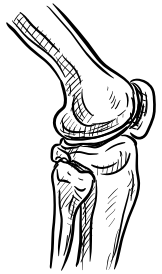
بسم الله الرحمن الرحيم



PHARMACOLOGY

Final | Lecture 1

Skin Pharmacology pt.1

Written by: Leen Mamoon
Layan Fawarseh

Reviewed by: Raneem AH

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا

رَمَضَانُ مُبَارَكٌ

REMEMBER FROM GENERAL PHARMACOLOGY

- Antibacterial agents work through four main mechanisms:
- 1. Inhibition of Cell Wall Synthesis
- 2. Inhibition of Protein Synthesis
- 3. Disruption of DNA or RNA Function
- 4. Other Mechanisms – Some antibacterial agents work through uncommon pathways, such as disrupting bacterial membranes or metabolic pathways

(رَبِّ اشْرَحْ لِي صَدْرِي * وَيَسِّرْ لِي أَمْرِي * وَاحْلُلْ عُقْدَةً مِّن لِّسَانِي * يَفْقَهُوا قَوْلِي)

Skin Pharmacology

- **In this lecture, We will discuss various drugs used to treat specific skin conditions. The skin, being the largest organ of the body, is susceptible to a wide range of diseases, Skin infections can be classified into bacterial, viral, and fungal infections. Each type requires distinct treatment approaches.**

Dr. Alia Shatanawi

Adverse Effects of Dermatologic Preparations

- **Burning or stinging sensation.** similar to the feeling of applying alcohol to the skin.
- **Drying and irritation**
- **Pruritus.**
- **Erythema.**
- **Sensitization.** leading to itching, dryness
- **Staining**
- **Superficial erosion.**

All drugs have potential side effects, but this does not mean that everyone who takes the drug will experience them. The likelihood of developing side effects depends on the percentage of people affected when using the drug.

Topical Antibacterial Agents

These drugs are primarily used to treat skin infections. For example, if a person sustains a cut on their hand, the wound may be exposed to environmental pathogens, including bacteria present on the skin's surface. To manage such infections, topical treatments such as creams or ointments are preferred over systemic therapy as they deliver the medication directly to the affected area while minimizing systemic side effects.

- **Gram-positive bacteria**
  - **Bacitracin**
  - **Gramicidin**
  - **Fusidic acid**
- **Gram-negative bacteria**
  - **Polymyxin B Sulfate**
  - **Neomycin**
  - **Genatamicin**

BACITRACIN

Bacitracin is a topical antibiotic that primarily functions as a cell wall synthesis inhibitor. Specifically, it inhibits the formation of the linear peptidoglycan chain, which is essential for bacterial cell wall integrity.

- **Active against streptococci, pneumococci, and staphylococci**
- **Also , most anaerobic cocci, neisseriae, tetanus bacilli, and diphtheria bacilli are sensitive.**
- **MOA???** Mechanism of Action

- **Side effects: Toxicity ??**

Allergic contact dermatitis occurs frequently, and immunologic allergic contact urticaria rarely. Bacitracin is poorly absorbed through the skin, so systemic toxicity is rare.

- Toxicity is primarily related to systemic absorption or systemic use, Fortunately, bacitracin is poorly absorbed through the skin, meaning it does not enter systemic circulation. Therefore, the risk of systemic toxicity is minimal.
- Bacitracin is associated with significant systemic toxicity, primarily nephrotoxicity (kidney toxicity), which can lead to acute renal failure. Due to this, systemic use is highly restricted.
- It's not available for oral use due to its toxicity. So it is used as an intramuscular injection for treating certain resistant infections, such as specific types of pneumonia in children.
- The side effects (allergic contact dermatitis) of bacitracin do not necessarily occur due to the drug itself. may not always be caused by bacitracin alone but could result from the vehicle or carrier used in the formulation (similar to how a drug is dissolved in water, oil or another medium)
- Urticaria is a skin condition characterized by itching, redness, and small physical changes in the affected area. It is usually an immunological response that occurs after exposure to a triggering chemical or irritant.

Neosporin is a combination antibiotic ointment that contains bacitracin, neomycin, and polymyxin B.
Why is this combination important?
Since skin infections can be caused by various microorganisms present in the environment, including both Gram-positive and Gram-negative bacteria, this combination helps prevent and treat infections more effectively.

- Frequently used in combination with other agents (polymyxin B and neomycin)
- Form: creams, ointments, and aerosol preparations **The differences between creams and ointments lie in their water and oil content, The choice between these forms depends on the site of infection, the specific condition being treated, and the patient's skin type.**

- **If a patient experiences pain at the site of infection, a local anesthetic, such as lidocaine, can be used.**

- Usually Antiinflammatory agents added
  - (Hydrocortisone)

Fusidic acid

Fucidin, is used for treating minor cuts or acne. While it may not be highly effective in all cases, it can provide relief and help minimize the risk of infection due to its antibacterial properties.

- **acts as a bacterial protein synthesis inhibitor**
- **Staphylococcus species, Streptococcus species, and Corynebacterium species.**

- often used topically in creams and eyedrops

Additions to fusidic acid could be prepared as well and they are used depending on the condition of the patient.
For example fusicort is a fusidic acid with cortisone added to it(anti inflammatory agent)
We must note that cortisone suppress the immune system so it may increase the infection;,however, in minor areas of skin infections it reduces signs and symptoms that's why patient's condition is important to be considered .

حَتَّىٰٓ إِذَا ضَاقَتۡ
عَلَيۡهِمُ ٱلۡأَرۡضُ بِمَا رَحُبَتۡ وَضَاقَتۡ عَلَيۡهِمۡ
أَنفُسُهُمۡ وَظَنُّوٓاْ أَن لَّا مَلۡجَأَ مِنَ ٱللَّهِ إِلَّآ إِلَيۡهِ
ثُمَّ تَابَ عَلَيۡهِمۡ لِيَتُوبُوٓاْ إِنَّ ٱللَّهَ هُوَ ٱلتَّوَّابُ
ٱلرَّحِيمُ ١١٨

POLYMYXIN B SULFATE

- **Gram-negative :Pseudomonas aeruginosa, Escherichia coli, enterobacter, and klebsiella.**
- **Proteus and serratia are resistant, as are all gram-positive organisms.**
- **Side effects: total daily dose applied to denuded skin or open wounds should not exceed 200 mg (the risk of systemic absorption is higher) in order to reduce the likelihood of toxicity "neurotoxicity and nephrotoxicity"**
  - **Allergic contact dermatitis NOT common.**

NEOMYCIN & GENTAMICIN

Neomycin

- **Aminoglycoside antibiotics** = protein synthesis inhibitor.
- **gram-negative :E coli, proteus, klebsiella, and enterobacter.**
- **SE: allergic contact dermatitis** ,only small percentage of patients get the side effect.

- **Gentamicin generally shows greater activity against P aeruginosa than neomycin.**
- **Gentamicin more active against staphylococci and group A β-hemolytic streptococci.**
- **Be careful with systemic toxicity : esp in renal failure** or **compromised kidney functions.**
- Any drug that is excreted in urine may cause toxicity as a side effect in patients with renal failure or **compromised kidney functions** which may be caused due to aging associated with cardiovascular or other diseases; that is because the kidney can't excrete all the amount of drug as expected, so the amount of drug in the body is increased.

Trichogenic*1 and Antitrichogenic*2 Agents

Further definitions regarding each * and some notes in the next slide.

- **Minoxidil (Rogaine):**
  - **Designed as an antihypertensive agent*3.**
  - Minoxidil is an potassium channel opener causing hyperpolarization of cell membranes.
  - Causing widening blood vessels (work as a vasodilator) , it allows more oxygen, blood, and nutrients to the follicles. may act as a nitric oxide (vasodilator) agonist. This may cause follicles in the telogen phase (resting phase) to shed, which are then replaced by thicker hairs in a new anagen phase (highly replicating phase).
  - **Effective in reversing the progressive miniaturization of terminal scalp hairs associated with androgenic alopecia*4.**
  - **Vertex balding is more responsive than frontal balding.**

Trichogenic and Antitrichogenic Agents - con.

*1 – Trichogenic: producing hair drug.
*2 – Antitrichogenic: Anti-producing hair drug.
*3 – Antihypertensive agent: lowering blood pressure agent.
*4 – Androgenic alopecia: hereditary baldness affected by dihydrotestosterne (secondary sex hormone), more in males but it can occur in females also.
- Side effects of minoxidil : Lowering blood pressure due to vasodilation → Hypotension (innocent – not a disease) → The body try to balances this by increasing heart rate → reflex tachycardia – especially in hyprtensive patient who are taking hypotensive medication (both drugs will increase heart rate)

Trichogenic and Antitrichogenic Agents

- **Minoxidil.**
- **Finasteride (Propecia)**
  - **5ά-reductase inhibitor which blocks the conversion of testosterone to dihydrotestosterne** → decreasing androgenic alopecia.
  - **Oral tablets.**
  - Side effects: **Can cause decreased libido, ejaculation disorders, and erectile dysfunction.**
  - Dihydrotestosterne is an important sex hormone so inhibiting its synthesis will cause problems in the sexual system as side effects - but it happens only among few patients because it is a small dose that doesn't cause a fully inhibition.

" رَبِّ ٱجۡعَلۡنِي مُقِيمَ ٱلصَّلَوٰةِ
وَمِن ذُرِّيَّتِيۚ رَبَّنَا وَتَقَبَّلۡ دُعَآءِ "

Trichogenic and **Antitrichogenic** Agents

- **Minoxidil** – Trichogenic.
- **Finasteride** – Trichogenic.
- **Eflornithine** – Antitrichogenic :
  - **Is an irreversible inhibitor of ornithine decarboxylase, therefore, inhibits polyamine synthesis. Polyamines are important in cell division and hair growth.**
  - **Effective in reducing facial hair growth in 30% of women when used for 6 months.**
  - For topical usage.

Acne treatment

- One of the most common skin diseases presenting to family physicians

- Considerable psychological impact on the quality of life Four main factors cause acne:

- **Excess oil (sebum) production.**
- **<u>Hair follicles clogged by oil and dead skin cells</u>** – salicylic acid can deal with that as it is an anti-keratogenic agent = removing sebum and layers of dead skin.
- **<u>Bacteria.</u>**
- **Inflammation**.

- The anaerobic bacterium <u>Cutibacterium acnes</u> (<u>Propionibacterium acnes</u>) is believed to play an important role in the pathophysiology of the common skin disease acne vulgaris.

- It may progress to: Comedonal Lesions → Inflammatory Lesions → Nodulocystic Lesions → Scaring (see next 4 slides).

Comedonal Lesions = black head

Inflammatory Lesions

Treatment here may be started

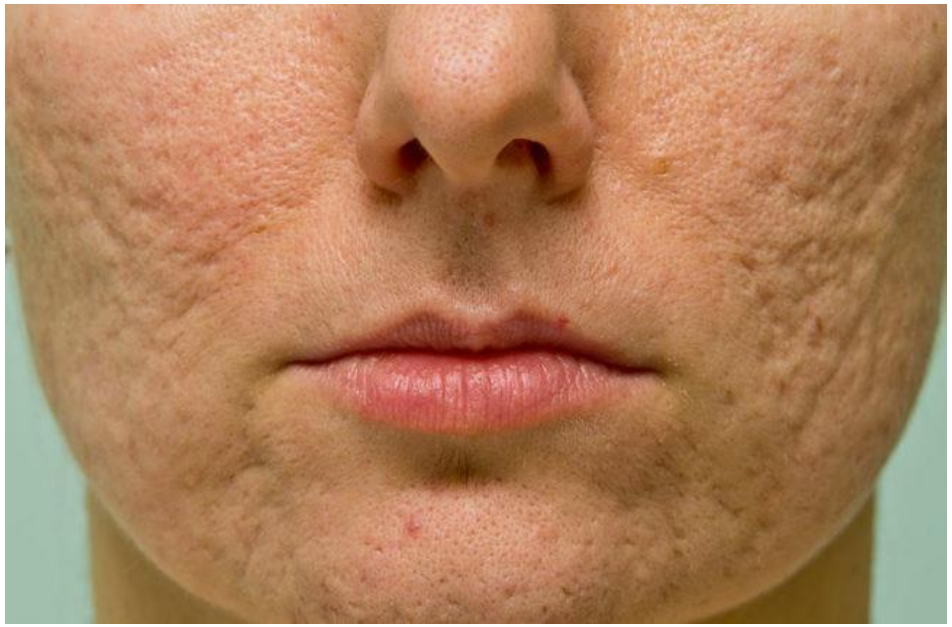
Nodulocystic Lesions

Pathologic & psychological impact should be taken in consider.

" رَبَّنَا ٱغۡفِرۡ لِي وَلِوَٰلِدَيَّ
وَلِلۡمُؤۡمِنِينَ يَوۡمَ يَقُومُ ٱلۡحِسَابُ "

Scaring

It is not Inevitable, so reaching to this stage should be avoided by giving an early treatment



For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide 13	(both drugs will **decrease** heart rate) ––	(both drugs will **increase** heart rate) The format of (trichogenic) and (antitrichogenic) was changed in order to differentiate the drugs and the explanations
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

فاسلْم فإنك قد نزلت بمنزلٍ
عند المليك تُضرُّ فيه وتنفع
تؤتى هواك إذا نطقت بحاجةٍ
فيه وتشفع عنده فيشفع

ما تنسوا أهلنا في غزة من
دعائكم في هذه الأيام الفضيلة
تقبّل الله طاعاتكم