

# **Dermatologic Pharmacology**

# Topical Antibacterial Agents

- Increasing the concentration gradient increases the mass of drug transferred per unit time
- *Stratum Corneum* is a reservoir for percutaneous drugs.
- Percutaneous drug **metabolism** and **receptor-binding** occur in *S.spinosum* and *basement membrane zone*.

Topical antibacterial agents include:

- 1- **Bacitracin**
- 2- Gramicidin (G+ve)
- 3- **Polymyxin B**
- 4- **Neomycin**
- 5- Gentamycin (G-ve)

*BACITRACIN:*

- Used with other agents ... given with anti-inflammatory drugs (hydrocortisone) ... more than one form.

Topical antibacterial agents in Acne include:

**Clindamycin ... Erythromycin ... Metronidazole ... Sodium Sulfacetamide.**

*CLINDAMYCIN*

- Risk for **Pseudomembranous Colitis** (low absorption)
- Allergic contact dermatitis is **uncommon**.
- The hydroalcoholic vehicle and foam formulation (Evoclin) may cause drying and irritation of the skin
- Available forms:
  - Clindamycin + Benzoyl Peroxide (Duac)**
  - Clindamycin + Tretinoin (Ziana)**

*METRONIDAZOLE*

- Effective in the treatment of **rosacea**
- This drug may act as an **anti-inflammatory** agent by direct effect on neutrophil cellular function
- Inhibitory effects of metronidazole on *Demodex brevis*.
- Metronidazole can cause severe tearing if applied near the eyes.
- The gel formula has **more side effects** than the cream, lotion, and noritate cream formulas.

*ERYTHROMYCIN*

- Erythromycin base is used rather than salt to facilitate penetration.
- Can develop antibiotic-resistant Staph.
- Benzamycin = Erythromycin + Benzoyl peroxide.

# Antifungal Agents

## Topical agents

| Drug               | Organism  |
|--------------------|---|
| -azole derivatives | Candida albicans  |
| Ciclopirox Olamine | Tinea versicolor  |
| -fine              | Tinea pedis, Tinea cruris, Tinea corporis                     |
| Tolnaftate         | -   |
| Nystatin           | Candida albicans ONLY<br><i>Forms: topical, oral, vaginal</i> |
| Amphotericin B     |   |

## Oral agents

| Drug   | Organism/disease  | Notes   |
|--|---|---|
| Some -azole derivatives<br>(Flucon-, Itracon-, Ketoconazole) | <ul style="list-style-type: none"> <li>• Systemic mycosis</li> <li>• Mucocutaneous candidiasis</li> </ul>         | <ul style="list-style-type: none"> <li>• Alter sterol synthesis; affects fungal permeability</li> <li>• Systemic side effects; <i>Hepatitis, elevated liver enzymes.</i></li> </ul> |
| Griseofulvin   | <ul style="list-style-type: none"> <li>• Epidermophyton</li> <li>• Microsporum</li> <li>• Trichophyton</li> </ul> | <ul style="list-style-type: none"> <li>• Many side effects</li> <li>• Prolonged treatment;</li> <li>• Scalp = 4-6 wk.<br/>Fingernails = 6 mn<br/>toenails = 8-18 mn</li> </ul>      |
| Terbinafine  | <ul style="list-style-type: none"> <li>• Onchomycosis</li> </ul>  | <ul style="list-style-type: none"> <li>• Ringworm of the nail</li> <li>• Prolonged treatment;</li> <li>• Fingernails = 6 wk.<br/>toenails = 12 wk.</li> </ul>                       |

*Ketoconazole* is used both topically and orally, but for different purposes:

Topically: yeasts (C.albicans).

Orally: Systemic mycosis, Mucocutaneous Candidiasis.

*Terbinafine* is used both topically and orally, but for different purposes:

Topically: T.pedis, T.Cruris, T.Corporis

Orally: Onchomycosis

## Topical Antiviral Agents

- -*Cyclovir* derivatives
- Synthetic **guanine** analogs
  - inhibitors of herpes virus
- If recurrent orolabial HSV infection: use ointments and creams.

## Immunomodulators

| Drug  | Uses  | MOA  |
|---|---|--|
| Imiquimod   | <ul style="list-style-type: none"> <li>- External warts (genital, perianal)</li> <li>- Actinic keratosis (face and scalp)</li> <li>- Basal cell carcinoma (the primary type)</li> </ul> | <ul style="list-style-type: none"> <li>- Goes to <b>peripheral mononuclear</b> cells to release <b>IF- <math>\alpha</math></b></li> <li>- Stimulates macrophages to release IL-1, IL-6, IL-8, TNF-<math>\alpha</math></li> </ul> |
| -Crolimus derivatives<br><b>Tacrolimus</b><br><b>Pimecrolimus</b> | <ul style="list-style-type: none"> <li>- Atopic Dermatitis</li> </ul>   | <ul style="list-style-type: none"> <li>- Inhibit <i>T-cell</i> activation</li> <li>- Prevents release of <b>cytokines</b> and <b>mast cell mediators</b>.</li> </ul>   |

## Ectoparasiticides

### *Permethrin*

- Kills:
  - P.Humanus
  - P.Pubis
  - S.Scabiei
- How to use it?
  - **Pediculosis**: apply cream for 10 min. then rinse with warm water
  - **Scabies**: apply cream for the whole body for 8-14 hrs.

### *Lindane*

- Hexachlorocyclohexane.
- 10% absorbed.
- Concentrated in fat tissue.
- Side effects: Neurotoxicity and Hematotoxicity.

### *Crotamitone*

- Scabicial and general antipruritic

### *Sulfur*

### *Malathion*

## Agents Affecting Pigmentation

### Depigmentation drugs (skin whitening)

| Drug         | MOA                 | Notes   |
|--------------|---------------------|---|
| Hydroquinone | Inhibits Tyrosinase | Temporary skin whitening                                  |
| Monobenzone  |                     | Toxic to Melanocytes<br>- causes permanent depigmentation |
| Mequinol     |                     | Used along with Hydroquinone for a temporary effect.      |

### Repigmentation drugs

| Drug                 | MOA                  | Notes  |
|----------------------|----------------------|--|
| -Oxsalen derivatives | Intercalate with DNA | - Treats vitiligo<br>- Needs photoactivation UV light<br>- Causes <i>Cataract</i> and <i>skin cancer</i> |

## Sunscreens and Sunshades

- What is the difference between the two?
  - Sunscreens: absorb UV light
  - Sunshades: Opaque materials that reflect light
- Examples:
  - Sunscreens: PABA and its esters (Para Amino Benzoic Acid)
  - Sunshades: Titanium Dioxide
- Uses:
  - Polymorphous Light Eruption (PLE)
  - Lupus
  - Erythematosis
  - Drug-induced Photosensitivity

## Acne Preparations

| Drug             | Uses                                    | MOA  | SE   | Notes  |
|------------------|---|--|--|--|
| Retinoic Acid    | <i>Fine lines and wrinkles</i>          | <ul style="list-style-type: none"> <li>-Increases RNA polymerase activity</li> <li>- Stabilizes lysosomes</li> <li>- Puts more Thymidine into DNA</li> <li>- Increases PGE2, cAMP, cGMP</li> <li>- Decreases cohesion between epidermal cells, and increases cell turnover = will lead to expulsion of open comedones and opens the closed ones.</li> <li>- <i>Promotes dermal collagen synthesis, angiogenesis, epidermis thickening</i></li> </ul> | Erythema<br>Dryness  | <ul style="list-style-type: none"> <li>- Teratogenic in animals</li> <li>- Also called <b>Tretinoin</b></li> </ul>                           |
| Isotretinoin     | Severe cystic acne                      | Inhibits sebaceous gland size and function   | <ul style="list-style-type: none"> <li>- Corneal capacities</li> <li>- Pseudotumor cerebri</li> <li>- IBD</li> <li>- Anorexia</li> <li>- Alopecia</li> <li>- Muscle pain</li> <li>- Joint pain</li> <li>- Lipid abnormalities</li> </ul> | <ul style="list-style-type: none"> <li>- Teratogenic</li> <li>- Given orally</li> <li>- Also called <b>Accutane</b></li> </ul>               |
| Benzoyl Peroxide | antimicrobial<br>Against <i>P.acnes</i> | Penetrates stratum corneum then converted to benzoid acid in dermis and epidermis  | Bleaching of hair  | <ul style="list-style-type: none"> <li>-Has peeling and comedolytic effects</li> <li>-combined with erythromycin/<br/>clindamycin</li> </ul> |
| Azelaic acid     | Antimicrobial                           |  |  |  |

Retinoic acid derivatives: **Adapalene** and **Tazarotene**

# Drugs for Psoriasis

## *Acetretin*

- Given orally
- Related to Isotretinoin
- SE: Hepatotoxicity, Teratogenic
- When taking this drug, *pregnancy and blood donation are contraindicated for 3 years.*

## *Tazarotene*

- Topical
- Anti-inflammatory and antiproliferative
- Teratogenic
- SE: Burning, stinging, peeling, erythema, localized edema.

## *Calcipotiene*

- Synthetic Vit D3 derivative.

## *Biologic Agents*

| Drug              | Info   |
|-------------------|--|
| <b>Alefacept</b>  | Immunosuppressive dimer fusion protein of <b>CD2</b> linked to the Fc portion of human IgG <sub>1</sub>  |
| <b>Efalizumab</b> | Recombinant humanized IgG <sub>1</sub> monoclonal antibody<br><br>Can cause Thrombocytopenia<br><br>Withdrawn; leads to PML (progressive multifocal leukoencephalopathy) |
| <b>Etanercept</b> | Dimeric fusion of <b>TNF</b> receptor linked to the Fc portion of IgG <sub>1</sub>   |