



MSS

PHARMACOLOGY

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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**

These are proteins synthesis inhibitor drugs, and they can be used topically to treat mild to moderate acne and they have anti bacterial effect as well

Combination therapy

(most of the time these drugs used in combination with other substances) ex of these combinations:

 **5% Benzoyl Peroxide and 3% Erythromycin**

 **5% Benzoyl Peroxide and 1% Clindamycin**

 **Topical antibiotics and Azelaic acid or Tretinoin**

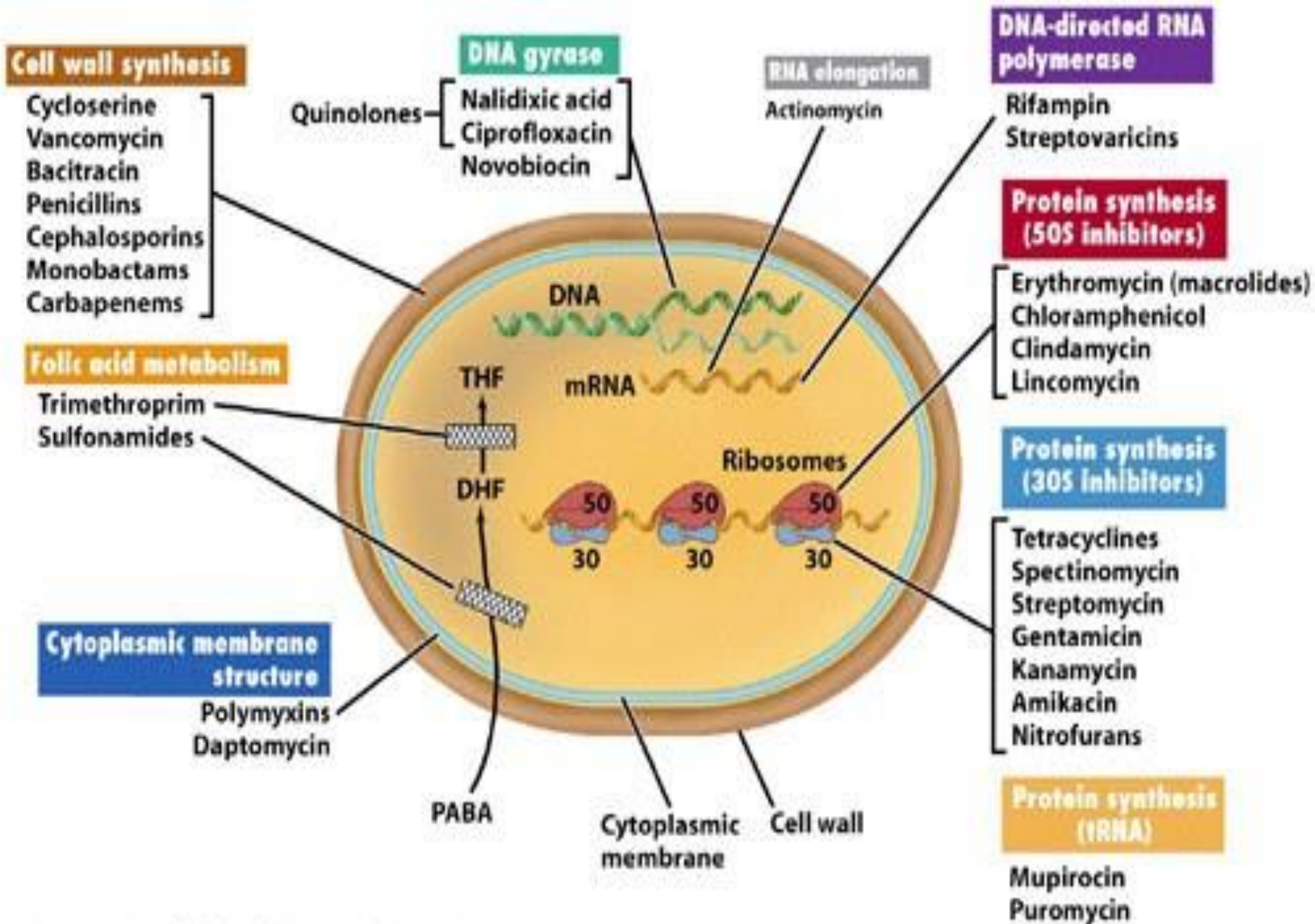


Figure 20-14 Brock Biology of Microorganisms 11/e
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Clindamycin

The topical side effects associated with these agents :

- **10% absorbed, so, possibility of *Pseudomembranous colitis*** (Caused by *Clostridium Difficile* ,and treated by Vancomycin or metronidazol)
- The hydroalcoholic vehicle and foam formulation (Evoclin)may cause drying and irritation of the skin, with complaints of burning and stinging.

Any drug contains alcohol can make drying of the area with *cracks or pustules*

- 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).

Side note from the doctor:

- **We never memorize the commercial name of drugs we only memorize the scientific name, even in the future you would prescribe the scientific name and give the patients the chance to choose between different companies which have different prices, unless there is a clinical indication for a specific form we must write the commercial name of the drug.**

Erythromycin

(To remind you it is a protein synthesis inhibitor working on 50S subunit of the ribosome).

- 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 (Flagyl)

We use it for parasitosis for ex: ameba

- 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

Rosacea when patient has a dilation in blood vessels in the skin that lead to redness and erythema, and it may cause a small pus-filled bumps in this case it is a kind of acne can coupled with rosacea



Metronidazole

- The mechanism of action is unknown

Demodex folliculorum is a small microorganism (parasite) that have been involved with rosacea, that can make inflammatory response

- 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

Systemic therapy means when we give a pill, tablet or capsule

Indications:

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

Remember nodulocystic acne :big acne filled with pus and disburse all over the body

Systemic therapy

Why don't we prescribe these drugs firstly ?because they have multiple side effects

 **Oral Antibiotics**

 **Isotretinoin**

 **Hormonal Therapy**

Doses are not for memorizing

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**

BD :twice daily

OD: once daily

Isotretinoin (Accutane) indicated in

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

Isotretinoin (RoAccutane) side effects



teratogenic

We don't give it during pregnancy, and even after stopping the medication the female patient must wait for a month or more (because it has a long half life) if she decides to get pregnant



mucosal dryness



photosensitivity



arthralgias (pain in muscles and joints)



alteration of liver enzymes



hypertriglyceridemia and hypercholesterolemia

Before we start treatment and every month while taking this drug the patient must perform many tests like: liver enzymes tests, and we look to lipid profile (triglyceride, cholesterol), if the patient has changing in these levels, we either lower the dose or stop drug for that patient for a period of time to make sure that everything goes back to normal.



Teratogenic in animals

-This drug can cause a certain type of cancer in animals, but nothing has been established yet in human.

-Some studies say that this drug causes some psychological problems such as depression

Isotretinoin (RoAccutane)

Its mechanism at the molecular or cellular level :

- ✚ 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.

All of these effects will increase the turn over or regeneration of the cells.

Physiologically:

- ✚ Decreases cohesion between epidermal cells and increases epidermal cell turnover. This will result in expulsion of open comedones(**black heads**)and the transformation of closed comedones into open ones.
the cells will expose more to shedding that is why we called this drug desquamative agent.
- ✚ Also, promotes dermal collagen synthesis, new blood vessel formation, and thickening of the epidermis, which helps diminish fine lines and wrinkles.

Isotretinoin (RoAccutane)

- this medication is taken from 6-9 months up to one year and the dose depend on the weight of the patient ,because the drug accumulate in the body ,so you have to have constant accumulation in the body.
- It can cause:1- dryness all over the body and that lead to nose bleeding ,so the doctor must prescribe moisturizer in the side of isotretinoin.2- photosensitivity reactions ,so patient must keep applying sunblock .3- dryness on the eye (recommend: using eye drop) .
- Moreover, the patient must drink a large amount of water.

Drugs for Psoriasis

Psoriasis : inflammatory condition .

- **Acitretin:** (Vitamin A derivative)
 - 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:** Tazarotene is a retinoic acid derivative ,and it can use to treat acne as well.
 - 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. **(another inflammatory condition)**
- 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.

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
- it Can cause upper respiratory symptoms that are similar to respiratory infection.**

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 (tyrosine kinase 2)
- 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

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. (immune suppressor),because the psoriasis is an immune response .

-It's convenient to use because it's only applied once daily

Drugs for Psoriasis

- **Biologic Agents:** (monoclonal antibodies)

- **Alefacept:**

- Immunosuppressive dimer fusion protein of CD2 linked to the Fc portion of human IgG₁.

- **Efalizumab:**

- Recombinant humanized IgG₁ monoclonal antibody.
- Withdrawn :progressive multifocal leukoencephalopathy (PML),
- Can cause thrombocytopenia.

- **Etanercept:** (Given IV)

- Dimeric fusion protein of TNF receptor linked to the Fc portion of human IgG₁.

Side note for the previous slide:

- **The part of the antibodies should be recombined with a humanize portion to reduce allergic reaction against foreign substances**

Anti-inflammatory Agents

- **Topical Corticosteroids:**

- Hydrocortisone.

- Prednisolone and Methylprednisolone.

- Dexamethasone and Betamethasone.

- Triamcinolone.

- Fluocinonide.

-The main stream therapy for psoriasis is corticosteroids

-They have different mechanisms of action, one of them that you have learned before ,when they inhibit the phospholipase A2 that produce arachidonic acid(which is central inflammatory mediator) and that lead to prevent a lot of inflammatory reactions.

The numbers are not for memorizing

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.

All of these are concentrations that depend on the area of the skin according to histological and anatomical variations on the skin layers (so that the penetration of the drugs differ from one area to another)

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.

For example :Triamcinolone is given as intralesional injection to treat scars by thinning the scare tissue .

Anti-inflammatory Agents

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

- **Topical Corticosteroids:**

- **Adverse Effects:**

- Suppression of pituitary adrenal axis.

- Systemic effects.

- Skin atrophy.

- Erythema.

- Pustules.

- Acne.

- Infections. **Because these drugs reduce inflammatory response in our body.**

- Hypopigmentation.

- Allergic contact dermatitis.

-The most important side effects are systemic side effects.

-As we know that the corticosteroids produce in our body by adrenal gland (endogenous source),so if the patient took exogenous source of corticosteroids ,the body stops the production of this hormone, so if the patient is taking systemic corticosteroids for the periods that is longer than 2 weeks or used for a large area of the skin we shouldn't stop treatment abruptly , we have to taper down the dose until we start produce corticosteroids again in our body.

Agents affecting Pigmentation

These drugs are used for depigmentation some dark area in the skin .

- Hydroquinone.
- Monobenzone. (It kills the cells that produce melanin in our body .)
- 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

There are certain conditions where we want to increase pigmentation like :albinism ,vitiligo.

So we need some drugs such as:

- **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.

Patients must reduce their exposure to the sun and put sun creams ,because these drugs are photoactivated .

Trichogenic and Antitrichogenic Agents

Trichogenic: the drugs that increase hair growth .

Minoxidil (Rogaine):

It works by opening K⁺ channels leading to hyperpolarization of the cell and that lead to closing of Ca²⁺ channels, which causing relaxation of vascular smooth muscles ,causing dilation of blood vessels leading to lowering the blood pressure.

- _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.**

This drug can enhance the growth of hair.

Trichogenic and Antitrichogenic Agents

- **Minoxidil.**
- **Finasteride (Propecia):**

_It can enhance the growth of hair .

- 5 α -reductase inhibitor which blocks the conversion of testosterone to dihydrotestosterone.
- Oral tablets.

It can cause side effects related to sexual functions :

- Can cause decreased libido, ejaculation disorders, and erectile dysfunction.

Trichogenic and Antitrichogenic Agents

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

It causes antitrichogenic effect

- Is an irreversible inhibitor of ornithine decarboxylase, therefore, inhibits polyamine synthesis. Polyamines are important in cell division and hair growth.

Ornithine decarboxylase :an enzyme that metabolizes ornithine into polyamine .

- Effective in reducing facial hair growth in 30% of women when used for 6 months.