

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

## **Pharmacology lecture (MSS)**

**Topical steroids, keratolytics and Antipruritics**

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## Preparations of topical cutaneous steroids

### 1- Ointments

It is a **greasy** vehicle; it administered for **thick hyperkeratotic** and **dry lesions (e.g. chronic eczema)**.

It is the most potent vehicle (they are the most occlusive)

Avoided on hair-bearing regions because it may result in folliculitis.

**2- Creams** - less potent than ointment but cosmetically better (they leave no greasy residue).

**3- Lotions:** less occlusive and greasy; well in hair-bearing regions.

**4- Gels** - like lotions, and more beneficial for the scalp as they do not cause greasy hair.

**5- Foams** - highly effective for steroid delivery to the scalp but are costly.

## Mechanisms of action

### Glucocorticoid activity

- 1- Anti-inflammatory (inhibition of phospholipase A2).
- 2- Immunosuppressant (decreasing lymphocytes)
- 3- Antiallergic effects.
- 4- Antimitotic effects.

### Mineralocorticoid activity

- 1- Vasoconstriction which leads to **poor healing**.
- The vasoconstrictor properties determines the potency of steroid.

### The European classification of topical steroids:

1. Weak (e.g. Hydrocortisone )
2. Moderate (e.g. Clobetasone butyrate 0.05% )
3. Potent (e.g. Mometasone furoate 0.05% & Betamethasone esters )
4. Very potent (e.g. Clobetasol propionate 0.05%).

## Pharmacokinetics

- Topical steroids are **absorbed** to the circulation when applied to thin epidermis (e.g. the **eyelid**, **genital** skin, and **face**) up to 300 folds compared to thicker regions of epidermis (like palms and soles).
- The penetration increases two- to ten-fold in **diseased states** (e.g. inflammation, scratches, and desquamation).
- The skin of **children** is more permeable to topical steroids.
- Avoid **High-potency steroids** in **face**, **genitalia**, & **intertriginous** areas.
- The **amount** of the applied steroid used affects its absorption. One fingertip unit (FTU) is equal to 0.5 grams.
- Topical corticosteroids are recommended for once - twice daily use.



## Therapeutic uses

✓ Topical steroids are FDA-approved for treating:

- 1-Psoriasis
- 2-Eczema
- 3-Lichen planus
- 4-Discoïd lupus erythematosus
- 5- Limited areas of vitiligo
- 6-Atopic dermatitis
- 7-Acute radiation dermatitis
- 8-Lichen simplex chronicus (neurodermatitis)
- 9-lichen sclerosis.

✓ Topical steroids are also effective for treating:

- 1- Hyper-proliferation disorders (e.g. **hyperkeratosis** & **skin tumors**).
- 2- Immunological disorders (e.g. **alopecia areata**, and **bullous pemphegoid**).
- 3- Inflammatory conditions (**contact dermatitis, sun burn & phimosis**).
- 4- Allergic conditions (e.g. **urticaria** and some **drug eruptions**).
- 5- Topical steroids are also used for treating **pityriasis rosea, sarcoidosis and other granulomas.**

## The adverse effects of topical corticosteroids

They can be divided into **local** and **systemic** effects.

A-Local adverse effects occur with **prolonged use** & their occurrence is based on the topical steroid **potency**, **vehicle**, and **application site**.

The most common local effects include:

1- Delayed wound healing.

2- Skin atrophy and striae.

3- Rosacea

5- Acne.

6- Spread of skin infections (viral, fungal, bacterial or parasitic)

7- Hypertrichosis.

8- Pigment alteration (leukoderma occurs with intralesional injection of triamcinolone).

4- Peri-oral dermatitis.

9- **Contact allergy with hydrocortisone.**



Steroid rosacea (erythema with or without pustules)



Skin atrophy is the most common adverse effect and occurs due to the **anti-mitotic** effect of topical corticosteroids  
The loss of connective tissue



Striae  
(stretch marks)

- **Tachyphylaxis** : the skin is developing **tolerance** to **topical steroids**, which leads to loss of vasoconstriction at the level of the capillaries.
- **Addiction of topical steroid** is a common clinical problem usually presented with **rosacea**, **thin facial skin** and **irritation**.
- ✓ Gradual withdrawal of topical steroids and using topical calcineurin inhibitors help the improvement.
  
- Systemic adverse effects are less likely to occur due to low cutaneous absorption; however, they can develop with the prolonged use of high-potency steroids on thin epidermal regions or in children.
  
- The systemic adverse effects include: **glaucoma**, **hypothalamic-pituitary axis suppression**, **Cushing** syndrome, hypertension, and hyperglycemia.



## Contraindications of topical steroids

**Absolute:** in previous allergy to the preparation.

**Relative:** 1-Bacterial infections (e.g. impetigo, cellulitis, erysipelas, etc).

2- In fungal infection including candida and dermatophytes.

3- Viral infections like herpes.

4- Wounds and ulcers.

## Topical calcineurin inhibitors

(**tacrolimus** & preclorimus) can be used alternative to topical steroids in different dermatological diseases (especially **vitiligo**, and **atopic dermatitis**).

Calcineurin inhibitors will not cause skin atrophy, srlia, rosecia, or tachyphylaxis.



## Keratolytic agents

Keratolytic agents are compounds that break down the outer layer of the skin and help it to bind moisture. They are designed to **dissolve skin flakes** and **scales**.

Removing the scales improve some skin diseases & minimizes dandruff, it also helps other topical medications to penetrate the skin better.

### Side Effects of Keratolytic agents:

1. Reddening of the skin
2. Burning or tingling sensation
3. **Sensitivity to UV light**
4. Peeling of the skin.

### 1- Lactic acid

**It exfoliates** the skin, stimulate skin cell renewal & keeps the skin hydrated.

Over-the-counter creams and lotions that contain lactic acid help to relieve symptoms of psoriasis and keratosis pilaris.

## 2- Urea

**Urea** is an organic compound known to soften the skin.

Urea is very safe even in high conc.

It also has **hydrating and anti-itching properties**, and helps other medications to penetrate the skin.

Topical application of urea in a cream or gel has been shown to effectively treat **atopic dermatitis**, eczema, **xerosis** (dry skin), psoriasis, keratosis pilaris “chicken skin”, as well as **brittle nails**.

## **3- Salicylic acid**

It is used to treat common conditions like acne, psoriasis, and dandruff.

Salicylic acid works as a keratolytic by breaking down connections between dead cells on the surface of the skin.

It is usually applied to the skin surface as a **cream or lotion** of small concentrations (e.g. **0.5-1%**) for acne and psoriasis, or **higher conc (up to 30%)** to treat **warts and corns or callus**.

Other examples of keratolytic agents:

- 1- Topical **tretinoin** and oral acitretin,
- 2- topical **coal tar**.
- 3- **glycolic acid**,
- 4- pyridithione zinc
- 5- All chemical peels

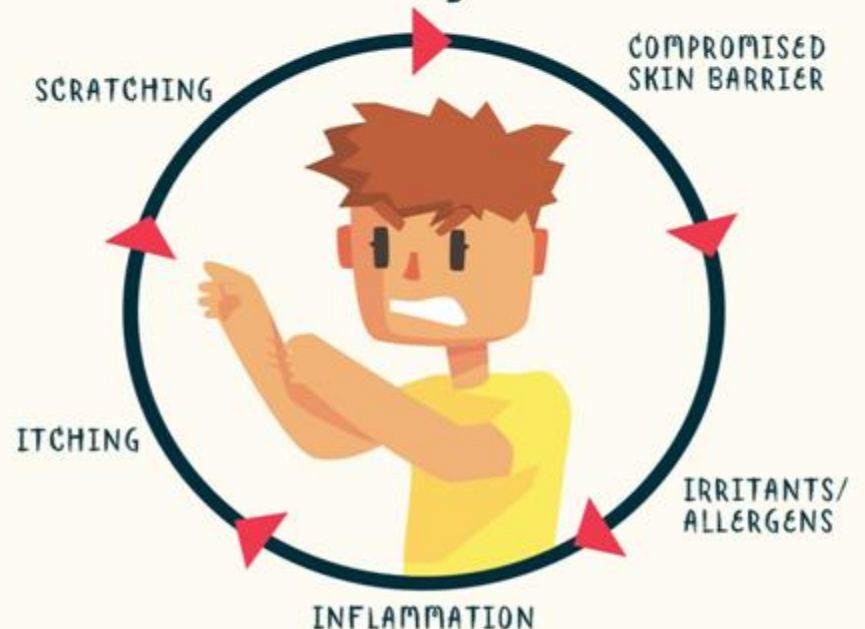
## Antipruritics

Antipruritics, or anti-itch drugs, are medications that inhibit itching ( pruritus).

### Treatment of itching:

- 1- Treat the cause.
- 2- General measures.
- 3- Topical medications.
- 4- Systemic medications.

### The itch-scratch cycle



# General measures

## INTERVENTION

Moisturization  
Cool environment  
Avoid irritants  
Break itch-scratch cycle  
Behavioural therapy, relaxation,  
stress reduction

## INDICATION

All patients  
All patients  
All patients  
All patients  
All patients, but especially for atopic  
dermatitis and other chronic itch

**Calamine (means Zinc) lotion** is an over-the-counter (OTC) medicine to treat mild itchiness (pruritus).

Calamine lotion contains zinc oxide & 0.5% ferric oxide (the iron oxide gives calamine lotion its distinctive pink color).

Additional ingredients include:

- Purified water.
- Glycerin.
- Calcium hydroxide.
- Phenol



Topical treatment	Indication
Corticosteroids	Inflammatory dermatoses
Calcineurin inhibitors	Inflammatory dermatoses
Capsaicin	Localized itch (eg, neuropathic)
Menthol	Localized itch (eg, neuropathic)
Pramoxine or eutectic mixture of lidocaine and prilocaine	Postburn, uremic, or neuropathic pruritus
Doxepin	Atopic dermatitis

➤ **Capsaicin** is an active component of **chili peppers**, It is a chemical irritant & triggers heat sensation from skin.

➤ **Menthol** (from mint ) chemically trigger the cold-sensitive receptors in the skin (cooling sensation), Menthol's analgesic properties are due to activation of  $\kappa$ -opioid receptors and blocking of voltage-sensitive sodium & calcium channels.

➤ **Pramoxine** (pramocaine) & **Lidocaine** are local anesthetics.

➤ **Doxepin** is a medication belonging to the tricyclic antidepressant.



## Systemic treatment

- 1- **Non-sedating antihistamines**: Urticaria, **insect bite reactions** and drug reactions.
- 2- First-generation **antihistamines (sedating)** for Nocturnal itch.
- 3-  **$\mu$ -Opioid receptor antagonists** for Cholestatic pruritus & atopic dermatitis.
- 4-  **$\kappa$ -Opioid receptor agonists** for **uremic pruritus**.
- 5- Antidepressants (**paroxetine, and sertraline**) palliative treatment in atopic dermatitis, **lymphoma**, solid **carcinoma**, **uremic** and **cholestatic** pruritus,

6-Doxepin in atopic dermatitis, HIV-related pruritus, allergic reactions, and urticaria.

7-Anticonvulsants (gabapentin & pregabalin) Uremic, Neuropathic pruritus.

8-Ursodeoxycholic acid for Intrahepatic cholestasis of pregnancy.

9- Oral immunosuppressants (cyclosporine, Azathioprine and Mycophenolate mofetil) in inflammatory dermatoses.

10 - Systemic corticosteroids in inflammatory dermatoses.



