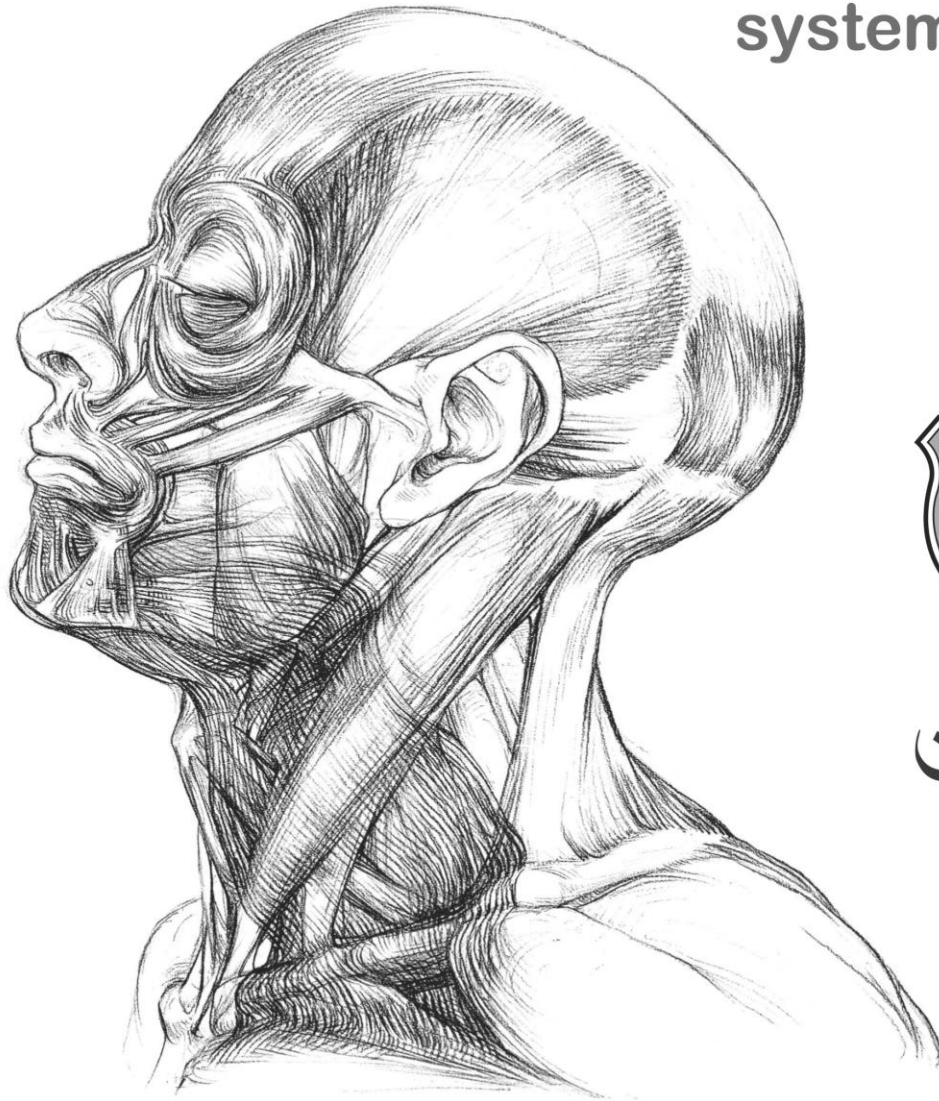


The skin &

Musculoskeletal

system



PHARMACOLOGY

SLIDES ☐

SHEET ☐

LECTURE # 2

DOCTOR: Alia Shatnawi

DONE BY: Jasmine Alzahiri

CORRECTION: Kamal Nasir

ANTIFUNGAL GROUPS

How do they work? They bind to a lipid called *Ergosterol* and they disrupt the equilibrium of the cell membrane of the fungi. Why do they target fungi and not target humans? Simply, we don't have *Ergosterol* in our body. There are a number of antifungal groups that are used topically and some may be used systematically.

What type of infections do antifungal agents treat? Fungal infections such as dermatophytes (*epidermophyton*, *microsporum*, and *trichophyton*) affecting skin, scalp and nails. Yeast (including *Candida albicans* and *Pityrosporum orbiculare*) affecting the body systematically.

Topical Antifungal Agents:

1. Clotrimazole
2. Econazole
3. Ketoconazole
4. Miconazole
5. Oxiconazole
6. Sulconazole

(Some may be given systematically or orally for persistent infections)

Systemic infection in association to fungi:

We have fungi in our normal flora such as oral cavity candida and in mucous membranes; so in immune-compromised patients the normal flora becomes opportunistic. However, people with an intact immune system may also be susceptible but it would be skin related rather than systematic. If the skin problems are persistent and start to enter in between the cracks of the skin because of *suckling of breasts* for example (such as the nursing mothers) we end up with a lot of fungal infections(systemic). And sometimes the only way to treat it is by systemic treatment even though it's a topical infection. Another example: *athlete's foot*. (Fungi grow in moist areas)

Oral Antifungal Agents

Azole Derivatives:

1. Griseofulvin: effective against dermatophytes and must be given for a long period of time until there are results because fungal infection is really resistant to treatment. Therefore:

- a) 4-6 weeks for the scalp
- b) 6 months for fingernails
- c) 8-18 months for toenails
- d) Has many side effects – such as liver toxicity (which is why topical administration is preferred)

2. Terbinafine

- a) Recommended for onychomycosis.
- b) 6 weeks for fingernails.
- c) 12 weeks for toenails.

Azole Derivatives:

- a) Fluconazole
- b) Itraconazole
- c) *Ketoconazole*

- They can affect the permeability of fungal cell membrane through alteration of sterol synthesis as mentioned before.
- Effective in systemic mycosis, mucocutaneous candidiasis (mostly occurs in immune-compromised patients), and other cutaneous infections
- Systemic side effects: hepatitis and liver enzyme elevations, and drug **interactions**.
- Inhibitors of cytochrome p450, slows down the break down of the certain drug, and therefore increase concentration of it in the blood resulting in increase of toxicity especially in low therapeutic index

Nystatin & Amphotericin B

1. Nystatin

- a) Route of administration: topically or ingestion (ex: mucosal candida infections)
- b) It is ineffective against dermatophytes.
- c) It only targets fungal infections in the oral cavity, esophagus, and small intestine since it is not absorbed systemically.
- d) It is used as a treatment for oral thrush in babies; drops of nystatin suspension are given.

2. Amphotericin B

- a) Route of administration: Systemically like in the case of mucocutaneous candidiasis
- b) Broader antifungal spectrum
- c) IV in the treatment of many systemic mycoses and to a lesser extent cutaneous candida infections but we must be very careful due to toxicity (monitor patients kidneys)

Topical Antiviral Agents

- 1. Acyclovir
- 2. Valacyclovir
- 3. Penciclovir
- 4. Famciclovir

- a) Route of administration: used topically as ointments or creams to treat for example *Herpes* infections, whether type 1 or 2.

How do they work?

They are guanine analogs that get incorporated into the structure of DNA and stop the synthesis of the VIRAL DNA. Acyclovir is converted by viral [thymidine kinase](#) to acyclovir monophosphate, which is then converted by host cell kinases to acyclovir triphosphate. Why only the viral and not the cellular DNA? Because there is more affinity for the viral and the concentration needed to inhibit cellular enzymes is 100 times more than what is needed to inhibit the viral enzyme.

It should be taken when the early signs of the dormant Herpes infection are seen; or else it will not be treated.

(10:00-20:00)

Immunomodulators

Definition: Drugs that target the immune system so they work on the cytokines and the WBCs.

Drug 1: Imiquimod

- a) Stimulates peripheral mononuclear cells to release anti-inflammatory cytokines like interferon- α and to stimulate macrophages to produce interleukins-1, -6, and -8 and tumor necrosis factor
- b) Mainly used to treat warts that mainly occur due to HPV (Human Papilloma Virus)
- c) Treats Actinic keratosis on the face and scalp. **Definition of actinic keratosis:** hyper-keratinization due to exposure of the UV light and may be pre-cancerous turning into squamous cell carcinoma.
- d) Also used for *Primary Basal cell carcinoma* (malignant but it is encapsulated) → very responsive for treatment

Drug 2: Tacrolimus

Drug 3: Pimecrolimus

- a) Useful for atopic dermatitis (eczema)—itchy, red skin that may become scaly and the cause of this condition is unknown but may be related with efficiency of immune system, allergies, or genetics
- b) Inhibits T-lymphocyte activation and prevents release of inflammatory cytokines and mast cell mediators.

- c) Black box warning- a label on the medicine from the FDA to spread awareness of special certain side effects, in this case, teratogenic (may cause certain types of cancers)

Ectoparasiticides

Definition: medicine that kills insects or small living microorganisms that may affect the skin

1. PERMETHRIN: (kills lice)

- a) Toxic to *Pediculus humanus*, *Pthirus pubis*, and *Sarcoptes scabiei*.
- b) Treatment of **Pediculosis**- cream applied (topically) for 10 minutes and then rinsed with warm water
- c) Treatment of **Scabies**- cream applied (topically) for the whole body
- d) Superinfection: because of itching—to prevent this from getting worse, we give antibacterial agents, pain killers, anti-itching agents (anti-histamine), or hydrocortisone (anti-inflammatory agent) to reduce swelling and redness in the area.

2. Lindane (hexachlorocyclohexane)

- a) 10% absorbed (don't memorize the concentration)
- b) Can cause neurotoxicity and hematotoxicity

3.Crotamiton

4.Sulfur

5.Malathion

(20:00-30:00)

Agents affecting Pigmentation of skin

COSMETIC DRUGS

Two reasons we may use these drugs

- a) Either people want to reduce the color of their skin

- b) Some conditions where we want to restore the pigmentation due to a certain disease

1. Hydroquinone

2. Monobenzene

- a) May be toxic to melanocytes resulting in permanent depigmentation (How?) Inhibits part of the melanocyte that are synthesizing the melanin substance, reducing the color of the skin

3. Mequinol

- a) Reduce hyperpigmentation of skin by inhibiting the enzyme *tyrosinase* present in the melanocyte, which will interfere with the biosynthesis of melanin.

Now we will talk about Repigmentation.

1. Trioxsalen & Methoxsalen

- a) Psoralens used for the repigmentation of depigmented macule of vitiligo. (**What is vitiligo?** Patches of skin lose their colors due to a problem in the melanocytes)
- b) Must cross-link the drugs so that they may work. When applying this drug, there must be photo activation by long-wave-length ultraviolet light (320-400nm) in order to get the beneficial effect
- c) Some side effects include skin cancer and cataracts.

Sunscreens and sunshades (sunblock includes both in it's composition)

- a) Sunscreen is a drug that absorbs the UV light such as PABA which converts the light to a harmless form.
- b) Sunshades are opaque materials that reflect light, like titanium dioxide.
- c) Sunscreen and sunshades should be used together therapeutically.
- d) Useful in polymorphous light eruption (when exposed to light and vesicles start to appear, usually found in first skinned people), lupus erythematosus, and drug induced photosensitivity.

Acne Preparations

Retinoic acid and derivatives:

1. **Retinoic acid**
2. **Adapalene**
3. **Tazarotene**

Retinoic Acid and Derivatives

1. Retinoic Acid (Tretinoin)

- a) Used when all other topical treatments do not work and the condition is very problematic to the patient, why? Because of its toxicity such as affecting the liver enzymes (so we must monitor the lipid profile every month, ALT and transaminase, the cholesterol, and make sure we don't have other infections due to dryness) along with bleeding, irritation, and even depression. Moisturizer, eye drops, sunscreen and sunshade should be used because the skin is fair now and the patient is at risk to get exposed to UV light.
- b) Stabilize lysosomes (degradation of components of the cell) so we can get rid of the exterior part of the pimples so it opens up the comedones, therefore easier to kill the insides.
- c) Increases the RNA polymerase activity and the incorporation of thymidine into DNA —important for the collagen synthesis
- d) Increase prostaglandin levels
- e) Increases PGE2, cAMP, and cGMP levels (increasing regeneration of the cells)
- f) It is applied for a long time, so after the patient stops the last pill a concentration of this drug stays in the body for 1 month. So it is important for women to use contraceptives to avoid pregnancy for at least 1 month as it is teratogenic.
- g) Decreases cohesion between epidermal cells and increases epidermal cell turnover. This will result in expulsion of open comedones and the transformation of closed comedones into open ones.

- h) Promotes dermal collagen synthesis, new blood vessel formation, and thickening of the epidermis, which helps diminish fine lines and wrinkles.
- i) Can cause erythema and dryness (so you must drink at least 2 L of water with this drug).
- j) Studies show that it is tumorigenic in animals and teratogenic in humans.
- k) Restricted for severe cystic acne that is resistant to standard treatment.

2. Isotretinoin (Accutane)—(commercial name is not required to memorize for the exam)

- a) Isomer to Tretinoin so they have very similar side effects and toxicity.
- b) Restricted for severe cystic acne resistant to standard treatment.
- c) Inhibits sebaceous gland size and function.
- d) Given orally.
- e) Toxic: dryness, itching, headache, corneal opacities, pseudotumor cerebri, inflammatory bowel disease, anorexia, alopecia, and muscle and joint pains. Also lipid abnormalities.
- f) Teratogenicity
- g) Once this drug is used skin becomes to UV light so sunscreen and sunshades are used to prevent any harm like cancer.

(30:00-40:00)

3. Benzoyl Peroxide

- a) Only topically
- b) Penetrates stratum corneum
- c) Causes killing of the bacteria *Proprio Acnes* (why? Formation of reactive oxygen species)
- d) Combines with erythromycin or clindamycin
- e) Can cause bleaching of hair and clothes

4. Azelaic Acid

- a) Works on dihydrotestosterone, which is responsible for secondary sexual traits as well as acne. Works by inhibiting the enzyme that converts testosterone to dihydrotestosterone.

Drugs for Psoriasis

Psoriasis: is an inflammatory condition affecting the skin, it can be localized, generalized, unknown causes (may be genetic, allergies, or immune system problems)

1. Acitretin

- a) Related to Isotretinoin (longer half life)
- b) Route of administration: Orally
- c) Teratogenic and hepatotoxic
- d) Not advised for patients to become pregnant for 3 years after stopping this treatment

2. Tazarotene

- a) Given topically to treat psoriasis
- b) Anti-inflammatory and anti-proliferative potential. It inhibits by inhibiting ornithine decarboxylase it is responsible of conversion of ornithine (amino acid) to polyamines, they are products that are very necessary for the proliferation of cells throughout the body so we inhibit the proliferation of these cells that form psoriasis by using this drug.
- c) Teratogenic
- d) Can cause burning sensation and localized edema of the skin when applied topically.

3. Calcipotriene

- a) Synthetic Vitamin D3 derivative, interfere with inflammatory process happening in psoriasis.

"Whether you think you can, or think you can't, you're right"