

MICROBIOLOGY

TEAM

431

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Red color: very important

Green color: the doctor explanation

Blue color: team's note

Orange color: doctor did not read it or explain it or read it quickly "not important"

RESPIRATORY FUNGAL INFECTIONS

- Affects Respiratory System
- Rout of infection?
Inhalation, through blood, through lymphatic system
- Oral Cavity, any role?
There are 74 different types of fungi in the oral cavity of a healthy host
- Respiratory fungal infections are less common than viral and bacterial infections.
Fungi are less virulent and large so they cannot reach the alveoli easily
- Are opportunistic infections
 - Diseases in immunocompromised mainly, rarely in healthy hosts
- Have significant difficulties in diagnosis and treatment.
The fungi is isolated but cannot be determined the significance of the fungi (colonization, contamination, or the cause of the disease. Fungi isolated from a clinical sample isn't grown easily (false negative most of the time)

Risk Factors (anything that depresses the immune system)

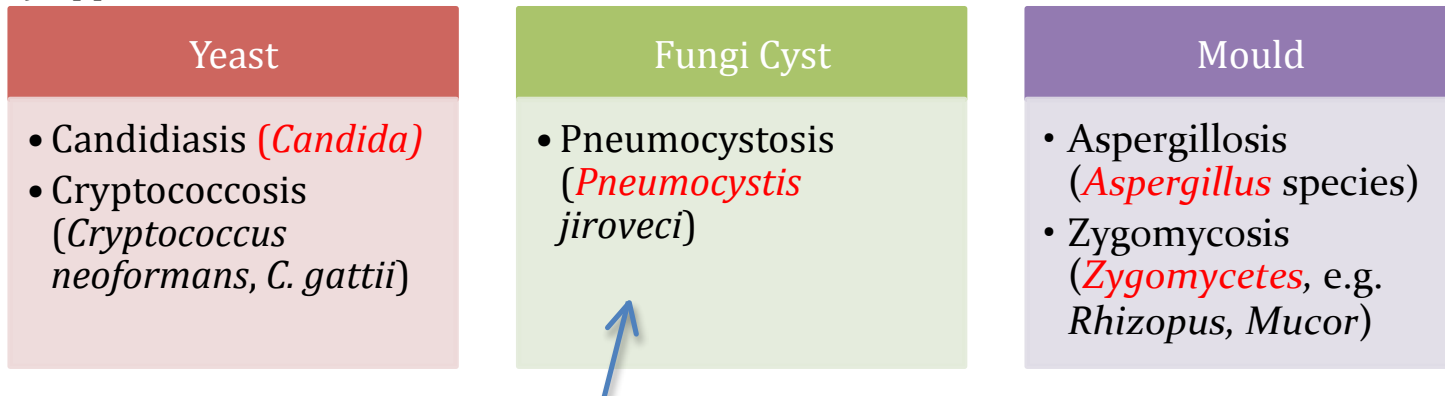
- AIDS
- Bone marrow/Organ transplantation
Because they take immunosuppressant drugs
- Cancer: leukemia, Lymphoma
- Drugs: Cytotoxic Drugs, **Steroids**
Any drug that inhibits the immune system
- Endocrine Related: Diabetes
- Organ failure

Other

- Increased survival of premature neonates
- More elderly pts.
- Long Stay in hospital mainly ICU
- Surgery
Due to exposing the patient to normal flora and airborne fungi
- Devices
Such as heart devices, artificial joints, any foreign object attached or in the body

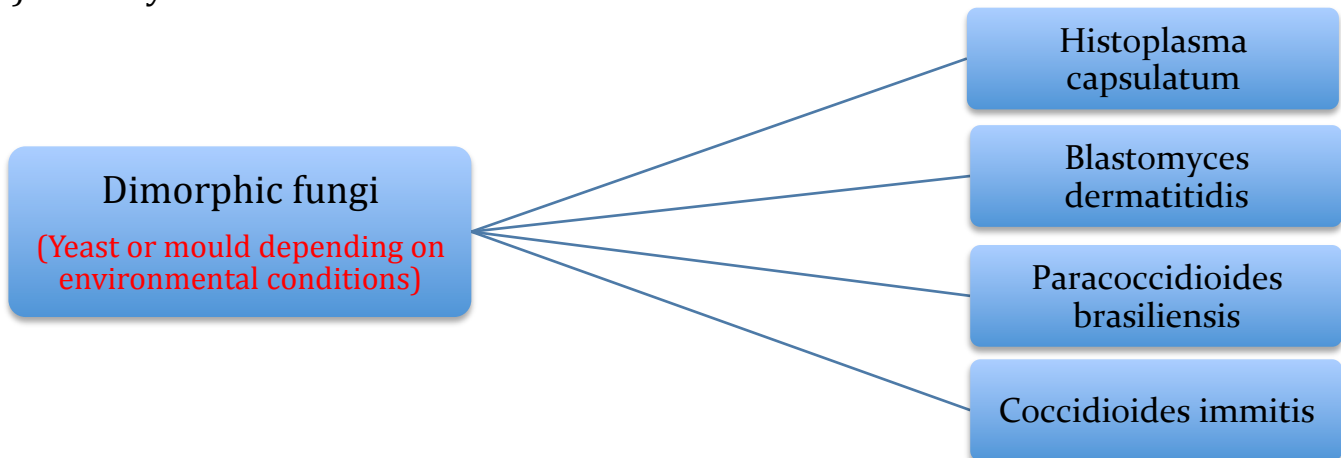
Etiology

1) Opportunistic



It was previously thought to be a parasite but lately conformed to be a fungi cyst
PCP abbreviation for pneumocystis carinii (previously known)

2) Primary Infections



Seen in healthy patients if seen in immunocompromised patients it is more severe and disseminates to other parts of the body not only the lungs

PRIMARY SYSTEMIC MYCOSES

- Dissemination seen in immunocompromised hosts
- Common in North America and to a lesser extent South America. Not common in other parts of the World. Especially in the soil of restricted habitats
- Etiology: dimorphic fungi. (Primary pathogens)
- Some are highly infectious (When exposed to only 10 spores you are likely to get the disease)

Examples:

- Blastomycosis,
- Histoplasmosis
- Coccidioidomycosis,
- Paracoccidioidomycosis

ASPERGILLOSIS (Any fungal infection obtained by aspergillus)

Disease of human and animals caused by fungi called *Aspergillus*

These include:

- (1) mycotoxicosis (toxins)
- (2) Allergy
- (3) Colonization (without invasion and extension in immunocompromised patients) in preformed cavities
- (4) Invasive, inflammatory, granulomatous, necrotizing disease of lungs
- (5) Systemic and disseminated disease.

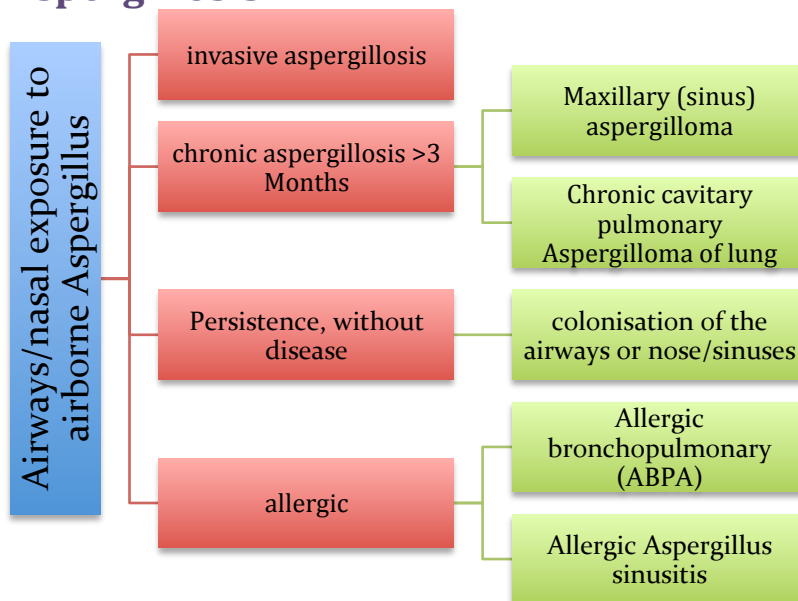
The type of disease and severity depends upon the physiologic state of the host (Either healthy or immunocompromised) and the species of *Aspergillus* causing the disease.

Aetiological Agents: *Aspergillus species*

Common species are:

- * *A. fumigatus* (causes invasive disease and is the most airborne fungi)
- * *A. flavus* (causes allergy)
- * *A. niger*
- * *A. terreus*
- * *A. nidulans*.

Classification of Aspergillosis



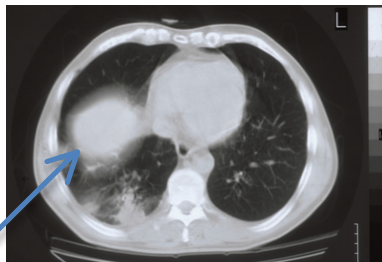
Difference between Chronic and invasive Aspergillosis

- **Chronic Aspergillosis :-**
- Also known as Colonizing aspergillosis, Aspergilloma, or Fungus ball (a ball in the lung)
- Signs: (Cannot be diagnosed by signs and symptoms only)
 - Cough
 - Hemoptysis (Hemoptysis: coughing up of blood or of blood-stained sputum from the lungs)
 - Variable fever (Mostly no fever but sometimes there is fever)
- Radiology:
 - Mass in the lung with **radiolucent crescent**

Invasive pulmonary Aspergillosis (Invade the lung tissue, more serious and fatal)

- Signs:
 - Cough
 - Hemoptysis
 - Fever
 - Pneumonia
 - Leukocytosis (raised white blood cell count)
- Radiology
 - **Lesion with halo sign**

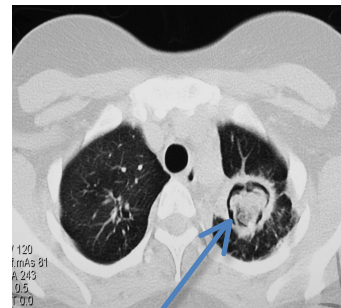
Invasive (AIDS)



Halo sign

Immunocompetent isn't given an antifungal agent surgery is the best choice

chronic



Air crescent

Air around the mass when seen it is most likely aspergilloma

Allergic Bronchopulmonary (ABPA)

In patients with history of:

- Asthma
- Bronchial obstruction
- Fever, malaise
- Eosinophilia (due to allergic reaction)
- Wheezing

Tests:

- Skin test reactivity (positive)
- Serum Antibodies (positive)
- Serum IgE > 1000 mg/ml
- Pulmonary infiltrates (seen on X-ray)

What is the link between airborne fungi and severe asthma?

- It triggers the asthma (in people who are allergic)
- Most common source of airborne fungi is the pillow

Air Quality

- Nosocomial pulmonary aspergillosis (found in the hospital atmosphere)
- >500 cases of postoperative aspergillosis are seen

A nosocomial infection also known as a hospital-acquired infection

Fungal Sinusitis

3 types:-

- A. Allergic
- B. Chronic
- C. Invasive

Allergic Aspergillus Sinusitis

1) Etiology:-

- a) The most common cause in KSA is "Aspergillus flavus"

2) Clinical course:

a) Signs and Symptoms:-

- i) Headache, nasal blockage, reduced smell, Nasal Polyps

b) Complications:-

- i) If not treated in immunocompromised patients the infection can disseminate to the eye then to the optic nerve then to the brain causing CNS infection called: (Rhino-cerebral aspergillosis) "very important"

3) Diagnosis

- a) Clinical and Radiology "CT scan mainly"
- b) Culture
- c) Measurement of IgE level, RAST test will be high in allergy
- d) Histology of mucosa.
- e) Precipitating antibodies.

4) Treatment :

- a) Depends on the type and severity of the disease and the immunological status of the patient "either medically ,surgery or both"

Diagnosis of aspergilosis

1. Specimen:

- A. Respiratory specimens: Sputum, BAL “Broncho-Alveolar Lavage”, Lung biopsy
- B. Other samples: Blood, etc.

2. Lab. Investigations:

A. Direct Microscopy:

Stain it by one of these: Periodic Acid Schiff (P.A.S); KOH, Giemsa, Greccott methenamine silver stain (GMS)

- B. “if it is aspergilosis will show fungal septated hyphae with Dichotomous branching “U-shaped”.

3. Culture on Sabouraud dextrose agar (SDR)

- A. For the Aspergillus culture:

Fungal media is better than Bacteriological media.

4. Serology:

- A. Looking for an anti-body against the Aspergillus in the serum

Using:

- I.D (Immunodiffusion)
- C.I. test

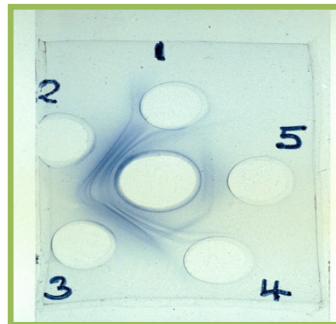
- B. ELISA test: looking for **GALACTOMANNAN** Antigen “the aspergillus antigen”

5. PCR:

- A. to detect the DNA of the Aspergillus in the serum”



PCR KIT



Immunodiffusion



Cultures for Aspergillus from sputum and BAL ***BAL is better**”

Management of acute invasive Aspergillus sinusitis

- ❖ biopsy for direct microscopy and culture for diagnosis
 - differential diagnosis :
 - 1- Between the aspergillus and other infection like:
Mucormycosis, Scedopsporium /Fusarium infection
 - 2- **between the invasive and non invasive aspergelosis.**
- ❖ Requires systemic antifungal therapy to minimize tissue destruction, spread to “face, eye, mouth, brain” and to cure.
- ❖ surgical removal “if needed”.

Choice of antifungal for aspergillosis

- **Voriconazole** (drug of choice unless drug interaction)
- Amphotericin B
- OR
- Posaconazole
- Itraconazole

Zygomycosis

- ❖ Pulmonary zygomycosis
- ❖ Rhinocerebral zygomycosis “very hard to treat”
- **Risk factors:**
 - ❖ Diabetic ketoacidosis
 - ❖ Granulocytopenia
 - ❖ Corticosteroid therapy
 - ❖ Malignancy
 - ❖ Hematopoietic stem cell transplantation (HSCT)
 - ❖ AIDS
 - ❖ Many others
- **Etiology:**
 - ❖ Zygomycetes
 - Non-septate hyphae.
 - e.g. Rhizopus, Mucor, Absidia.
 - Angioinvasion: invasion of blood vessels causing thrombosis leading to pulmonary infarction and hemorrhage.

Pulmonary Zygomycosis

- ❖ Fever, pulmonary infiltrates refractory to antibacterial therapy.
- ❖ Consolidation, nodules, cavitations, pleural effusion, hemoptysis
- ❖ If not treated infection may extend to chest wall, diaphragm and pericardium.
- ❖ Most seen in the immunocompromised patients
- ❖ **Early recognition and intervention are critical**

Diagnosis:

- **Specimen:**
 - Respiratory specimens: Sputum, BAL, Lung biopsy,
 - **Other samples**
- **Lab. Investigations:**
 - **Direct Microscopy:**
 - **Staining** Periodic Acid Schiff (P.A.S); KOH, Giemsa, Greccott methenamine silver stain (GMS)
 - will show broad **non-septate fungal hyphae** Culture on SDA
- **Serology: Not available**

❖ Treatment

- **Amphotericin B (Drug of choice)**
- Posaconazole
- Surgery in most cases

Questions:-

- 1) Which one of the following is not an opportunistic organ?
 - a) Histoplasma
 - b) Zygomycetes
 - c) Aspergillus
 - d) Candida
- 2) Galactomannan Antigen is used to identify which fungi
 - a) Candida
 - b) Aspergillus
 - c) Paracoccidioides
 - d) Zygomycosis
- 3) Direct microscope of acute Aspergillus sinusitis will show?
 - a) Non-Septate fungal hypha.
 - b) Septate fungal hypha
 - c) Budding yeast cells
 - d) Hat-shaped cysts
- 4) Direct microscope of Zygomycete will show?
 - a) Non-Septate fungal hypha.
 - b) Septate fungal hypha
 - c) Budding yeast cells
 - d) Hat-shaped cysts
- 5) Which of the following is the most common cause of invasive aspergillosis?
 - a) Aspergillus Fumigatus
 - b) Aspergillus Flavus
 - c) Aspergillus niger
 - d) Aspergillus terreus
- 6) Which of the following is the DRUG OF CHOICE FOR aspergillosis
 - a) Posaconazole
 - b) Amphotericin B
 - c) Voriconazole
 - d) Itraconazole

Answers:

- 1- A
- 2- B
- 3- B
- 4- A
- 5- A
- 6- C