

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

FINAL | Lecture 2

Skin Pharmacology (pt.2)

Written by: Mahmoud Aljunaidi
Ahmad Darwish

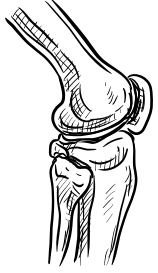
Reviewed by: Mahmoud Aljunaidi



وَإِنْ تَتَوَلَّوْا يَسْتَبَدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَلَكُمْ
اللهم استعملنا ولا تستبدلنا



رَمَضَانَ مُبَارَكٌ



PHARMACOLOGY



Quiz on the last lecture!

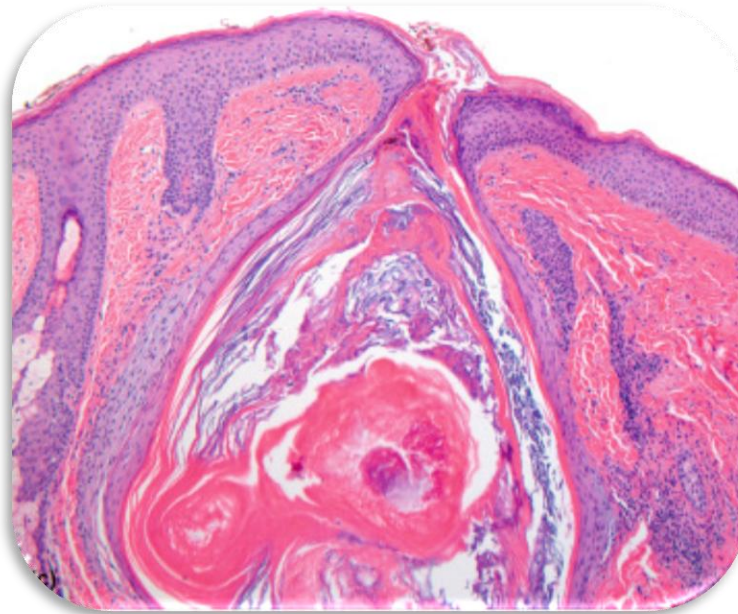


Figure (1): Acne vulgaris

REMEMBER FROM GENERAL PHARMACOLOGY

- Bacteriostatic refers to an agent that **inhibits** bacterial **growth**, while bactericidal describes an agent that **kills** bacteria.
- A special side effect associated with Clindamycin is pseudomembranous colitis.
- Clindamycin and erythromycin are antibiotics that inhibit bacterial protein synthesis.

Does that ring a bell?

- Acne develops when **excess oil** (sebum) is produced, leading to **clogged hair follicles**. As a result, **bacteria** (*Cutibacterium acnes*) thrive in these clogged pores, causing infection. The body then initiates an **immune response** against the clogged pores and bacteria, which explains the pathophysiology of acne.
- Acne progresses as follows,
 - **Comedonal** lesions, if inflamed → **Inflammatory** lesions → **Nodulocystic** lesion, if not treated early → **Scarring**.
- Depending on the stage/kind of acne, proper treatment is indicated.
 - ✓ As acne progresses, more extensive treatment is given.

Lotion VS. Cream VS. Gel VS. Solution

| Feature | Lotion | Cream | Gel | Solution |
|----------------------------|-----------------------------|-----------------------------|-------------------------------|--------------------------------|
| Consistency | More liquid than cream | Thicker than lotion | Contains more oily substances | More watery than lotion |
| Water Content | More than cream | Less than lotion | - | More than lotion |
| Oil Content | Some oil | More than lotion | More than lotion/solution | Low |
| Best for Skin Type | Suitable for all skin types | Best for dry/sensitive skin | Recommended for oily skin | Ideal for oily skin |
| Application on Hairy Areas | - | - | Unsuitable | Better for hairy areas |
| Alcohol Content | - | - | - | Can contain alcohol |
| Effect of Alcohol | - | - | - | Dries skin, removes excess oil |

There are further comparisons, but this is what was mentioned in the lecture.

Topical Therapy (Indications)

Usually given for:

- comedonal acne
- mild to moderate inflammatory acne

Topical Therapy

Depending on the type of the skin (oily/dry) and the condition, we choose the preparation's type:

- Cream **for** sensitive or dry skin.
- Lotion **for** any skin type.
- Gel **for** oily skin **as it has high oil content.**
- Solution **for** oily skin

Topical Therapy (Anti Comedonal Agents)

[] = Concentration

- Topical Retinoids, [] = 0.025% - 0.5%
 - Retinoids are vitamin A derivatives.
- Azelaic acid
- Salicylic acid

Topical Retinoids (Adapalene, Differin)

Topical Retinoids 0.025% - 0.5%

- Because of their photosensitivity, it's better to apply them at night.
- Always apply test dose.
- Start at low concentrations.
- Although their systemic manifestations are minimal (not easily absorbed), they should be Avoided in pregnancy, **category X**; affect fetus.

➤ Remember, **category X** means that it has confirmed risk, thus contraindicated in pregnancy.



Topical Retinoids (Adapalene, Differin)

➤ Side Effects:

- When the drug is first applied, it causes a temporary exaggeration of acne, known as **pustular flare**.

➤ Why the exaggeration?

- Acne lesions, including deep-seated pustules and comedones, may already be present beneath the skin's surface. The medication promotes skin cell turnover and exfoliation, which helps unclog pores and bring these lesions to the surface more quickly.
- **Photosensitivity.**
- **Skin irritation and erythema.** (common topical side effect)
- **Dryness, forcing people to use moisturizers, and peeling.**

Mnemonic: Retinoids Side effects: Puppies Frequently Irritate Eager Dogs

Pu = **P**ustular flare, **F**requently = **P**hotosensitivity, **I**rritate = irritation, **e**ager = **e**rythema, **D**ogs = **D**ryness

Azelaic Acid 15-20%

➤ Mechanisms:

1. **Competitive inhibitor of mitochondrial oxidoreductases and of 5 alpha-reductase, inhibiting the conversion of testosterone to 5-dihydrotestosterone, giving it the potential to treat baldness when used in combination with other agents. (Remember Finasteride, a trichogenic drug).**
 - Acne can be due to hormonal changes during puberty, where dihydrotestosterone levels increase, enhancing acne.
 - Azelaic Acid affects acne by lowering secondary sex hormones levels.
2. **It also possesses bacteriostatic activity to both aerobic and anaerobic bacteria including Propionibacterium acnes.**
3. **It possesses an anti-inflammatory and antioxidant properties, clearing free radicals that can be damaging to the skin.**

Azelaic Acid 15-20% – Continued.

- Can be produced chemically, but also naturally from **Malassezia furfur** (pathogen of tinea versicolor)
- **Applied twice daily.**

➤ **Side Effects**

- **Acid, so erythema and irritation.**
- **Decrease in pigmentation, therefore, it can be used clinically to treat hyperpigmentation.** (see next slide)

! Any acidic drug can cause erythema and irritation.

Mnemonic: Azelaic Acid Soothes New Eruptions, Improving Dermal Clarity.
Soothes = BacterioStatic, New = Number 2 (twice) , Eruptions= erythema, improving = irritation, improving dermal clarity = decrease in pigmentation (by meaning or just the D in dermal)).

Azelaic Acid – Clinical correlation.

- Azelaic acid reduces pigmentation by **inhibiting** ⁽¹⁾**tyrosinase**, making it effective in treating hyperpigmentation disorders like ⁽²⁾**melasma** and ⁽³⁾**post-inflammatory hyperpigmentation**.
- By suppressing tyrosinase, azelaic acid decreases melanin production in melanocytes.

⁽¹⁾ an enzyme critical for melanin synthesis, ⁽²⁾ hyperpigmentation that is common in pregnant women,
⁽³⁾ hyperpigmentation caused by inflammation.

Azelaic Acid 15-20%

- **Evens skin tone. It decreases pigmentation, inhibiting an enzyme called tyrosinase that leads to hyperpigmentation, or dark patches of skin.**
- **Due to its antibacterial and anti-inflammatory properties, Azelaic acid is used to treat mild to moderate acne, both comedonal acne and inflammatory acne.**
- **It belongs to a class of chemicals called dicarboxylic acids.**
- **It works by killing acne bacteria that infect skin pores.**
- **It also decreases the production of keratin, keratolytic as it's an acid.**
- **Azelaic acid is also used as a topical gel treatment for rosacea, due to its ability to reduce inflammation**

Salicylic Acid 0.5 - 2%

- Like other acids, it has a **Keratolytic** activity, dissolves the keratinized layer of the skin.
- **It belongs to the same class of drugs as aspirin (salicylates).**
- **Anti-inflammatory capability.**
- **Can reduce swelling and redness and unplugging blocked skin pores to allow pimples to shrink.**
- **Used for comedonal lesions, mild to moderate lesions.**
- **applied twice daily**
- **High doses are used for hyperkeratinization of the skin, as in: Warts (HPV) and Corns (مسمار اللحم).**
- **Side effects: skin dryness; keratolytic, and irritation; acid.**

Salicylic Acid 0.5 - 2%

- For high doses, the risk of systemic absorption, thus toxicity, should be considered.
- As it's related to aspirin, it **shouldn't** be given to patient with aspirin sensitivity or a patient with a condition that aspirin is contraindicated.

- **Topical Therapy (Anti Inflammatory Agents)**

- **Benzoyl Peroxide 2.5 - 10%**

- It releases H_2O_2 , so it has free radicals and oxygen.
- Anaerobic bacteria are sensitive for oxygen, so it **Exhibits bactericidal effects against Cutibacterium acnes.**
- As it can form an acid (Benzoic acid), it has **Keratolytic effects to prevent and clear clogged pores, and anti-inflammatory properties to reduce redness and swelling.**
- **Avoid leaving for long periods of time on the skin to minimize irritation.**
 - Benzoyl peroxide is a potent irritant, and the skin requires time to accommodate to its effects. Consequently, treatment typically begins with a once-daily application, gradually increasing to twice daily as the **skin develops tolerance**. Additionally, it is not advisable to apply benzoyl peroxide before sleep, as **prolonged** contact with the skin during the night can lead to **increased irritation**.
- **dryness of skin**

Mnemonic: Benny kills Acne, irritating Dry skin. Benny = Benzoyl, kills = keratolytic + bactericidal, Acne = Anti - inflammatory, irritating = irritation, Dry skin = dryness of skin

Topical Therapy (Anti Inflammatory Agents)

Some Antibacterial agents can be used topically and/or systemically for the treatment of Acne, agents used topically include:

- **Clindamycin.**
- **Erythromycin** (can also be used systemically).
- **Apply twice** daily for the treatment of acne.
- **A common adverse effect is skin dryness.**
- **Clindamycin and erythromycin** (Antibacterial) **may also be employed in Combination therapy, examples include:**
 - **5% Benzoyl Peroxide and 3% Erythromycin**
 - **5% Benzoyl Peroxide and 1% Clindamycin**
 - **Topical antibiotics and Azelaic acid or Tretinoin**

Clindamycin

- When clindamycin is applied topically it is **10% absorbed systemically**, so, there still exists a **possibility of *Pseudomembranous colitis* in susceptible individuals**.
 - Recall that pseudomembranous colitis is a serious side effect associated with clindamycin.
- **Formulations of clindamycin include:**
 1. **The hydroalcoholic vehicle and foam formulation (commercial name: Evoclin), may cause drying and irritation of the skin, with complaints of burning and stinging.**
 - Individuals with certain skin types may experience irritation from the hydroalcoholic vehicle formulation. In such cases, transitioning to the water-based gel is recommended, as it is generally better tolerated and less likely to cause irritation.
 2. **The water-based gel and lotion formulations; well tolerated and less likely to cause irritation. Allergic contact dermatitis is uncommon.**

Clindamycin is also available in fixed-combination topical gels with benzoyl peroxide (commercial names: Acanya, BenzaClin, Duac), and with tretinoin (commercial name: Ziana).

!! The Dr. Said it is not required to memorize the commercial names, memorize the combination by scientific name only.

Erythromycin

- In topical preparations, erythromycin base rather than a salt is used to facilitate penetration.
- One of the possible complications of long-term topical therapy is the development of antibiotic-resistant strains of organisms, including staphylococci.
- Adverse local reactions to erythromycin solution may include a burning sensation at the time of application and drying and irritation of the skin.

Metronidazole

- Metronidazole is often mistakenly classified as an antifungal due to its similarity in name to the azole class of antifungal agents. However, Metronidazole is not an antifungal; it is primarily an antiparasitic and antibacterial agent, effective against anaerobic bacteria.
- **Effective in the treatment of rosacea (الوردية).**
- **Rosacea: common skin condition that causes blushing or flushing and visible blood vessels in your face. It may also produce small, pus-filled bumps (becoming pustular rosacea, a subtype of rosacea). These signs and symptoms may flare up for weeks to months and then go away for a while.**



Metronidazole

- **The mechanism of action is unknown.**
 - **but it may relate to the inhibitory effects of metronidazole on *Demodex brevis* (a parasite believed to be a contributing factor to the development of pustular rosacea); This drug may act as an anti-inflammatory agent by direct effect on neutrophil cellular function**
 - **Adverse local effects include dryness, burning, stinging and excessive tearing.**
 - **Caution should be exercised when applying metronidazole near the eyes to avoid excessive tearing.**

Systemic therapy

Indications – reasons for therapy:

- **Moderate inflammatory acne non-responsive to topical therapy, the drugs that have been mentioned previously).**
- **Nodulocystic acne**

Types of *systemic therapy* :

- **Oral Antibiotics**
- **Isotretinoin**
- **Hormonal Therapy**

Oral Antibiotics (used for 3-6 months)

- **Tetracycline 500mg X BD**
- **Doxycycline 100mg X BD**
- **Minocycline 100mg X OD**
- **Erythromycin 500mg X BD**
- **combined with topical therapy**

- OD = "Once Daily".
- BD = Bis in Die, which is Latin for "Twice a Day".

- Tetracycline, doxycycline, and minocycline are commonly employed in the systemic treatment of acne due to their combined **antibacterial** and **anti-inflammatory** effects on *Propionibacterium acnes*.
- Furthermore, doxycycline has been shown to inhibit matrix metalloproteinases (**MMPs**), enzymes responsible for the degradation of the extracellular matrix (ECM). By suppressing MMP activity, doxycycline promotes the **preservation of ECM** and **collagen**, ultimately contributing to **improved skin** structure and appearance.

Isotretinoin (Accutane) indicated in

- **severe nodulocystic acne**
- **Non-responsive acne**
- **severe psychological distress**

Isotretinoin (RoAccutane) side effects

- Isotretinoin is not immediately prescribed due to the **numerous potential side effects** associated with its use:

1. **Teratogenic**, never prescribed for pregnant women because it will cause fetus malformation.
 1. Remember isotretinoin is a Vit A derivative.
2. **mucosal dryness**, so it's prescribed with moisturizers and eyedrops.
3. **photosensitivity**, so use of sunscreen is essential.
4. **Arthralgias**.
5. **Alteration of liver enzymes**.
6. **hypertriglyceridemia and hypercholesterolemia**, so regular monitoring of triglycerol and cholesterol is essential.

- **Tumerogenic in animals**

Isotretinoin May Pose A Little Catastrophe Increasing Lipid Targets.

May = Mucosal dryness, Pose= Photo sensitivity, A = Arthralgias, Little = Alteration of liver enzymes., Catastrophe = increase in cholesterol, Targets= Teratogenic.

The catastrophe means it has a lot of side effects and not immediately prescribed, Lipid targets = hypertriglyceridemia

Isotretinoin (RoAccutane)

- **Retinoic Acid (Tretinoin):** is the acid form of Vitamin A.
- **Stabilizes lysosomes, increases RNA polymerase activity, increases PGE₂, cAMP, and cGMP levels** (both cAMP and cGMP are vasodilators), and increases the incorporation of thymidine into DNA, so more cell regeneration.
- **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.
- **Also, promotes dermal collagen synthesis, new blood vessel formation, and thickening of the epidermis, which helps diminish fine lines and wrinkles.**
- **Women should avoid becoming pregnant for at least one month after discontinuing isotretinoin treatment, as the drug can remain in the body for up to one month.** Additionally, women should **refrain from donating blood** while undergoing treatment with isotretinoin, as the donated blood could potentially be **transfused to a pregnant woman**, thereby posing a **risk to the developing fetus**.

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 | 16 | aerobic | anaerobic |
| V1 → V2 | | | |

Additional Resources:

رسالة من الفريق العلمي:

سُورَةُ الْبَقَرَةِ

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

شَهْرُ رَمَضَانَ الَّذِي أُنْزِلَ فِيهِ الْقُرْآنُ هُدًى لِلنَّاسِ
وَبَيِّنَاتٍ مِّنَ الْهُدَى وَالْفُرْقَانِ فَمَن شَهِدَ مِنْكُمُ
الشَّهْرَ فَلْيَصُمْهُ وَمَن كَانَ مَرِيضًا أَوْ عَلَى سَفَرٍ فَعِدَّةٌ
مِّنْ أَيَّامٍ أُخَرَ يُرِيدُ اللَّهُ بِكُمُ الْيُسْرَ وَلَا يُرِيدُ بِكُمُ
الْعُسْرَ وَلِتُكْمِلُوا الْعِدَّةَ وَلِتُكَبِّرُوا اللَّهَ عَلَى مَا
هَدَاكُمُ وَلَعَلَّكُمْ تَشْكُرُونَ ﴿١٨٥﴾

تقول عائشة رضي الله عنها: (كان رسول الله صلى الله عليه وسلم يجتهد في
العشر الأواخر ما لا يجتهد في غيره) رواه مسلم.

النبي صلى الله عليه وسلم قال: (التمسوها في العشر الأواخر من رمضان، ليلة
القدر في تاسعة تبقى، في سابعة تبقى، في خامسة تبقى).

احرصوا على العمل في ما تبقى من شهر رمضان، لعلنا لا ندرك الذي يليه.
هدانا الله وإياكم، ووفقنا لما فيه خير الأمة وصلاحها.
دعواتكم لنا بالتوفيق.