PASSION ACADEMIC TEAM YU - MEDICINE

Sheet# 8 - MICROBIOLOGY

Lec. Date :

Lec. Title : Respiratory Fungal Infection

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RESPIRATORY SYSTEM

RESPIRATORY FUNGAL INFECTION

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- Fungi are not “virulent” But they are good at taking advantage “Opportunistic”

The pathogenesis of the eukaryotes depends only on the responses of the immune system wither it’s combatant or compromised.

Thus, if an individual immune system is competent the fungus usually will not cause an infection.

The fungus ability to infect someone depends on the bulk formation (fungal growth). Unlike bacteria that depends mainly on the toxins that it released to force an infection.

The toxins that the fungus produce have no big effect on the normal healthy human.

Fungal biology

Eukaryotes

- Non-motile
- Aerobic
- Saprophytic or parasitic
- Cell wall contains glucan and chitin
- Cell membrane contains ergosterol

Chitin is very important in medicine because it's used for the production of medical thread that is used for surgical sutures , and it's natural means no need for another surgery to remove them.

Etiology

The most pathogenic, because it could live in either conditions.

YEAST	MOULD FUNGI	DIMORPHIC FUNGI
Opportunistic		**Primary Infectious**
Candidiasis (Candida and other yeast)	Aspergillosis (Aspergillus species)	Histoplasma capsulatum
		Paracoccidioides brasiliensis
Cryptococcosis -Cryptococcus neoformans, -C. gattii	Zygomycosis (Zygomycetes, e.g. Rhizopus, Mucor)	Blastomyces dermatitidis
	Other Mould	Coccidioides immitis

Pathogenesis

- Toxins: produced but not relevant to human infections

The problem of the the fungal infections that it interacts and interfere with the physiological metabolism of the host cell, which means there is symmetry with the host cell.

- Disease from:
  - Bulk of organisms
  - Immune response to them or their byproducts

And this symmetry has 2 effects:

1. **Interfering in the metabolism**
2. **Anti-fungal usage can affect on the host cell also because A. They are similar B. anti-fungal have low specificity.**

That's why when the treatment is in IV form it needs to be done in the hospital because the responses are unknown and sometimes could be deadly.

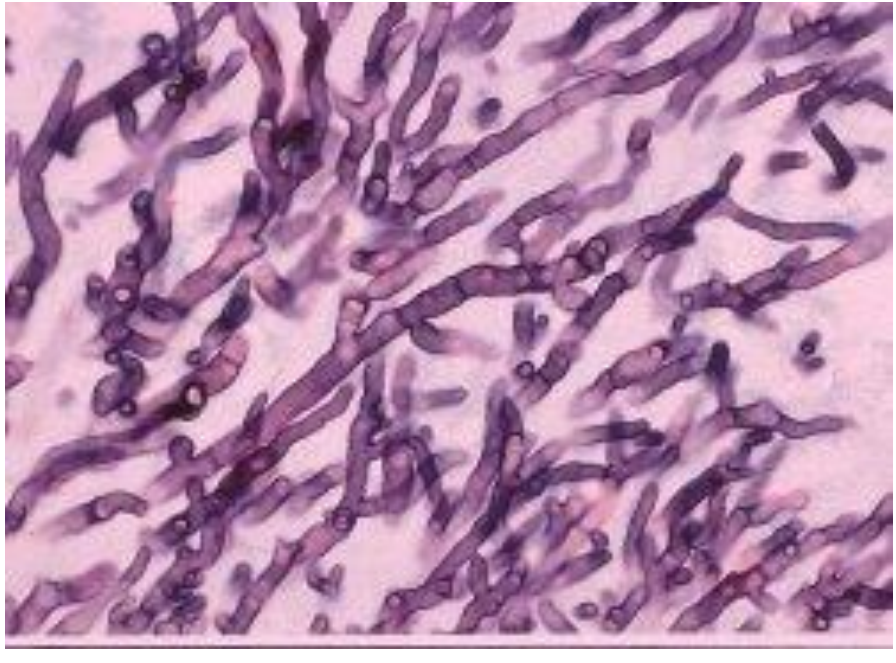
PRIMARY SYSTEMIC MYCOSIS

- Infections of the respiratory system, (Inhalation)
  Inhalation of spores.
  In patient's that are immune compromised the fungal genus could disseminate to other parts of the body.
- Dissemination seen in immunocompromised hosts
- Common in North America and to a lesser extent in South America.

ASPERGILLOSIS

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

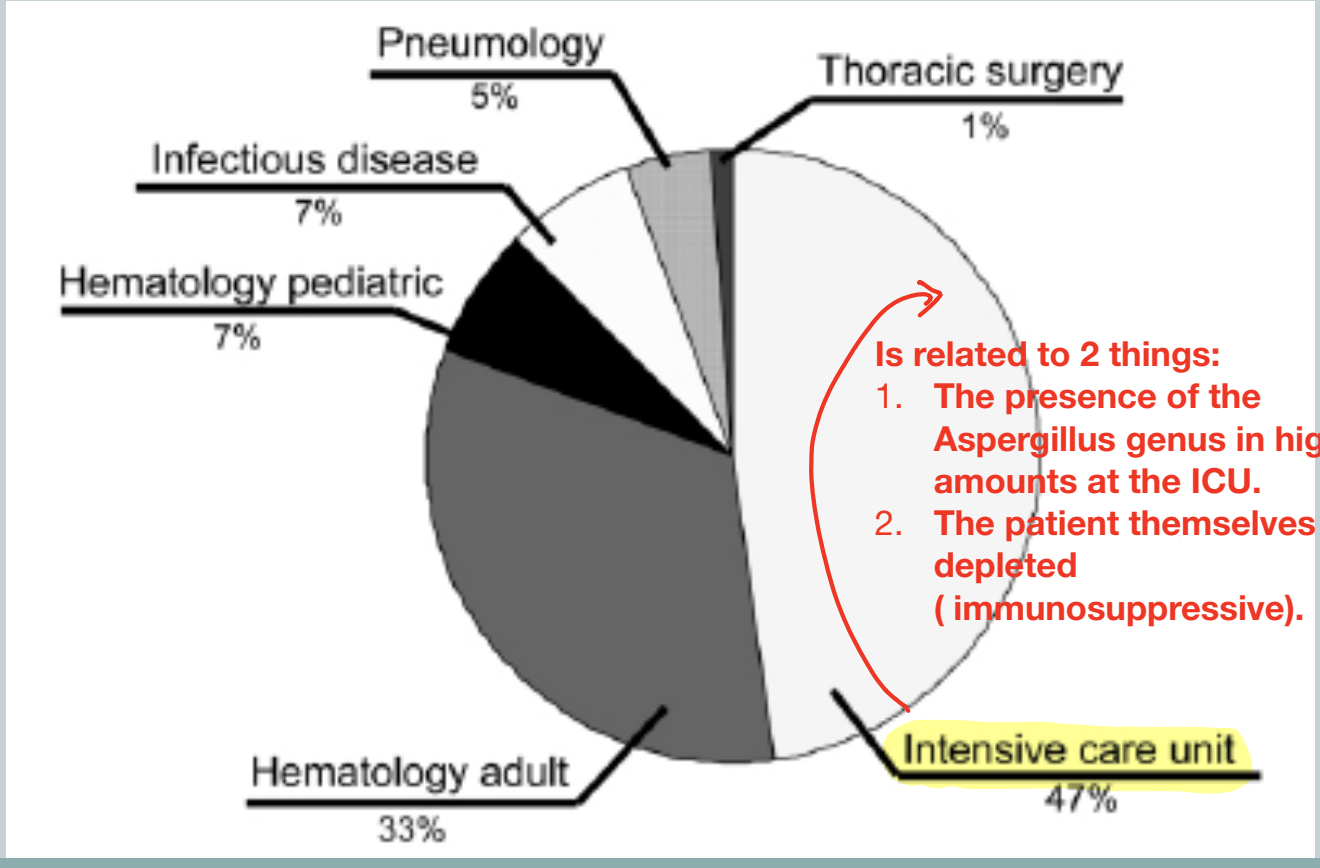
The main disease for the aspergillus is lung infection
Which is pneumonia-like infection.



Risk Factors

- Transplant Patients "e.g. bone marrow"
- Malignancy "leukemia, lymphoma"
- AIDS
- Diabetes
- And many others
  - any thing that leads to immunosuppression
    - ex:- pregnancy.

Where in the hospital does invasive aspergillosis occur?



CLASSIFICATION OF ASPERGILLOSIS

acute Invasive Aspergillosis

Signs: Cough , hemoptysis, fever, Leukocytosis

Radiology will show lesions with halo sign

Chronic Aspergillosis

Aspergilloma OR Aspergillus fungus ball

Signs include: Cough, hemoptysis, variable fever

Radiology will show mass in the lung , radiolucent crescent

If this white small mass is less than 3mm it isbenign if more than 3mm it is malignant, but this is not enough because we also needs a biopsy of the lung to know the type of tumor.

Allergic Aspergillosis

Hyper production of the IGE

Allergic bronchopulmonary (ABPA)

Allergic Aspergillus sinusitis

Etiology

Aspergillus species, common species are:

- A. fumigatus " Invasive"
- A. flavus, "Allergic""
- A. niger
- A. terreus
- A. nidulans

The diagnosis of fungus is always the same.

Unlike bacteria which have a diverse types of cultures the fungus cultures are specific and limited.

Diagnosis

- Speciemen:
  - Respiratory specimens: Sputum, BAL, Lung biopsy, Other samples: Blood

Lung biopsy is taken when we are looking for further investigation.

- Microscopiy: Giemsa Stain, Grecott methenamine silver stain (GMS) Will show fungal septate hyphae

Side note : Aspergillus species have septate hyphae.

- Culture: on SDA

SDA (Sabouraud dextrose agar).

- Serology: Test for Antibody , ELISA
- PCR: Detection of Aspergillus DNA in clinical samples

Clues to the diagnosis of IA

Excess wheezing (consider tracheobronchitis)

Are similar to the wheezing sound of the asthma patients.

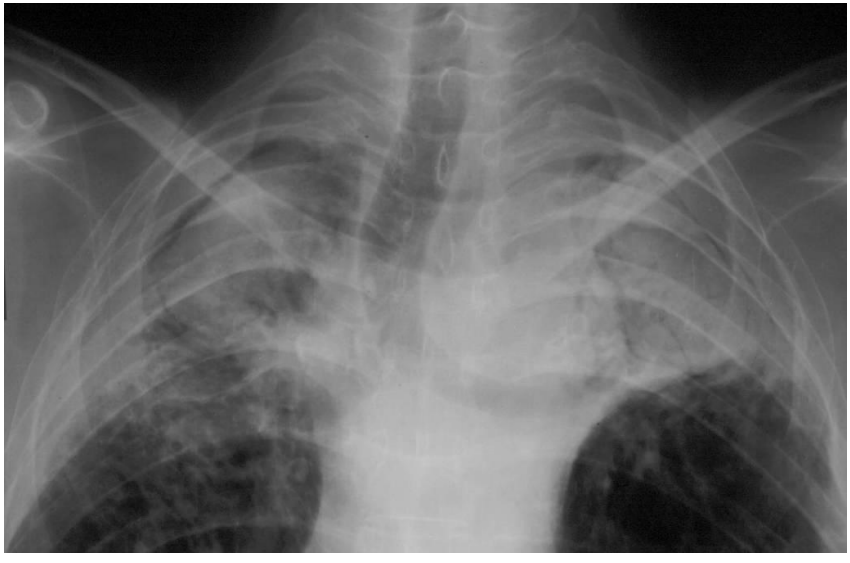
- Worsening infiltrates in ān ‘exacerbation’ (66%)
- Bilateral infiltrates (55%)
- Culture of Aspergillus

Infiltration is a way to distinguish between the causative agents, is it lobar or non-lobar, bi or uni lateral.

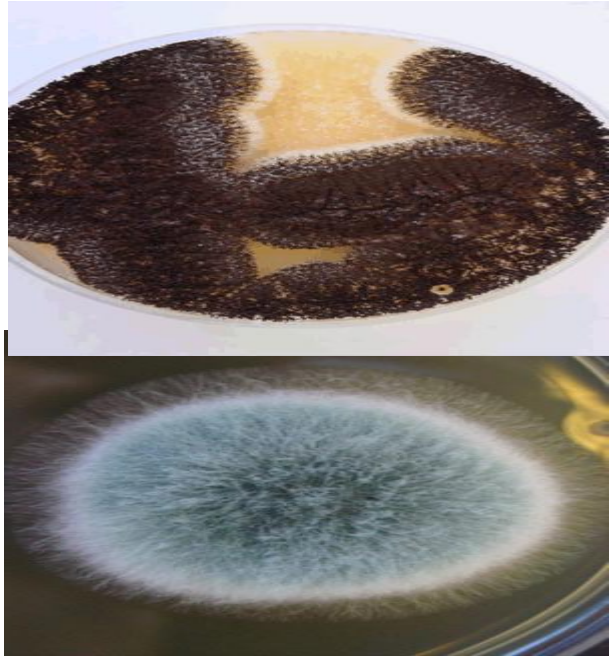
- High corticosteroid exposure recently

Not enough by it self to assume that a patient have aspergillosis.

- Do NOT expect fever (38%), chest pain or haemoptysis



Chronic cavitary pulmonary aspergillosis with bilateral aspergillomas complicating sarcoidosis



Treatment

Antifungal: Voriconazole “Drug of choice”

Alternative therapy: Amphotericin B, Itraconazole, Caspofungin

ALLERGIC BRONCHO-PULMONARY ASPERGILLOSIS

- Clinical Features: “Symptoms of Asthma”
  - Bronchial obstruction
  - Fever, malaise
  - Eosinophilia
  - Wheezing +/-
  - Skin test reactivity to Aspergillus
  - Serum antibodies to Aspergillus
  - Serum IgE > 1000 ng/ml ⇒ **The main aspect to differentiate between allergic aspergillosis and acute aspergillosis.**
  - Pulmonary infiltrates

FUNGAL SIINUSITIS

Side note : the fungus always start at the lung and then disseminate to other parts of the body and can cause (real cerebral infection), which is infection of the nasal passage and in the ocular region and in brain.

Clinical Features:

- Nasal polyps – and other symptoms of sinusitis
- In immunocompromised, Could disseminate to – eye craneum (Rhinocerebral)
- Aspergillus sinusitis has the same spectrum of Aspergillus disease in the lung

Etiology:

Most common in desert and dry areas.

Common in KSA is ***Aspergillus flavus***

"In addition to *Aspergillus*, there are other fungi that can cause fungal sinusitis"

Diagnosis

- Clinical and Radiology
- Histology
- Culture
- Precipitating antibodies useful in diagnosis
- Measurement of IgE level

Treatment

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

Pathogenic fungus are less than 300 species which is small number compared to bacteria

Zygomycosis

- Pulmonary Zygomycosis
- Rhinocerebral Zygomycosis

Risk Factors

The same risk factors with Aspergillosis.

- Transplant Patients
- Malignancy
- AIDS
- Diabetic Ketoacidosis
- And many others

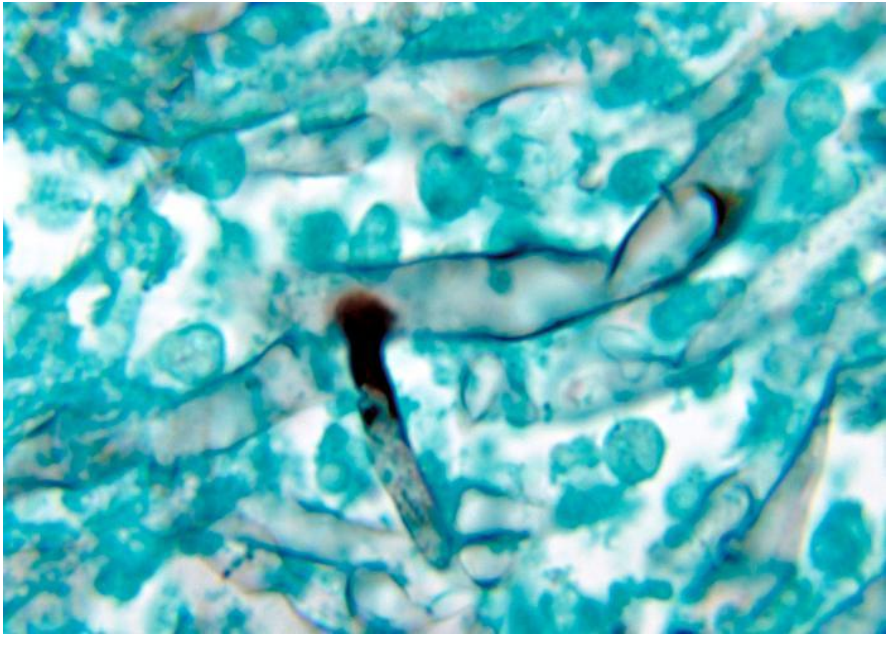
This condition shown in the picture needs surgery

a patient with rhinocerebral mucormycosis.

PULMONARY ZYGOMYCOSIS

- Acute disease
- Features include: Consolidation, Nodules, pleural effusion, hemoptysis

The lodged areas for the fungus are the soft tissue, then these fungus consolidates by exudate to form a firm and rigid solid tissue.



Etiology:

Zygomycetes , Non-septate hyphae. e.g. **Rhizopus**

Diagnosis

-Speciemen: Sputum, BAL, Lung biopsy

-Microscopiy: Giemsa, Grecott methenamine silver stain (GMS)

Will show broad non- septate fungal

-Culture: on SDA "No cycloheximide"

Treatment

- ✓ Amphotericin B
- ✓ Surgery

Pneumocystosis “Pneumocystis pneumonia”

No infiltration

- It’s interstitial pneumonia of alveolar area
- Affect immuno-compromised patients, especially AIDS patient.

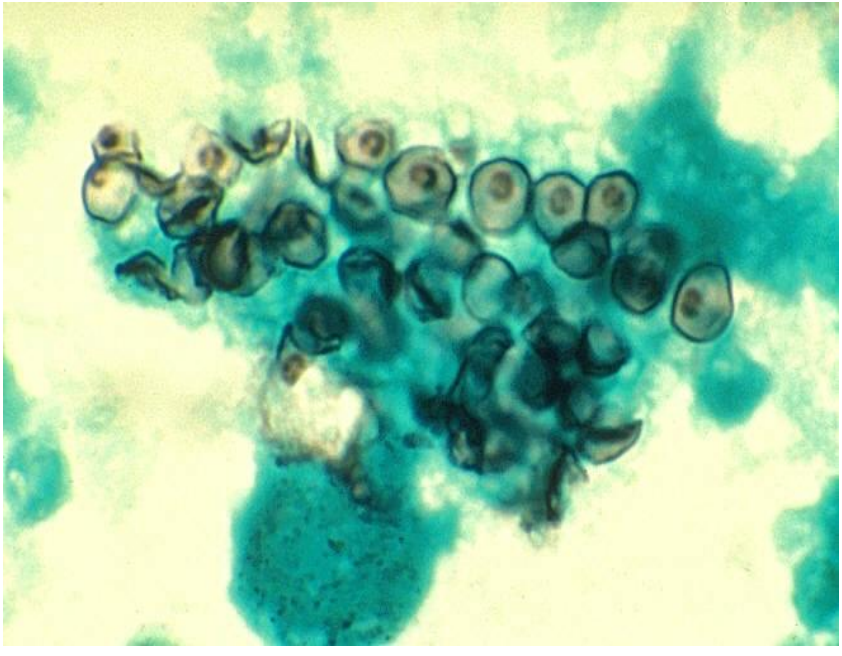
Etiology:

Pneumocystis jiroveci → Zoonotic fungal infection

"Previously thought to be protozoan parasite, but later has proven to be a fungus"

Found In

- Rodents (rats), other animals (goats, horses)
- Humans may contract it during childhood



Diagnosis

- Speciemen: Bronchoscopic specimens (B.A.L.), Sputum, Lung biopsy tissue.
- Histological sections or smears stained by GMS stain
- Immunofluorescence have better sensitivity, positive result will show cysts of hat-shape, cup shape, crescent

Treatment

- Trimethoprim-sulfamethoxazole
- Dapsone

Histoplasmosis

- Organism: Histoplasma capsulatum
  - Dimorphic soil organism
- Habitat: soils with high N content
- Pathogenesis: inhalation of spores

Histoplasmosis

Pathophysiology:

- Spores transform to yeast in lung, elicit cellular immunity as per TB
  - Hematogenous dissemination
  - skin test reactivity (histoplamin)

Clinical: mimics TB

- May disseminate early (infancy, immunodef.)
- May cause acute nodular/cavitary lung disease
- May reactivate years later

Blastomycosis

- Organism: Blastomyces dermatitidis
  - Dimorphic soil organism
- Habitat: humid woodlands
- Pathogenesis: inhalation of spores

Blastomycosis

Pathophysiology:

- Spores transform into yeast in lung, disseminate.
- No good antigen test to describe exposed population

Clinical:

- Acute or chronic lung disease (nodular/cavitary)
- Disseminated disease
  - skin
  - bone
  - urinary tract

Cryptococcosis

- Organism: Cryptococcus neoformans
  - yeast with thick polysaccharide capsule
- Habitat:
  - worldwide
- Pathogenesis: inhalation of yeast

Cryptococcosis is almost associated with HIV, thus almost all patients with HIV have cryptococcosis neoformans.

Similar to M.tuberculosis.

Cryptococcosis

Pathophysiology:

- transient colonization

OR

- acute/chronic lung disease

OR

- CNS invasion

Clinical:

When it disseminate to the brain, and this type is very severe.

Meningoencephalitis

- acute or chronic
- fever, headache, stiff neck, loss of vision
- complicated by hydrocephalus
- cryptococcal antigen for diagnosis

Candidiasis (Opportunistic organism)

- Organism: Candida albicans (yeast).
- Habitat: normal human flora

Causes :

1. **oral thrush**
2. **Vaginitis**
3. **UTI**

The pregnant women are susceptible for the Candida albicans because they have low immunity.

Candidiasis

Pathogenesis:

- Skin or mucosal integrity
- Normal bacteriologic flora
- Neutrophil function or CMI

→ which happens because of the drug abuse.

Clinical settings:

- Moisture, antibiotics, pregnancy
- HIV infection
- Intravenous catheters
- Chemotherapy or marrow ablation

Candidiasis

Diagnosis:

- Gram stain may help
- Infection and colonization may be difficult to distinguish

Because they look like bacteria.

Treatment:

- Remove the breach in defenses, if possible

If we do a smear to the candid albicans we will find something special called (Germ Tube).

Candida needs to be cultured within 37c just like the normal body temperature.

Mucormycosis

- Organism: species of Mucorales, genera Rhizopus and Mucor
  - Mold without a yeast phase
- Habitat:
  - Everywhere, worldwide
- Pathogenesis:
  - Inhalation of spores

Clinical:

- The most acute and fulminant fungal infection known
- Pneumonia progressing to infarction
- Sinusitis progressing to brain abscess