Topical Antimicrobial Drugs
Figure 34.2
Cross section of the skin.
Skin

• The largest organ system of the body.
• It has many essential functions including:
  ✓ Serving as a protective barrier.
  ✓ Helping to regulate temperature.
  ✓ Offering defense against infections and toxic chemicals.
  ✓ Serving as a source of vitamin D.
  ✓ Providing sensation to touch, temperature, sexual pleasure, and pain.

❖ Skin disorders, such as acne and dermatitis, are among the top reasons that patients seek medical attention.

❖ Pharmacological approaches to correct skin abnormalities including infections, can be administered topically or systemically, depending on the nature and extent of the disorder.
Acne vulgaris

- Acne vulgaris (common acne) is a common skin disorder that is characterized by pimples, comedones, pustules, and sometimes nodules and scarring.
- Comedones are clogged hair follicles (pores) in the skin, which can be open (blackhead) or closed (whitehead).
- Acne occurs due to alterations in pilosebaceous units—skin structures that contain a hair follicle and a sebaceous (oil) gland.
- Androgens stimulate sebaceous glands, thereby producing sebum that leads to follicular keratinization and obstruction.
- Propionibacterium acnes, part of the normal skin flora, can enter the clogged pore and multiply, causing redness and inflammation and leading to papillary, pustular, and cystic acne.
- Treatments for acne help to reduce sebum production or control P. acnes.
- Use of oral contraceptives may help decrease circulating levels of free androgen and reduce symptoms of acne.
A. Retinoids

- Retinoids are derivatives of vitamin A that are highly effective in the treatment of acne, as well as other skin conditions such as psoriasis and photoaging.

- **Tretinoin** [TRET-in-oin] and **isotretinoin** [eye-so-TRET-i-noyn] are **first-generation retinoids** that are used for the management of **acne**.

- **Third-generation retinoids** include **adapalene** [a-DAP-a-leen] and **tazarotene**

- *Third generation* agents are less irritating and more effective than first generation retinoids and are considered **first-line therapy** for comedonal and inflammatory acne.

- These agents are applied **topically** with the exception of **isotretinoin** (Roaccutane®), which is an **oral drug**.

- *Due to* the adverse effect profile, use of **isotretinoin should be reserved for** severe cystic acne.
Mechanism of Action:

- Retinoids influence a wide variety of biological activities, including cellular proliferation and differentiation, immune function, inflammation, and sebum production.

- Third-generation agents:
  - Do not influence sebum production. Unlike the first-generation agents.
  - They are comedolytic and anti-inflammatory.

- The molecular actions of retinoids are mediated through nucleic retinoic acid receptors. Once bound to the receptors, retinoids function as transcription factors that enhance initiation of transcription.
Adverse effects

- Irritation, dryness, and skin peeling are all complications with the use of retinoids.
- **Photosensitivity** is also an adverse effect, and patients should be cautioned to wear sunscreen.
- Other adverse effects include dry mucous membranes and dry eyes.
- Suicide or suicide attempts have been associated with the use of oral *isotretinoin*.
- There is a very high risk of birth defects if pregnancy occurs while taking *isotretinoin*.
- This drug as well as other retinoids are contraindicated in pregnancy.
B. Benzoyl peroxide

- **Benzoyl peroxide** [BEN-zoyl per-OX-ide] *is considered the first-line* agent for mild to moderate acne with no inflammation.
- The mechanism of action includes **antiseptic effects** against *P. acnes* as well as opening of the pores.
- **Benzoyl peroxide** *is a topical agent that is available* in many over-the-counter acne treatment products, as well as some prescription products.
- **Dry skin, peeling, and irritation** are local adverse effects.
C. Salicylic acid

- Topical *salicylic [sal-i-SIL-ik] acid*, a $\beta$-hydroxy acid, *penetrates the* pilosebaceous unit and works as an exfoliant to clear comedones.
- Its comedolytic effects are not as pronounced as those of the retinoids.
- The drug has mild anti-inflammatory activity and is keratolytic at higher concentrations.
- *Salicylic acid is used as a treatment for mild acne* and is available in many over-the-counter facial washes and medicated treatment pads.
- Mild skin peeling, dryness, and local irritation are adverse effects.
D. Azelaic acid

- Azelaic [aze-eh-LAY-ik] acid, a dicarboxylic acid, has antibacterial activity against *P. acnes* as well as anti-inflammatory actions.
- Azelaic acid normalizes keratinization and is anticomедogenic.
- It is available as a topical preparation for the treatment of mild to moderate inflammatory acne.
- It is generally well tolerated, with mild skin irritation as the most common adverse effect.
E. Antibiotics

- *P. acnes* is a gram-positive rod that is associated with inflammatory lesions in acne.
- For moderate to severe acne with inflammatory lesions, use of topical or oral antibiotics is useful for inhibition of *P. acnes*.
- Topical formulations of *erythromycin* and *clindamycin* (preferred) are available.
- These agents may be combined with *benzoyl peroxide or the retinoids* for better effectiveness.
Dapsone

- a synthetic sulfone is available as a topical gel that treats acne.
- Its mechanism of action in the treatment of acne is unknown.

Metronidazole as a topical agent is useful in adult acne, also known as rosacea.

- Oral antibiotics commonly used for the management of moderate to severe acne include minocycline, doxycycline, and erythromycin.
- Erythromycin is used infrequently due to gastrointestinal adverse effects.
Topical Antibacterial Agents

- Organisms such as *staphylococci* and *streptococci* can cause folliculitis, abscesses, fasciitis, cellulitis, impetigo, and many *pus-forming infections*.

- Several gram-positive and gram-negative bacteria cause infections that are not limited to the skin and may cause serious diseases, since they can spread and become systemic infections.

  ✓ **A. Gram-positive infections**
    - *Bacitracin* [bas-i-TRAY-sin] is a peptide antibiotic active against many gram-positive organisms.
      - It is used mainly in topical formulations.
      - If used systemically, it is toxic.
      - *Bacitracin is mostly used for the prevention of skin infections after burns or minor scrapes.*
      - It is frequently found in *combination* products with *neomycin* and/or *polymyxin*.
- **Mupirocin** [mue-PIR-oh-sin] is a protein synthesis inhibitor that is useful in treating impetigo (a contagious skin infection caused by streptococci or staphylococci and other serious gram positive skin infections, including infections caused by *methicillin-resistant* Staphylococcus aureus.

- **Retapamulin** [RE-te-PAM-ue-lin]
  - Is a newer protein synthesis inhibitor that treats impetigo.
  - Adverse effects are minimal with these agents and usually consist of mild local skin reactions
B. Gram-negative infections

- **Polymyxin** [paw-lee-MIX-in] is a cyclic hydrophobic peptide that disrupts the bacterial cell membrane of gram-negative organisms.

- It is commonly combined with **neomycin and bacitracin** ("triple antibiotic") in topical products used for the prevention of skin infections after minor skin trauma.

- **Neomycin** [nee-oh-MY-sin] in combination with other agents.

- **Gentamicin** can be used to treat skin infections caused by gram-negative organisms such as Pseudomonas, E. coli, and Klebsiella sp.

- Topical use of these agents rarely causes systemic side effects.

- Rare adverse reactions such as allergic dermatitis and other sensitivities occur with **neomycin**.
AGENTS USED IN ECTOPARASITIC INFECTIONS

• **Ectoparasites** are parasites that live on the skin of animals from which they derive nutrition.

• **Pediculosis** (infestation with lice) and **scabies** (caused by *Sarcoptes scabiei*, human mite; are common ectoparasitic infections.

• Lice infestations may be caused by *Pediculus capitis* (head louse) *Pediculus corporis* (body louse), or *Pthirus pubis* (pubic or crab louse).
Treatments for ectoparasitic infections.

- **Lindane** [LIN-dane] is a cyclohexane derivative that is available as a cream or shampoo.

- *Lindane* is toxic when absorbed by the parasite and is an effective pediculicide (kills lice) and scabicide.

- **Permethrin** [per-METH-rin] is a synthetic pyrethroid that is neurotoxic to lice (1% nonprescription) and is effective in 5% concentration by prescription to treat scabies.

  - *Permethrin is preferred over lindane for the treatment of lice and scabies, since lindane can cause neurotoxicity.*

- **Oral ivermectin** is an alternative treatment for lice and scabies.

- **Synergized pyrethrins** (pyrethrins [pye-REE-thrins] with piperonyl butoxide [pye-PER-oh-nil bue-TOX-ide]) is a nonprescription product approved to treat head and pubic lice.

- **Pyrethrins** are pesticides and piperonyl butoxide prevents the lice from metabolizing the pyrethrins, thereby enhancing their effect.

- Due to a low risk of toxicity, this agent is considered a first-line treatment for pediculosis.

- **Crotamiton** [crow-TAmi-ton] is a scabicide and has antipruritic functions.

  - Its mechanism of action is unknown.
ECTOPARASITICIDES

Crotamiton EURAX
Lindane
Permethrin ELIMITE, NIX
Pyrethrins RID