Diversity of Fungi and Fungal Infections

Objectives:

1.To provide students with an overview of the common medically important yeasts and mold fungi.

2. To provide students with an overview of the major fungal diseases that threatens human health.

3. To give a fundamental knowledge about the antifungal agents, their mechanisms of action, and spectrum.

Color index

Important

*Further explanations

LECTURE ELVEN

Fungi can cause harm or a diseases to humans (Mycotic Diseases) by :

- Hypersensitivity (1) (Allergy) (ex. Touching fungi, inhaling fungal spores)
- Mycotoxicoses (ex. Eating toxic fungi, or food that is contaminated with toxins produced by fungi)
- Infections

HOW THE INFECTION IS ACQUIRED?:

- Endogenous (2), Colonization (overgrowth of normal flora)
- Inhalation (Airborne)
- Contact (mostly cause skin infections)
- Trauma

(1) Fungi are one of the most common causes of allergies.
(2) It means acquiring the infection from our own normal flora

TYPES OF FUNGAL INFECTIONS (MYCOSES):

(the severity of infections depend upon the patient's condition)

Superficial mycoses:
- Affect the outer layer of the skin or hair shaft.
- No immune response. (Because it's superficial)

Cutaneous mycosis: (Dermatophytosi
- Infection of th skin, hair or nails
- caused by a group of keratinophilic fungi, called dermatophyte

Subcutaneous mycoses:
- Fungal infections involving the dermis, subcutaneous tissues, muscle and may extend to bone.
- Usually they are initiated by trauma.

Primary systemic mycoses:
- Caused by primary pathogens (4)
- Contracted by inhalation, start as respiratory disease
- Geographically restricted (endemic), north and South America

Opportunistic mycoses:
- Diseases in immunocompromised host.

Risk factors, -
Examples:
- HIV/AIDS
- Hematopoietic stem cell transplant (HSCT)
- Solid organs transplantation
- Malignancies
- Neutropenia
- Diabetes

(3)Love keratin

4)They are the microorganisms that cause diseases in healthy individual.

THE FUNGI:

A) Opportunistic Fungi: — Only immunocompromised host get the disease

- Normal flora (ex. Candida spp)
- Ubiquitous in our environment (Aspergillus spp. And Zygomycetes spp)

B) Primary Pathogens: — Any host can get the disease

- Dermatophytes
- Endemic geographically restricted.

DIAGNOSIS OF FUNGAL INFECTION:

- **Clinical features (**clinical presentation**):**
  History, risk factors, etc.

- **Imaging (**x-ray, CT scan, etc.)
  Good value in diagnosis and therapy monitoring

- **Lab Investigations:**
  Histopathology
  Microbiology

(ANTIFUNGAL AGENTS)

To kill fungi, we use antifungal agents.

TARGETS FOR ANTIFUNGAL AGENTS:

Cell membrane:

A) Polygene: (Amphotericin B and Nystatin (5))

Mechanism of Action **Amphotericin B** (MOA):

- Binds to ergosterol within the fungal cell membrane resulting in formation of pores, which permit leakage of intracellular contents, and lead to **death**.
- Spectrum of Activity (a **broad antifungal spectrum)**
  Active against most fungi that cause human disease.

B) Azole:

Ex.Fluco**nazole**. (Only for yeasts)
Ketoco**nazole.**
Itraco**nazole.**
Vorico**nazole.**

أهم شيء تعرفون الاسمين هذول على كلام الدكتور نفسه

Mechanism of Action:

- Inhibits synthesis of ergosterol, the major sterol of fungal cell membrane. (Once the synthesis of ergosterol is inhibited, the fungus will live of the ergosterol stored, when its finished the fungus will eventually **die**)

(5) Name of drugs.

TARGETS FOR ANTIFUNGAL AGENTS:

على كلام الدكتور أهم شيء هذه

Cell wall:

Echinocandins

Ex. Caspo**fungin**, Mica**fungin** and Anidula**fungin.**

Mechanism of Action:

- Inhibits glucan synthase, the enzyme complex that forms glucan (6) polymers in the fungal cell wall.
- Spectrum of Activity (**Restricted spectrum of activity**)

  Active against Candida spp and Aspergillus spp

(6) Glucan polymers are responsible for providing rigidity to the cell wall.

DNA/RNA synthesis:

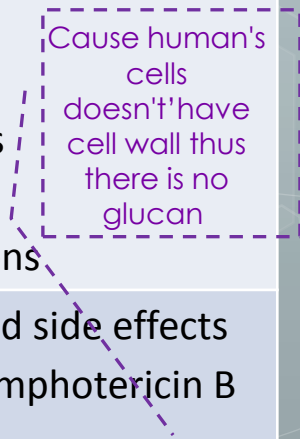
Flucytosine(7)

Mechanism of Action:

- Fungal RNA miscoding.
- Interfering with DNA synthesis.
- Spectrum of Activity (**Restricted spectrum of activity**)
  - **Active against**
  - Candida species
  - Cryptococcus neoformans.
  - Monotherapy: Flucytosine cannot work alone (the fungus will develop **resistance**).

7) work only against yeast.

TARGET	GROUP	MECHANISM OF ACTION	ANTIFUNGAL AGENTS	SPECTRUM OF ACTIVITY	COMMENTS
Cell membrane	Polyenes	Binds to ergosterol within cell membrane, formation of pores which lead to cell death	Amphotericin B, Nystatin	Broad antifungal spectrum which includes most fungi	Serious toxic side effects (nephrotoxicity)
	Azoles	Inhibit the synthesis of ergosterol	Ketoconazole Itraconazole Fluconazole Voriconazole Posaconazole Miconazole clotrimazole	Fluconazole has a limited or no activity against mould fungi Voriconazol is the drug of choice for Aspergillosis Posaconazole has broader spectrum of activity than other azoles	Not effective against zygomycosis (except posaconazole) Adverse Effects Drug Interactions
Cell wall	Echinocandins	Inhibits glucan synthasis, (glucan polymers in the fungal cell wall)	Caspofungin Micafungin Anidulafungin	Good activity against *Candida spp ,Aspergillus spp* Limited or no activity against other fungi	Less toxicity and side effects compared to amphotericin B and azoles
DNA/RNA synthesis	Pyrimidine analogues	Fungal RNA miscoding Interfering with DNA synthesis	Flucytosine	Restricted spectrum of activity *Candida* species *Cryptococcus neoformans*	Monotherapy now limited (Resistance)



MCQS

Subcutaneous mycoses are fungal infections that involve:

Hair b) Skin c) Muscles (a

Cell membrane is the target for polyene and azole.

T b) F (a

Related videos:

http://youtu.be/b5rluxtABGA

THANK YOU

Thousands of candles can be lighted from a single candle, and the life of the candle will not be shortened. Happiness never decreases by being shared."

— Buddha

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