

Skin Pharmacology

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Adverse Effects of Dermatologic Preparations

- **Burning or stinging sensation.**
- **Drying and irritation**
- **Pruritus.**
- **Erythema.**
- **Sensitization.**
- **Staining**
- **Superficial erosion.**

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.



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

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



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

Trichogenic and Antitrichogenic Agents

- **Minoxidil (Rogaine):**
 - **Designed as an antihypertensive agent.**
 - Minoxidil is a potassium channel opener causing hyperpolarization of cell membranes.
 - Causing widening blood vessels, it allows more oxygen, blood, and nutrients to the follicles. may act as a nitric oxide agonist. This may cause follicles in the telogen phase to shed, which are then replaced by thicker hairs in a new anagen phase
 - **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)**
 - **5 α -reductase inhibitor which blocks the conversion of testosterone to dihydrotestosterone.**
 - **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.

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**
- ✚ **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



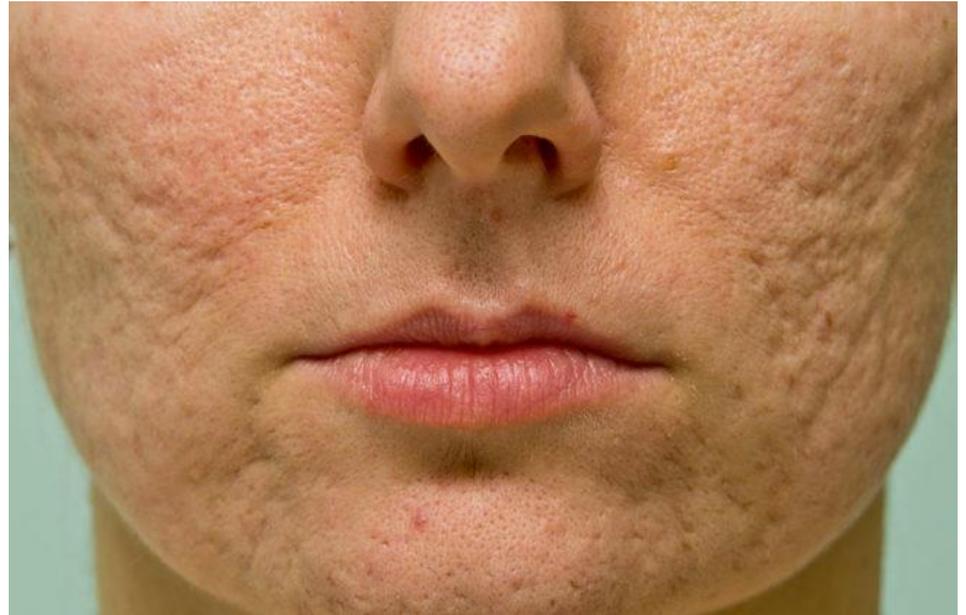
Inflammatory Lesions



Nodulocystic Lesions



Scaring



Topical Therapy (Indications)

-  **comedonal acne**
-  **mild to moderate inflammatory acne**

Topical Therapy

-  **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)

✚ Topical Retinoids 0.025% - 0.5%

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

✚ Side Effects:

- pustular flare
- photosensitivity
- skin irritation and erythema
- dryness and peeling

Avoid in Pregnancy



Azelaic Acid 20%

- ✚ **competitive inhibitor of mitochondrial oxidoreductases and of 5 alpha-reductase, inhibiting the conversion of testosterone to 5-dehydrotestosterone. It also possesses bacteriostatic activity to both aerobic and anaerobic bacteria including Propionibacterium acnes**
- ✚ **applied twice daily**
- ✚ **Side Effects**
 - **erythema and irritation**
 - **decrease in pigmentation**

Salicylic Acid 0.5 - 2%

-  **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**

Topical Therapy) (Anti Inflammatory Agents)

 **Benzoyl Peroxide 2.5 - 10%**

**exhibits bactericidal effects against
Cutibacterium acnes**

 **apply once to twice daily**

 **always apply test dose**

 **avoid use at night**

 **dryness of skin**

Topical Therapy (Anti Inflammatory Agents)

- + Clindamycin.**
- + 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**

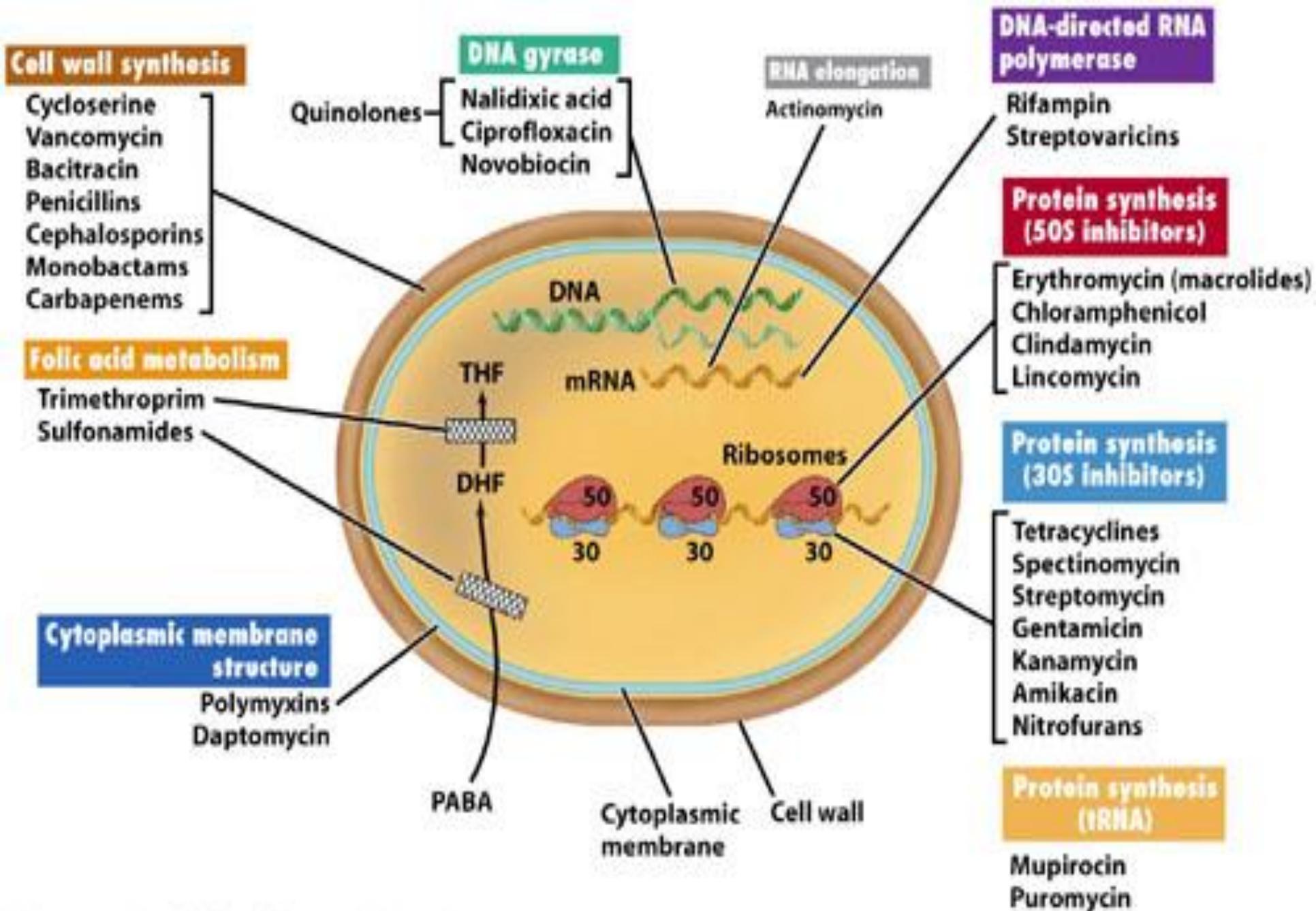


Figure 20-14 Brock Biology of Microorganisms 11/e
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Clindamycin

- **%10 absorbed, so, possibility of *Pseudomembranous colitis***
- The hydroalcoholic vehicle and foam formulation (Evoclin)may cause drying and irritation of the skin, with complaints of burning and stinging.
- The water-based gel and lotion formulations..... well tolerated and less likely to cause irritation. *Allergic contact dermatitis is uncommon* .
- Clindamycin is also available in fixed-combination topical gels with benzoyl peroxide (Acanya, BenzaClin, Duac), and with tretinoin (Ziana.)

Erythromycin

- In topical preparations, erythromycin base rather than a salt is used to facilitate penetration
- One of the possible complications of topical therapy is the development of antibiotic-resistant strains of organisms, including staphylococci
- Adverse local reactions to erythromycin solution may include a burning sensation at the time of application and drying and irritation of the skin
- Clindamycin is also available in fixed-combination topical gels with benzoyl peroxide (Acanya, BenzaClin, Duac), and with tretinoin (Ziana.)

Metronidazole

- Effective in the treatment of rosacea .
- Rosacea: common skin condition that causes blushing or flushing and visible blood vessels in your face. It may also produce small, pus-filled bumps. These signs and symptoms may flare up for weeks to months and then go away for a while



Metronidazole

- The mechanism of action is unknown
 - ✚ but it may relate to the inhibitory effects of metronidazole on *Demodex brevis*; This drug may act as an anti-inflammatory agent by direct effect on neutrophil cellular function
 - ✚ Adverse local effects include dryness, burning, and stinging .
 - ✚ Caution should be exercised when applying metronidazole near the eyes to avoid excessive tearing.

Systemic therapy

Indications:

- **Moderate inflammatory acne non-responsive to topical therapy**
- **nodulocystic acne**

Systemic therapy

-  **Oral Antibiotics**
-  **Isotretinoin**
-  **Hormonal Therapy**

Oral Antibiotics (used for 3-6 months)

-  **Tetracycline 500mg X BD**
-  **Doxycycline 100mg X BD**
-  **Minocycline 100mg X OD**
-  **Eythromycin 500mg X BD**
-  **combined with topical therapy**

Isotretinoin (Accutane) indicated in

-  **severe nodulocystic acne**
-  **non responsive acne**
-  **severe psychological distress**

Isotretinoin (RoAccutane) side effects

-  **teratogenic**
-  **mucosal dryness**
-  **photosensitivity**
-  **arthralgias**
-  **alteration of liver enzymes**
-  **hypertriglyceridemia and hypercholesterolemia**

-  **Tumerogenic in animals**

Isotretinoin (RoAccutane)

- ✚ **Retinoic Acid(Tretinoin):** is the acid form of Vitamin A. Stabilizes lysosomes, increases RNA polymerase activity, increases PGE₂, 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.

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.
- **Calcipotiene:**
 - Synthetic vitamin D₃ derivative

New Drugs for Psoriasis

Apremilast(Otezla)

- psoriasis and psoriatic arthritis .
- It may also be useful for other immune system-related inflammatory diseases .
- The drug acts as a selective inhibitor of the enzyme phosphodiesterase 4 (PDE4) and inhibits spontaneous production of TNF-alpha from human rheumatoid synovial cells.

Apremilast

Side Effects

– diarrhea

–nausea.

–stomach pain.

–vomiting.

–headache.

–sore throat, cough, and fever.

–sneezing, runny nose, and nasal congestion.
e-to-severe psoriasis demonstrating superior efficacy to apremilast

New Drugs for Psoriasis

Deucravacitinib (Sotyktu)

- A new oral treatment option for adults with plaque psoriasis.
- moderate-to-severe plaque psoriasis
- It is a once-daily oral medication with its clinical trials in moderate-to-severe psoriasis demonstrating superior efficacy to apremilast
- MOA: Allosteric inhibitor of TYK2
- Side effects:runny nose, congestion, or sore throat, sore on mouth, lips, gums, tongue or roof of mouth, acne.

New Drugs for Psoriasis
Roflumilast (Zorvye) cream

Selective, long-acting inhibitor of the enzyme phosphodiesterase-4 (PDE-4). It has anti-inflammatory effects.

- **chronic plaque psoriasis**
- an effective topical therapy for use on all psoriasis-affected areas including body, face, and intertriginous areas



New Drugs for Psoriasis

Tapinarof (Vtama)

Tapinarof (Vtama) is a topical (on the skin) medication used to treat plaque psoriasis in adults.

- MOA: immune modulation, skin-barrier normalization, and antioxidant activity.
- It's convenient to use because it's only applied once daily

Drugs for Psoriasis

- **Biologic Agents:**

- **Etanercept:**

- Dimeric fusion protein of TNF receptor linked to the Fc portion of human IgG₁
- approved for the treatment of psoriasis, psoriatic arthritis, and ankylosing spondylitis in adults

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.**