



Doctor 021

MSS

PHARMACOLOGY

#1



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Commented [U1]:

Dermatologic Pharmacology

Variables affecting Pharmacologic Response:

Regional variation in drug penetration.

Concentration gradient.

Dosing schedule.

Vehicles and occlusion.

توضيح النقاط في السلايد القادم

These variables are for the drugs that are administered to the skin surface.

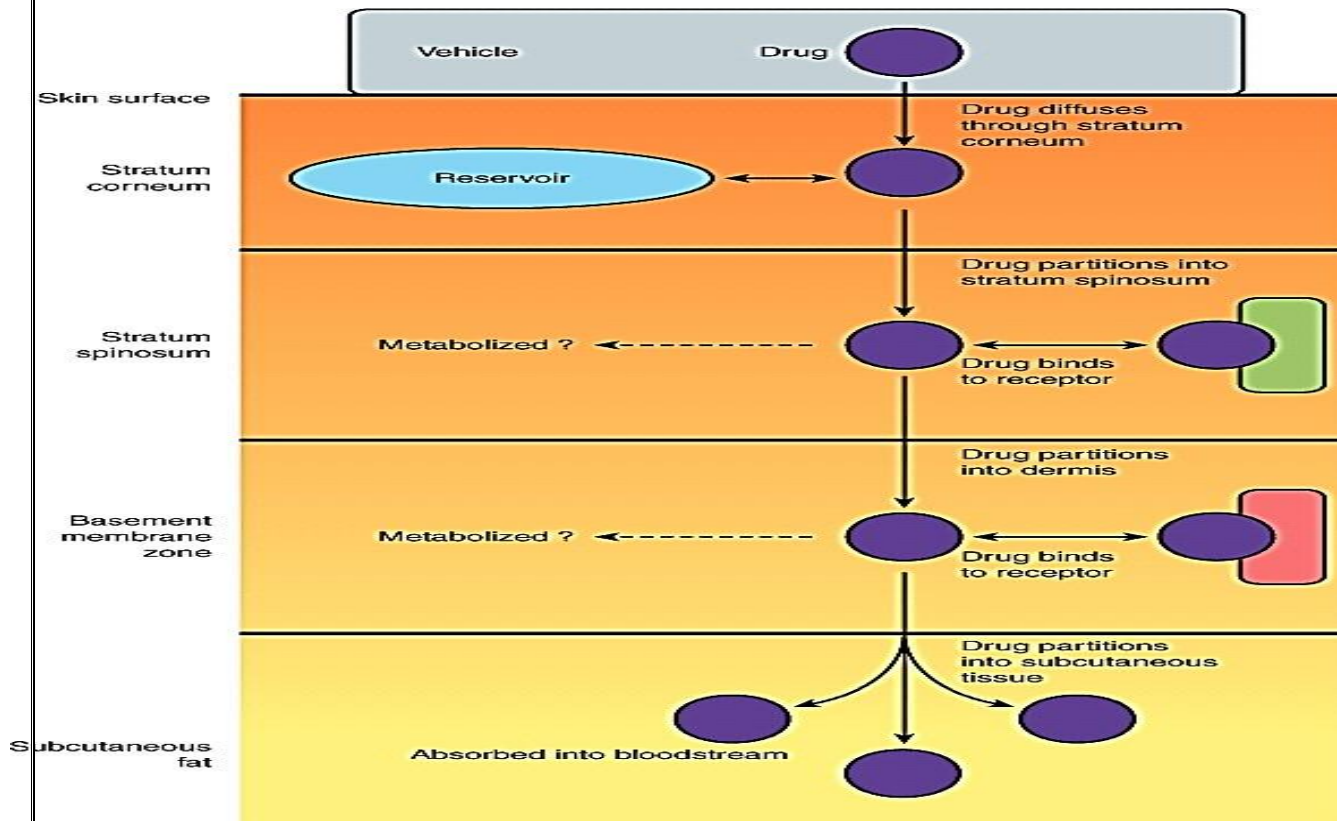
1: **Regional variation** for example the palm of hand is more keratinized and more resistant to the permeation of the drugs than the dorsum, so the amount of the drug will be different, we have special parts like the area surrounding the eye, so we can't apply the same kind of feet drugs to that sensitive area because of the structural differences.

2: **Concentration gradient** most compounds will be transferred from area of high concentration to area of low concentration, typically we have a high concentration outside and that will help moving the drug to the inside, and sometimes in order to increase the permeation we can apply occlusion, which mean to put a gauze (شاش) above the drug which help in conserving the high concentration outside so there will be continuous permeation of drug through the skin.

3: **Dosing schedule**

4: **Vehicles** help us recognize and determine which kind of drug formulation we use. *vehicle*: a *carrier* the material we put drug in and allow it to be transferred from that tube into our body. Examples (on vehicles for the drugs that are administered topically to skin surface) are: creams, gels, ointments, serum, shampoo, tinctures (alcohol based) ... etc, depends on area of skin we cure.

Percutaneous Absorption.



Source: Katzung B.G., Masters S.B., Trevor A.J.; *Basic & Clinical Pharmacology*, 11th Edition; <http://www.accessmedicine.com>
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We have different skins layers, we need our drug to work locally, stratum corneum works as a reservoir so the drug gets accumulate their and will be released at longer period of time through the skin layers to reach its target, usually the drug target is within the layers of the skin and there's no need to reach the circulation, 99% of skin formulation works by this way.

According to which area is being treated and the condition, the structure type is chosen; for example, in very hyper keratinized area it's better to have more Vaseline like structure in order for drug to penetrate to help moisturize the area.



The lotion has high water content in comparison to the ointment, which is more lipophilic, according to which area of skin I treat and which condition we treat, for example in high keratinized area we need better permeation so we need more Vaseline like structure to penetrate and help moisture that area. Tropical treatments are used to avoid systemic side effect advantages of tropical treatments are quickly delivery and limit systemic absorption and this limit the side effects.

Permeation is not absorption.

Absorption: وصول الدواء للدورة الدموية

Permeation: عبور الدواء عبر طبقات الجلد

So... Penetration or Absorption??

Absorption means for the drug to reach the circulation or the blood stream, *penetration* means that the drug penetrates or pass through the skin layers to reach the inner part of skin or the deep layers of skin. In dermatological pharmacology or skin pharmacology the concept **penetration** is used, and this is important because curing the site of the disease topically is needed without any systemic effects (without reaching the drug the blood stream).

The advantages of topically administered drugs:

- 1- Quick delivery to the site of action.
- 2- Limiting systemic absorption, so the side effects of the drug.

Dermatologic Formulations

- Tinctures. (alcohol based like iodine and dyes)
- Wet dressings.
- Lotions.
- Gels.
- Powders. (for bacterial infection in wounds to keep it dry)
- Pastes.
- Creams.
- Ointments.

Adverse Effects of Dermatologic Preparations

- Burning or stinging sensation.
- Drying and irritation
- Pruritus. (حكة)
- Erythema. (احمرار)
- Sensitization.
- Staining.
- Superficial erosion.

TABLE 61-1
Local cutaneous reactions to topical medications.

Reaction type	Mechanism	Comment
Irritation	Non-allergic	Most common local reaction
Photoirritation	Non-allergic	Phototoxicity; usually requires UVA exposure
Allergic contact dermatitis	Allergic	Type IV delayed hypersensitivity
Photoallergic contact dermatitis	Allergic	Type IV delayed hypersensitivity; usually requires UVA exposure
Immunologic contact urticaria	Allergic	IgE-mediated type I immediate hypersensitivity; may result in anaphylaxis
Non-immunologic contact urticaria	Non-allergic	Most common contact urticaria; occurs without prior sensitization

- Irritation... most likely in alcohol based drugs, they cause burning or stinging sensation.
- Urticaria: one kind of inflammatory skin condition or reactive, there's itching and redness in that area of skin, it's called: الشرىة . It's an IgE mediated response.

The patient should be exposed to the drug once before to form the IgE against that drug.

- Photoirritation: the drug reacts with the UVA.

Topical Antibacterial Agents

- **Gram-positive bacteria**
 - Bacitracin
 - Gramicidin
 - Fusidic acid

- **Gram-negative bacteria**
 - Polymyxin B Sulfate
 - Neomycin
 - Genatamicin

BACITRACIN

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

- 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.



Bacitracin:

- Antibiotic vs antibacterial:
- *Antibiotic*: comes from a natural source or microorganisms, it can work against a wider spectrum of microorganisms.
- *Antibacterial*: they come from the factory, and it works only against bacteria.
- No need to memorize the specific spectra of bacteria, just know the general type (gram-positive OR gram-negative).
- MOA... (mechanism of action): Cell wall synthesis inhibitor but not a beta lactam.
- Side effects: May cause systemic toxicity if applied to a large amount of denuded skin or burned skin, so it's applied only topically.
- When we use a topically or anti-inflammatory agent the systemic side effect will be less, but this does not negate the systemic side effect
- An advantage of poorly absorbed drugs: the systemic side effects will be lesser.

- Frequently used in combination with other agents (polymyxin B and neomycin)
- Form: creams, ointments, and aerosol preparations
- Usually Anti inflammatory agents added - (hydrocortisone)



- **Corticosteroids** are a big important family of anti-inflammatory drugs that are used a lot in skin disorders.
- Usually skin infections are combined (means there's more than one type of microorganisms cause the infection, a lot of time there's gram-negative and gram-positive together) so the use is of drugs present in formulations that include multiple drugs, examples of these formulations:
 - 1- Polymyxin b sulfate.
 - 2- Fusidic acid.

Side effects of polymyxin b sulfate:

- If applied on intact skin, side effects are rare... if applied on denuded skin or open wounds, it may be cause systemic side effects like neurotoxicity and nephrotoxicity.

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 in order to reduce the likelihood of toxicity
“neurotoxicity and nephrotoxicity”
 - Allergic contact dermatitis NOT common.

Fusidic acid

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

often used topically in creams and eyedrops



Adding a hydrocortisone or corticosteroids is very important for curing the inflammation because hydrocortisone is an anti-inflammatory.

Inflammatory symptoms: swelling itching, etc.

The inflammatory reaction can happen due to an infection or due to an allergy.

Eczema is an allergic reaction that is treated with an anti-inflammatory drug like hydrocortisones, it will relieve the symptoms but not the condition.

NEOMYCIN & GENTAMICIN

Neomycin

- Aminoglycoside antibiotics
- gram-negative :E coli, proteus, klebsiella, and enterobacter.
- SE: allergic contact dermatitis
- 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
- Hospital acquired resistant

Aminoglycosidic antibiotics: protein synthesis inhibition (bacteriostatic).

Gentamicin can cause renal toxicity so we must care about patient with renal failure
Or low creatinine clearance.

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.
- Hair follicles clogged by oil and dead skin cells.
- Bacteria.
- Inflammation

Excessive oil production and Hormonal disturbances are also a cause, (progesterone and estrogen)

✚ The anaerobic bacterium *Cutibacterium acnes* (*Propionibacterium acnes*) is believed to play an important role in the pathophysiology of the common skin disease acne vulgaris.

Comedonal Lesions

Black heads

Mild

Happens because the excessive production of oil with exposure to the environmental dirt.



Inflammatory Lesions

Body exacerbated response to comedonal lesions



Nodulocystic Lesions

Bigger bumps they contain more pus they dispersed more around the body
Severe (more developed condition).



Can be diminished by collagen injection, filler injection, laser treatments...

Not easily inversed...

Scaring is genetically predisposed, some people are more predisposed than others

Scaring




Topical Therapy (Indications)

 comedonal acne


 mild to moderate inflammatory acne


Topical Therapy (Treatment Vehicle)

 cream → sensitive or dry

skin  lotion → any skin

type

 gel → oily skin

 solution → oily skin

Topical Therapy (Anti Comedonal Agents)

 **Topical Retinoids 0.025% - 0.5%**

 **Azelaic acid**

 **Salicylic acid**

Topical Retinoids (Adapalene, Differin)

The scientific name.

The commensial name

Vitamin a derivative



Topical Retinoids 0.025% - 0.5%

- apply at night
- always apply test dose
- start at low concentrations
- avoid in pregnancy

It's a teratogenic agent. category x agent

Avoid in Pregnancy



-  **Side**

Effects:

- **pustular flare** Pimples containing pus
- **photosensitivity**
- **skin irritation and erythema** مقشر للحبوب
- **dryness and peeling**

Azelaic Acid 20%



competitive inhibitor of mitochondrial oxidoreductases and of 5 alpha-reductase, inhibiting the conversion of testosterone to 5- dihydrotestosterone. It also possesses bacteriostatic activity to both aerobic and anaerobic bacteria including

Propionibacterium acnes

(dihydrotestosterone is a secondary sex characteristic and increase the acne)



applied twice



daily

Effects

- **erythema and irritation**

Azelaic Acid 20%

- **decrease in pigmentation**

Salicylic Acid 0.5 - 2%

Is used in washes

 **keratolytic. It belongs to the same class of drugs as aspirin (salicylates)**

 **Can reduce swelling and redness and unplugging blocked skin pores to allow pimples to shrink**

 **applied twice daily**

 **skin dryness and irritation**

Keratolytic: يذوب طبقة الكيراتين

. مسامير اللحم, black head or warts, Can be used in keratosis,

التركيز 10% في حالة مسمار اللحم

Topical Therapy (Anti Inflammatory Agents)

Very effective and Have bleach effect

 **Benzoyl Peroxide 2.5 - 10%**

exhibits bactericidal effects against Cutibacterium acnes

 **apply once to twice daily**

 **always apply test dose**

 **avoid use at night** Because its irritant

 **dryness of skin**

Topical Therapy (Anti Inflammatory Agents)




 **Clindamycin.**

Glycosides family of anti-biotics

 **Erythromycin.**

- **apply twice daily**
- **skin dryness**

*Combination
therapy*

-  **5% Benzoyl Peroxide and 3% Erythromycin**
-  **5% Benzoyl Peroxide and 1% Clindamycin**
-  **Topical antibiotics and Azelaic acid or
Tretinoin**