بسم الله الرحمن الرحيم

Treatment of Psoriasis, vitiligo, and allergic skin diseases

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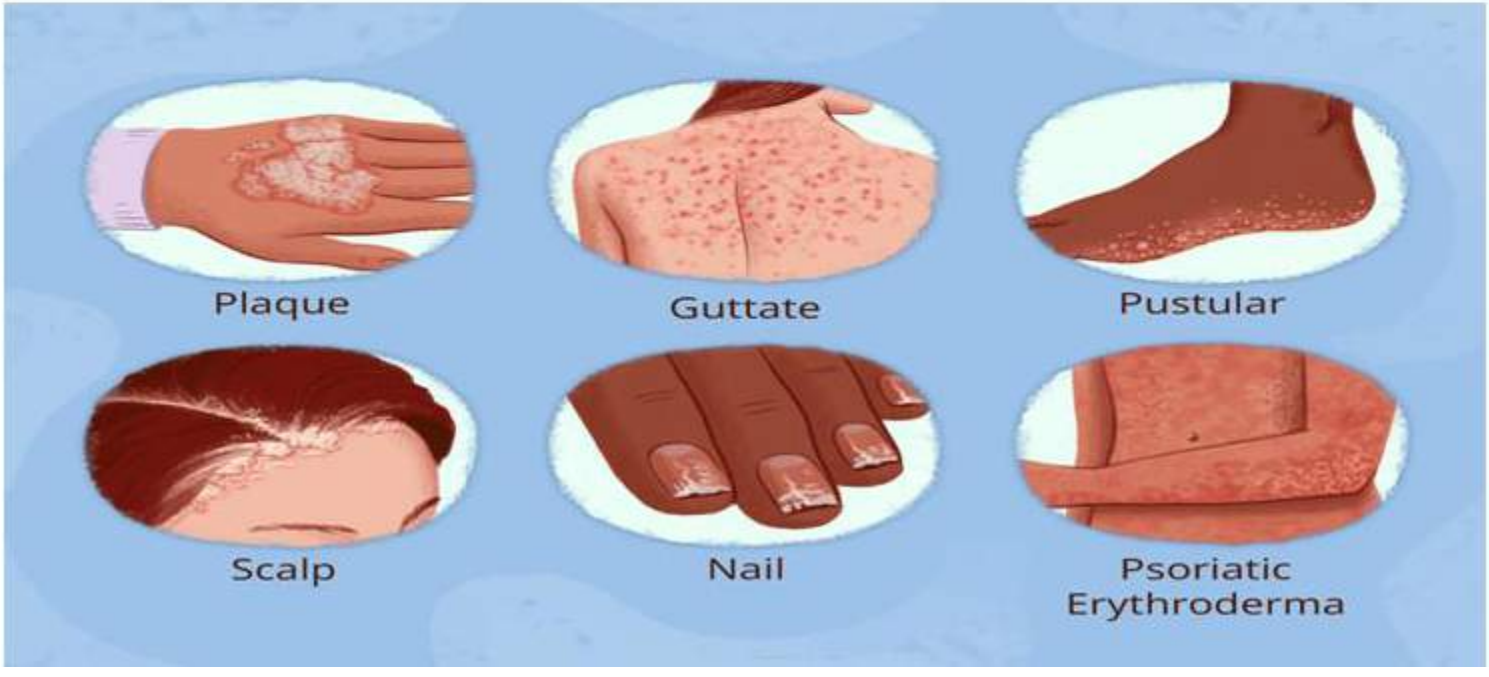
Psoriasis

- Psoriasis is a chronic papulosquamous disease affecting skin and joints.
- Hyperproliferation of keratinocytes & abnormal keratinization occurs. Lymphocytes & neutrophils are involved. Skin infections are rare due to rapid desquamation of epithelium.
- Clinically; lesions vary but redness and white silvery scales predominate.
- Medications &phototherapy can improve skin, joint, nail lesions, and to improve the quality of life for patients.
- No definitive complete cure for psoriasis till now.



Topical treatment of psoriasis

It is preferred for patients with limited psoriasis (less than 10% of body surface)

1-Topical corticosteroids

- ↓proliferation of keratinocytes, ↓ inflammation & Promote vasoconstriction.
- Betamethasone ointment is more effective than creams. Clobetasol propionate ointment is extremely potent (used once weekly in severe cases).
- long-term use can cause potential local and systemic side effects.
- Low to mid potency steroids are used during pregnancy.

2- Vitamin D3 analogues (e.g. calcipotriol, and tacalcitol)

- Prevent proliferation of keratinocytes and enhance their maturation.
- It has immunomodulatory effects on T-cells and neutrophils.
- Mild irritation occurs, so avoid calcipotriol with salicylic acid.
- Excessive administration **(>100 gm weekly**) can evoke **hypercalcemia**
- The classic 1st line treatment of psoriasis: Combination of topical steroids and topical calcipotriol.
- It is effective in **scalp psoriasis**, and Safe with phototherapy.

3- Topical calcineurin inhibitors

- **Tacrolimus** ointment and **pimecrolimus** cream
- prescribed for the treatment of **psoriasis in gentalia, face and intertriginous** areas (low uptake systemically)
- They inhibit T-Cell functions
- They are **safe during pregnancy** but not safe during lactation.
- They don't cause the adverse effects seen with topical steroids.

4-Tazarotene gel

- One of the **topical retinoid** which regulate keratinocyte differentiation
- It is irritant and sensitize the skin to UV radiation (so , doses of therapeutic phototherapy should be decreased)
- Avoided during pregnancy (teratogenicity) and avoided during lactation.
- Avoided in erythrodermic psoriasis.

5- Moisturizers

Petrolatum jelly, **glycerin** & other non-medical moisturizers can be used to fasten recovery. **Ceramide** **(medical moisturizer)** is effective but expensive.

6- Coal tar

- Anti-inflammatory, anti-pruritic and may **inhibit DNA synthesis** (reducing keratinocyte over-proliferation).
- It may be combined with topical steroids.
- Used mainly for scalp psoriasis (**shampoo**)
- Side effects: bad odor, contact dermatitis, staining, erythema, folliculitis.
- Avoided during pregnancy
- Dithranol paste: like coal tar but more irritant and very effective.

7-Topical keratolytics (urea & salicylic acid)

- **Salicylic acid combined with topical steroids** especially for **scalp lesions**.
- Topical salicylic acid should be avoided during pregnancy
- Systemic salicylic poisoning (tinnitus, metabolic acidosis, and Vomiting) occurs in high conc. (5-10%) with prolonged use.

Systemic treatments are commonly used for severe disease.

Methotrexate	Acitretin	Cyclosporine
Folic acid antagonist (anticancer drug)	Activates retinoid receptors (Vitamin A related drug)	Inhibits calcineurin (immunosuppressive drug)
Antiproliferative	Regulate keratinization	Inhibit T cell function
Oral or IM	Oral	Oral
Not safe in pregnancy	Not safe in pregnancy	Safe in pregnancy
Adverse effects 1. Bone marrow depression 2. Hepatotoxicity 3. GIT ulceration and bloody diarrhea 4. Crystalluria 5. Teratogenicity	Adverse effects 1. Muco-cutaneous dryness 2. photosensitivity 3. GIT disturbances 4. arthralgia 5. Elevated triglyceride 6. Elevated liver enzymes 7. Teratogenicity (even after 2-3 years of stopping the drug)	Adverse effects 1. Hypertension 2. nephrotoxicity 3. Secondary infections 4. Hyperuricemia 5. Hyperlipidemia 6. Hypertrichosis and hirsutism 7. Drug interactions

Biological agents for psoriasis and psoriatic arthritis

- Monoclonal antibodies that binds and inactivate inflammatory cytokines
- They are highly effective in the treatment of moderate & severe psoriasis and psoriatic arthritis .
- Most of biologics are **safe during pregnancy**
- They are given by injections (usually S.C.). Examples:

1. IL-12/23 inhibitor (Ustekinumab)
2. TNF inhibitors (Adalimumab)
3. IL-17 inhibitors (Secukinumab)

Common adverse effects:

- Injection site reactions and **Hypersensitivity** reactions
- Reactivation of hepatitis B or tuberculosis

Phototherapy for psoriasis

The main types of phototherapy used to treat psoriasis include

- Psoralen plus UVA (PUVA)
- Broadband UVB

Treatment of vitiligo

Vitiligo is characterized by **absence of pigment in the skin**, secondary to the loss of melanocytes (autoimmune disease)

Topical treatment

1- Topical calcineurin inhibitors (e.g. **tacrolimus**)

Tacrolimus inhibit calcineurin and decreases the formation of interleukin 2 leading to **inhibition of activation of lymphocytes** and dendritic cells.
Tacrolimus also **induce melanoblast proliferation.**

2- Topical vitamin D3 analogs

- They inhibit T-cell activity, ↑ **melanocyte and of melanin production**.
- not effective as monotherapy but are useful as adjuvants to other therapies .

3- Topical corticosteroids

Useful for **localized skin lesions of vitiligo to avoid their side effects**.

4- Topical and intralesional injection of 5- fluorouracil (5-FU)

5-FU **stimulates follicular melanocytes migration** and increases the number of melanosomes in keratinocytes.

5-FU can be injected intradermal in vitiligo lesions or used as a **cream** applied following epidermal abrasion (to enhance the absorption)

5- Methotrexate gel.

MTX is a folate antagonist leads to **decrease the number of T cells.**

6- Prostaglandin F2 alpha analogs like latanoprost (eye drops for glaucoma).

It **increase melanogenesis.**

7- Janus kinase (JAK) inhibitors: e.g., tofacitinib

It causes downregulation of the JAK-STAT pathway & ↓**interferon-gamma** which is involved in cell-mediated immunity in vitiligo.

Phototherapy in vitiligo

1. PUVA
2. Narrow band UVB
3. Excimer light laser

Systemic treatments of vitiligo

1- Systemic Corticosteroids.

They **suppress the immune response** &used in rapidly progressive active vitiligo to **stabilize the disease** and allow re-pigmentation

Systemic Corticosteroids pulse therapy (intermittent) is preferred to decrease the potential side-effects.

2-Oral JAK inhibitors (Tofacitinib)

Adverse effects: upper respiratory infections, **weight gain**, arthralgia and mild elevation of lipid levels.

3- Apremilast.

It is phosphodiesterase 4 inhibitor that ↑ intracellular cAMP and ↓ production of (IL-23, IL-17, TNF-α and IFN-γ) and an **increase** in anti-inflammatory mediators, such as **(IL-10).**

4- Antioxidants

Treatment of atopic dermatitis

Atopic dermatitis also known as **atopic eczema** is a common, chronic relapsing, and remitting inflammatory skin. The skin barrier is disrupted, and bacterial colonization is common.

➢ **Good skin hygiene** and the **use of emollients (medical moisturizers)** are recommended for chronic treatment

- Topical corticosteroids are first-line treatment during exacerbations.
- Topical calcineurin inhibitors can be used for sensitive sites (e.g. face).
- Crisaborole cream is approved for mild to moderate atopic dermatitis in patients over the age of two years. It is a phosphodiesterase-4 inhibitor which reduces cytokines.
- Adjunctive treatments like Bleach baths, oral antihistamines and wet dressings are potentially helpful adjunctive therapies when patients have a flare of atopic dermatitis. Topical antibiotics to fight infections.

Systemic therapies and phototherapy are effective in patients with moderate-to-severe disease and not responsive to topical therapies

1- Oral prednisolone (corticosteroid) is used to treat flares of atopic dermatitis.

2- JAK inhibitors (abrocitinib & **Upadacitinib**): very effective in in moderate-to-severe atopic dermatitis via blocking signaling of multiple cytokines.

3- Immunosuppressive drugs

Ciclosporin and other immunosuppressive drugs could be used for treating severe atopic dermatitis.

4-Dupilumab

Dupilumab is a monoclonal antibody that blocks interleukins 4 & 13 (key drivers of atopic dermatitis). It is an immunomodulator, not an immunosuppressant.

5-Phototherapy

Phototherapy with narrowband ultraviolet B (UVB) results in significant improvement in most patients with atopic dermatitis.


THANK
YOU!