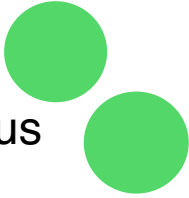


## Immunomodulators

Imiquimod.

Tacrolimus.

Pimecrolimus



## Ectoparasiticides

Permethrin

Lindane.

Crotamiton.

Sulfur.

Malathion.



## Agents affecting Pigmentation

depigmentation.

Hydroquinone.

Monobenzone.

Mequinol.

## Agents affecting Pigmentation

repigmentation

Trioxsalen.

Methoxsalen.

## Sunscreens and Sunshades

para amino benzoic acid (PABA)  
(Sunscreens)

titanium dioxide(Sunshades)

## Acne Preparations

Retinoic Acid and Derivatives:

Retinoic Acid( Tretinoin).

Adapalene.

Tazarotene.

Isotretinoin( Accutane).



Not derivatives of Retinoic acid

Benzoyl Peroxide

Azelaic Acid

### Drugs for Psoriasis

Acitretin.



Tazarotene.



Calcipotiene

**Biologic Agents (monoclonal antibody)  
for psoriasis:**

Alefacept.

Efalizumab.

Etanercept.

### Keratolytic and Destructive Agents

Salicylic acid.

Propylene Glycole.



Urea:

Podophyllum Resin and Podofilox.

Flurouracil.

Nonsteroidal Anti-inflammatory Drugs.

Aminolevulinic Acid

### Anti-inflammatory Agents

Topical Corticosteroids:

Hydrocortisone.

Prednisolone and Methylprednisolone.

Dexamethasone and Betamethasone.

Triamcinolone.

Fluocinonide.

Tar compounds.



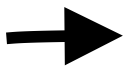
neurotoxicity



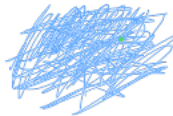
nephrotoxicity



hematoxicity



hepatotoxicity



Teratogenicity

# Immunomodulators

- **Imiquimod:**
- **Stimulates peripheral mononuclear cells to release interferon- $\alpha$  and to stimulate macrophages to produce interleukins-1,-6, and -8 and tumor necrosis factor- $\alpha$ .**
- **Uses:**
  - **For external genital and perianal warts.**
  - **Actinic keratosis on the face and scalp.**
  - **Primary basal cell carcinoma.**
- **Tacrolimus.**
- **Pimecrolimus.**
  - **Useful for atopic dermatitis.**
  - **Inhibit T-lymphocyte activation and prevent release of inflammatory cytokines and mast cell mediators**
  - **(Black box warning)**

# Ectoparasiticides

- **Permethrin:**
  - Toxic to *Pediculus humanus*, *Pthirus pubis*, and *Sarcoptes scabiei*
  - Pediculosis: cream applied for 10 minutes and then rinsed off with warm water.
  - Scabies: cream applied for the whole body for 8-14 hours.
- **Lindane (Hexachlorocyclohexane):**
  - 10% absorbed and concentrated in fatty tissues.
  - Can cause neurotoxicity and hematotoxicity
- **Crotamiton.**
- **Sulfur.**
- **Malathion.**

# Agents affecting Pigmentation

- Hydroquinone.
- Monobenzone.
- Monobenzone may be toxic to melanocytes resulting in permanent depigmentation.
- Mequinol
  - Reduce hyperpigmentation of skin by inhibiting the enzyme tyrosinase which will interfere with biosynthesis of melanin.

# Agents affecting Pigmentation

- Trioxsalen.
- Methoxsalen.
  - Are psoralens used for the repigmentation of depigmented macules of vitiligo.
  - Must be photoactivated by long-wave-length ultraviolet light (320-400nm) to produce a beneficial effect.
  - They intercalate with DNA.
  - Can cause cataract and skin cancer.

# Sunscreens and Sunshades

- **Sunscreens absorb UV light.**
  - **Examples are para amino benzoic acid (PABA) and its esters.**
- **Sunshades are opaque materials that reflect light, like titanium dioxide.**
- **Useful in polymorphous light eruption, lupus erythematosus, and drug –induced photosensitivity.**

# Acne Preparations

*tetra*

- **Retinoic Acid and Derivatives:**
  - Retinoic Acid.
  - Adapalene.
  - Tazarotene.



# Acne Preparations

- **Retinoic Acid and Derivatives:**

- **Retinoic Acid( Tretinoin):** is the acid form of Vitamin A. Stabilizes lysosomes, increases RNA polymerase activity, increases PGE<sub>2</sub>, cAMP, and cGMP levels, and increases the incorporation of thymidine into DNA.
- **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.**
- **Can cause erythema and dryness.**
- **Tumorigenic in animals**

# Acne Preparations

- **Isotretinoin( Accutane):**
  - Restricted for severe cystic acne resistant to standard treatment.
  - Inhibits sebaceous gland size and function.
  - Given orally.
  - Toxic: dryness, itching, headache, corneal opacities, pseudotumor cerebri, inflammatory bowel disease, anorexia, alopecia, and muscle and joint pains. Also lipid abnormalities.
  - Teratogenicity

# Acne Preparations

- **Benzoyl Peroxide:**
  - Penetrates the stratum corneum or follicular openings and converted to benzoic acid within the epidermis and dermis.
  - Has antimicrobial activity against *P. acnes* and peeling and comedolytic effects.
  - Can be combined with erythromycin or clindamycin.
  - Potent contact sensitizer.
  - Can cause bleaching of hair or colored fabrics.
- **Azelaic Acid:**
  - Has antimicrobial activity and inhibits conversion of testosterone to dihydrotestosterone.

# Drugs for Psoriasis

- **Acitretin:**
  - Related to isotretinoin.
  - Given orally.
  - Hepatotoxic and teratogenic.
  - Patients should not become pregnant for 3 years after stopping treatment, and also should not donate blood.

# Drugs for Psoriasis

- **Tazarotene:**

- Topical.

- Anti-inflammatory and antiproliferative actions.

- Teratogenic. Also, can cause burning, stinging, peeling, erythema, and localized edema of skin.

- **Calcipotriene:**

- Synthetic vitamin D<sub>3</sub> derivative

# Drugs for Psoriasis

- **Biologic Agents:**

- **Alefacept:**

- Immunosuppressive dimer fusion protein of CD2 linked to the Fc portion of human IgG<sub>1</sub>.

- **Efalizumab:**

- Recombinant humanized IgG<sub>1</sub> monoclonal antibody.
    - Withdrawn :progressive multifocal leukoencephalopathy (PML),
    - Can cause thrombocytopenia.

- **Etanercept:**

- Dimeric fusion protein of TNF receptor linked to the Fc portion of human IgG<sub>1</sub>.

# Anti-inflammatory Agents

- **Topical Corticosteroids:**
  - Hydrocortisone.
  - Prednisolone and Methylprednisolone.
  - Dexamethasone and Betamethasone.
  - Triamcinolone.
  - Fluocinonide.

# Anti-inflammatory Agents

- **Topical Corticosteroids:**
  - **Absorption:**
    - 1% of hydrocortisone applied to the ventral forearm.
    - 0.14 times of hydrocortisone applied to the plantar foot.
    - 0.83 times of hydrocortisone applied to the palm.
    - 3.5 times of hydrocortisone applied to the scalp.
    - 6 times of hydrocortisone applied to the forehead.
    - 9 times of hydrocortisone applied to the vulvar skin.



# Anti-inflammatory Agents

- **Topical Corticosteroids:**
  - **Absorption:**
    - Absorption increased with inflammation.
    - Increasing the concentration does not proportionally increase the absorption.
    - Can be given by intralesional injection.

# Anti-inflammatory Agents

- **Topical Cortcosteroids:**
  - **Dermatologic disorders very responsive to steroids:**
    - Atopic dermatitis.
    - Seborrheic dermatitis.
    - Lichen simplex chronicus.
    - Pruritus ani.
    - Allergic contact dermatitis.
    - Eczematous dermatitis.
    - Psoriasis

# Anti-inflammatory Agents

- **Topical Cortcosteroids:**

- **Adverse Effects:**

- Suppression of pituitary-adrenal axis.
    - Systemic effects.
    - Skin atrophy.
    - Erythema.
    - Pustules.
    - Acne.
    - Infections.
    - Hypopigmentation.
    - Allergic contact dermatitis.

# Anti-inflammatory Agents

- Topical Corticosteroids.
- Tar compounds:
  - Mainly for psoriasis, dermatitis, and lichen simplex chronicus
  - Can cause irritant folliculitis, phototoxicity, and allergic contact dermatitis.

# Keratolytic and Destructive Agents

- **Salicylic acid:**
  - Solubilizes cell surface proteins resulting in desquamation of keratotic debris.
  - Keratolytic in 3-6% concentration, but destructive in higher concentrations.
  - Can result in salicylism due to systemic absorption.
  - Locally, can cause **urticaria**, **anaphylactic** and erythema multiforme reactions, irritation, inflammation, and ulceration.

# Keratolytic and Destructive Agents

- **Salicylic acid:**
- **Propylene Glycole:**
  - Usually used as a vehicle for organic compounds.
  - Used alone as a keratolytic agent in concentrations of 40%- 70%, with plastic occlusion, or in gel with 6% salicylic acid.
  - Minimally absorbed, oxidized in liver to lactic acid and pyruvic acid.
  - Develops an osmotic gradient through the stratum corneum, thereby increasing hydration of the outer layers of skin.

# Keratolytic and Destructive Agents

- Salicylic acid.
- Propylene Glycole.
- Urea:
  - Has a **humectant** activity, i.e. softening and moisturizing effect on the stratum corneum.
  - Increases water content as a result of its **hygroscopic** characteristics.
  - Decreases the unpleasant oily feel of dermatologic preparations.
  - When absorbed, it is excreted in urine.

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# Keratolytic and Destructive Agents

- **Salicylic acid.**
- **Propylene Glycole.**
- **Urea:**
- **Podophyllum Resin and Podofilox:**
  - An alcoholic extract of *Podophyllum peltatum*(  
Mandrake root or May apple).
  - Used in the treatment of condyloma acuminatum and  
other verrucae.
  - Cytotoxic activity with specific affinity for the  
microtubule protein of the mitotic spindle.
  - Can cause N, V, muscle weakness, neuropathy, coma,  
and even death.

# Keratolytic and Destructive Agents

- **Salicylic acid.**
- **Propylene Glycole.**
- **Urea:**
- **Podophyllum Resin and Podofilox.**
- **Flurouracil:**
  - Antimetabolite that resembles uracil and inhibits thymidylate synthetase, thus interferes with DNA and may be RNA synthesis.
  - Used in multiple actinic keratosis.

# Keratolytic and Destructive Agents

- Salicylic acid.
- Propylene Glycole.
- Urea:
- Podophyllum Resin and Podofilox.
- Flurouracil.
- Nonsteroidal Anti-inflammatory Drugs:
  - 3% gel formulation diclofenac.

# Keratolytic and Destructive Agents

- **Salicylic acid.**
- **Propylene Glycole.**
- **Urea:**
- **Podophyllum Resin and Podofilox.**
- **Flurouracil.**
- **Nonsteroidal Anti-inflammatory Drugs.**
- **Aminolevulinic Acid:**
  - Used in actinic keratosis.
  - After topical application(20%) and exposure to light, produces a cytotoxic superoxide and hydroxyl radicals.

# Antipruritic Agents

- **Doxepine:**
  - Potent H<sub>1</sub> and H<sub>2</sub> receptor antagonist.
  - Can cause drowsiness and anticholinergic effects.
- **Pramoxine:**
  - Is a topical local anesthetic agent.

# Trichogenic and Antitrichogenic Agents

- **Minoxidil (Rogaine):**
  - Designed as an antihypertensive agent.
  - Effective in reversing the progressive miniaturization of terminal scalp hairs associated with androgenic alopecia.
  - Vertex balding is more responsive than frontal balding.

# Trichogenic and Antitrichogenic Agents

- **Minoxidil.**
- **Finasteride (Propecia):**
  - **Finasteride (is a trichogenic agent) is a 5 $\alpha$ -reductase inhibitor that blocks the conversion of testosterone to dihydrotestosterone ( DHT) DHT is the androgen responsible for androgenic alopecia in genetically predisposed men for androgenic alopecia in genetically predisposed men.**
  - **Oral tablets.**
  - **Can cause decreased libido, ejaculation disorders, and erectile dysfunction.**

# Trichogenic and Antitrichogenic Agents

- **Minoxidil.**
- **Finasteride.**
- **Eflornithine:**
  - 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.



# Drugs for Leishmania

Caused by three *Leishmania species*:

*L.tropica* causes: Cutaneous leishmaniasis or oriental sore.

*L. braziliensis* causes: Mucocutaneous leishmaniasis.

*L. Donovanii* causes: Visceral leishmaniasis

# Sodium Stibogluconate

**Pentavalent antimonial**

**Binds to SH groups on proteins.**

**Typical preparations contain 30% to 34% pentavalent antimony by weight as well as *m*-chlorocresol added as a preservative.**

**Also, inhibits phosphofructokinase**

**Local, IM or slow IV, irritant.**

**Given for 20-28 days.**

**Drug of choice for all forms of leishmaniasis.**

**Resistance is increasing, especially in India.**

**Cough, V, D, myalgia, arthralgia, ECG changes, Rash, Pruritus.**

# Amphotericin

- **Antifungal agent, difficult to use, and toxic.**
- **Alternative therapy for visceral leishmaniasis, especially in areas with high resistance.**

# Miltefosine

- **For visceral leishmaniasis.**
- **Given orally, for 28 days.**
- **Causes V & D, hepatotoxicity, nephrotoxicity, and it is teratogenic.**

# Pentamidine

- **Inhibits DNA replication.**
- **Also, DHF reductase inhibitor**
  
- **Given IM or IV injection and Inhalation**
- **Binds avidly to tissues, not the CNS.**

# Pentamidine

## **Leishmaniasis:**

Alternative to Na stibogluconate

## ***Pneumocystis jiroveci:***

Treatment and prophylaxis of patients who cannot tolerate or fail other drugs.

## **Trypanosomiasis:**

For early hemolympathic stage.

# Pentamidine

- **Adverse Effects:**
- **Rapid Infusion: Hypotension, tachycardia, dizziness.**
- **Pain at the injection site.**
- **Others: Pancreatic, Renal, and Hepatic toxicity.**

# Antilepromatous Drugs

- **Dapsone and Sulphones:**
  - Related to sulphonamides.
  - Inhibit folate synthesis.
  - Resistance develops.
  - Combined with Rifampin and Clofazimine.
  - Also used for *Pn. Jeroveci* in AIDS patients.
  - Well absorbed and distributed.
  - Retained in the skin, muscle, liver and kidney.



# Antilepromatous Drugs

- **Dapsone and Sulphones:**
  - Hemolysis, particularly in G-6-PD deficiency.
  - GIT intolerance
  - Fever, Pruritus, Rashes.
  - Erythema Nodosum Leprosum:  
suppressed by steroids or  
thalidomide.

# Antilepromatous Drugs

- **Rifampin:**
  - Discussed with antituberculous drugs.
- **Clofazimine:**
  - Binds to DNA.
  - Stored widely in RES and skin.
  - Released slowly from storage sites,  $t_{1/2} = 2$  months.
  - Given for sulphone-resistant or intolerant cases.
  - Causes skin discoloration (red-brown to black) and GIT intolerance.