

# DERMATOLOGICAL PHARMACOLOGY

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### BASES AND VEHICLES

#### OBJECTIVES

Following completion of this material the student should:

1. understand the principles of the interactions of drugs with the skin.
2. understand the various bases and vehicles used in dermatological preparations.

#### I. ABSORPTION

##### A. FACTORS

1. Area of skin
1. Solubility of drug in vehicle

1. Lipophilicity of drug

1. Condition of skin

## B. DRUG DELIVERY SYSTEMS

1. Systemic absorption

- a. transdermal systems

1. Topical

- a. acute lesions

- b. subacute lesions

- c. chronic lesions

## II. VEHICLES

### A. WET PREPARATIONS

1. baths, soaks, wet dressings

1. inherent cleansing and antipruritic

1. or, medicated for additional antipruritic, astringent, antimicrobial activity

### B. POWDERS

1. zinc oxide, talc (magnesium silicate), titanium dioxide

- a. reduce friction and absorb moisture

- b. used in intertriginous regions or inert carriers for antiparasitic and fungistatic agents.

### C. SHAKE LOTION

1. Suspensions of fine powders

1. Calamine lotion - originally zinc carbonate are colored by iron salts as impurities

1. now - zinc oxide with ferric oxide added for color

#### D. EMULSIONS

1. less drying than lotions

#### E. CREAMS OR HYDROPHILIC OINTMENTS

1. intermediate between drying preparation (wet) and ointments
1. high percentage water
1. polyethylene glycols
  - a. consistency of oil, cream or wax depending on molecular weight
  - b. water soluble and dissolve water soluble drugs

#### F. PASTES

1. suspension of powder in ointment

#### G. OINTMENTS

1. grease or oil as vehicle
1. provide protection of skin
1. penetrate chronic, thickened lesions well
1. should not be used in hairy areas --> folliculitis

### III. ACTIONS OF DRUGS APPLIED TO SKIN

#### A. ANTIPRURITIC

1. protects against stimulation of scratching, friction, changes in temperature
1. phenols - reduce itching by action on sensory reception

#### B. ASTRINGENT

1. mild protein precipitants

### C. KERATOSPLASTIC

1. salicylic acid (1-2%)
1. coal tar
1. reducing agents-sulphur, chrysarobin and pyrogalllic acid in low concentrations

### D. KERATOLYTIC

1. damage cornified layer, then sloughed off
1. salicylic acid (5-20%)
1. resorcin (resorcinol) (2-30%)
1. chrysarobin (0.1-10%)
1. anthralin (0.1-5%)
1. see lecture on Psoriasis for more

## PHOTOPHARMACOLOGY

### OBJECTIVES

After studying the information in this section the student should:

1. understand the agents used in prevention and treatment of sunburn.
2. understand the possibility of photoallergic and phototoxic reaction to drugs.
3. understand the treatment of vitiligo.

### DRUGS

#### SUNBURN

titanium dioxide

zinc oxide

p-amino-benzoic acid (PABA)

benzophenones

anthranilates, cinnamates, salicylates

#### IV. SUNBURN

##### A. PATHOLOGY

- 1 Ultraviolet spectrum 200-400 nm.
  - a. 320-400 nm - UVA
    - i. photochemotherapy
    - ii. photosensitivity
  - b. 290-320 nm - UVB
    - i. sunburn and tanning
  - c. 200-290 nm - UVC
    - i. germicidal region
- 2 Other factors
  - a. wind
  - b. humidity
- 3 Vascular changes-biphasic
  - a. Immediate, faint, transient reddening of skin - fades within 30 min.of exposure
  - b. delayed erythema, 2-6 hours, peaks 10-24 hrs
- 4 Other effects of exposure to solar radiation

##### B. PREVENTION-SUNSCREENS

- 1 Opaque agents
  - a. Titanium dioxide

b. zinc oxide

2 Agents which absorb u.v. light

a. p-amino-benzoic acid (PABA) and esters, pentyl p-dimethylaminobenzoate (padimate A) and ethyl-hexyl p-dimethylaminobenzoate (padimate O) - UV absorption -290-320 (UVB)

b. benzophenones - UV absorption - 250-360 (UVB + UVA)

c. cinnamates - UV absorption - 290-320 (UVB)

d. salicylates - UV absorption - 290-320 (UVB)

e. anthranilates - UV absorption - UVA

3 Factors influencing efficacy

a. substantivity - creams > alcohols, esters > PABA

b. sun protection factor (SPF)

c. skin sensitivity

i. Type I - Always burns, never tans SPF 12-15

ii. Type II - Usually burns, sometimes tans SPF 4-12

iii. Type III - Occasionally burns, gradually tans SPF 2-4

iv. Type IV - Minimally burns, readily tans SPF 0

v. Type V - Rarely burns, tans profusely

vi. Type VI - Never burns, deeply pigmented

v. PHOTSENSITIVITY: Reaction due to chemical reactivity of systemically or topically administered drug, perfume or cosmetic

A. EXPOSURE TO SUNLIGHT

1 brief

2 warm or cold weather

- 3 may occur long after use of agent

#### B. PHOTOTOXICITY

- 1 "sunburn" reaction
- 2 erythema, edema, blisters, hyperpigmentation, desquamation most common reaction

#### C. PHOTOALLERGY

- 1 resembles contact allergies
- 2 immediate wheal and flare reactions
- 3 delayed papular, erythematous or eczematous rashes

#### D. TREATMENT

- 1 as ordinary sunburn
- 2 cold water compresses, emollients, cool baths
- 3 topical steroids
- 4 Systemic steroids in severe reaction
- 5 prevention - sunscreens

## DRUGS WHICH MAY CAUSE PHOTSENSITIVITY REACTION

\*Reactions occur frequently

### ANTICANCER DRUGS

\*Dacarbazine (DTIC-Dome)  
Fluorouracil (Fluoroplex; and others)  
Methotrexate (Mexate; and others)  
Procarbazine (Matulane)  
Vinblastine (Velban)

### TRICYCLIC ANTIDEPRESSANTS

### ANTI-HISTAMINES

Cyproheptadine (Periactin)  
Diphenhydramine (Benadryl; and others)

### ANTIMICROBIALS

\*Demeclocycline (Declomycin; and others)  
Griseofulvin (Fulvicin-U/F; and others)  
\*Nalidixic acid (NegGram)  
Tetracyclines  
Sulfanamides

### ANTIPARASITIC DRUGS

\*Bithionol (Bitin)  
Pyrvinium pamoate (Povan)  
Quinine (many manufacturers)

### ANTIPSYCHOTIC DRUGS

### DIURETICS

Acetazolamide (Diamox)  
Amiloride (Midamor)  
Furosemide (Lasix)  
Metolazone (Diulo; Zaroxolyn)  
Quinethazone (Hydromox)  
Thiazides

### HYPOGLYCEMICS

Acetohexamide (Dymelor)  
Chlorpropamide (Diabinese; Insulase)  
Glipizide (Glucotrol)  
Glyburide (DiaBeta; Micronase)  
Tolazamide (Tolinase)  
Tolbutamide (Orinase; and others)

### NONSTEROIDAL ANTI-INFLAMMATORY

Ketoprofen (Orudis)  
Naproxen (Naprosyn)  
Phenylbutazone (Butazolidin; others)  
Piroxicam (Feldene)  
Sulindac (Clinoril)

### SUNSCREENS

6-acetoxy-2,4,-dimethyl-m-dioxane (preservative in sunscreens)  
Benzophenones (Aramis; Clinique; and others)  
Cinnamates (Aramis; Estee Lauder; and others)  
Oxybenzone (Eclipse; PreSun; and others)  
PABA esters (Eclipse; Block Out; Sea & Ski; and others)  
Para-aminobenzoic acid (PABA - Pabagel; Pabanol; PreSun; and others)

### OTHERS

\*Amiodarone (Cordarone)  
\*Bergamot oil, oils of citron, lavender, lime, sandalwood, cedar (used in many perfumes and cosmetics; also topical exposure to citrus rind oils)  
Benzocaine  
Captopril (Capoten)  
Carbamazepine (Tegretol)  
Contraceptives, oral  
Disopyramide (Norpace)  
Gold salts (Myochrysin; Solganol)  
Hexachlorophene (pHisoHex; and others)  
Isotretinoin (Accutane)  
6-methylcoumarin (used in perfumes, shaving lotions, and sunscreens)  
Musk ambrette (used in perfumes)  
Quinidine sulfate and gluconate

(adapted from Medical Letter 28, Issue 713, 1986)

## VI. VITILIGO

### A. CLINICAL MANIFESTATIONS

- 1 loss of melanin pigmentation
- 2 depigmentation first appears in areas of frequent injury - hands, knees, elbows
- 3 areas enlarge, merge - may go to total vitiligo
- 4 areas susceptible to injury by u.v. light

### B. TREATMENT

#### 1 Corticosteroids

- a. Repigmentation - mechanism unknown
- b. topical for isolated vitiligo
  - i. triamcinolone acetonide (0.1% cream)
  - ii. total repigmentation in 20-30%
  - iii. 4-6 months or longer
  - iv. fluorinated steroids should not be used on face due to atrophy and telangiectasia
- c. systemic
  - i. effective as topical
  - ii. long term therapy
  - iii. not recommended

#### 2 Psoralens

- a. 8-methoxypsoralen (methoxsalen) - OXSORALENR
- b. trimethylpsoralen (trioxsalen) - TRISORALENR
- c. activated by ultraviolet A - 320 - 400 nm
- d. cause melanocyte hypertrophy, proliferation

- e. increase melanosome transfer
  - f. melanocytes which survive in hair follicles, therefore no response in hairless areas or white hair
  - g. initial therapy followed by 2 hours of u.v. light
  - h. every other day treatment
  - i. increase dose or light exposure after every two treatments
  - j. 50-100 treatments over 6-12 months
  - k. methoxsalen - side effects - excessive burns, pruritus, edemabulae formation, nausea: long term - cataracts (ophthalmic exams, UVA absorbing glasses), premature aging, cancers
- 3 Depigmenting agents
- a. in extensive vitiligo
  - b. 20% monobenzone (BENOQUINR) - topical to pigmented skin
  - c. twice daily, hypopigmentation 3 to 4 months, depigmentation - 1year

## **TOPICAL ANTI-INFECTIVES AND CORTICOSTEROIDS**

### **OBJECTIVES**

After studying the material in this lecture the student should:

1. Understand the principles and rationale of the use of topical anti-infectives.
2. Know the effective antiseptics.
3. Understand the principles of the use of topical antibiotics.
4. Know the principles and agents used in the treatment of superficial fungal infections.
5. Understand the principles of topical corticosteroid use in dermatological disorders.

## DRUGS

### Antiseptics

Alcohols - ethanol, isopropanol  
Triclocarban - COAST , DIAL , ZEST , others  
Hydrogen Peroxide  
Chlorhexidine Gluconate - HIBICLENS , HIBISTAT  
Chlorine Compounds, Chlorophors  
Iodine, Iodophors - BETADINE , PHARMADINE , others  
Phenolic Compounds - PHISOHEX , LIFEBOUY , IRISH SPRING

### Topical Antibiotics

Bacitracin - generic, BACIGUENT , mixtures  
Neomycin - generic, MYCIGUENT , mixtures  
Polymyxin B - mixtures

### Antifungal Agents

Imidazoles  
clotrimazole - LOTRIMINR, GYNE-LOTRIMIN , MYCELEX , MYCELEX-G  
Miconazole - MICATIN , MONISTAT-DERM , MONISTAT 7 , MONISTAT 3  
Ketoconazole - NIZORAL  
Griseofulvin  
Tolnaftate - AFTATE , TINACTIN , ZEASORB-AF

## VII. TOPICAL ANTI-INFECTIVES

### A. PROPERTIES

- 1 Germicidal rather than germistatic activity.
- 2 High germicidal potency
- 3 Broad spectrum - at most sites do not have problems with superinfection
- 4 Rapid onset and sustained activity
- 5 Lipid solubility - favors germicidal activity
- 6 Dispersibility
- 7 Good therapeutic index

8 Germicidal kinetics important

9 Germicidal efficacy

## B. TOPICAL GERMICIDES VS. SYSTEMIC ANTIBIOTICS

1 In most cases systemic antibiotics are superior in treatment of wounds and infections.

2 Intolerance to systemic drugs

3 Burns and superficial fungal infections

## C. ANTISEPTICS

1 Principles of Use

a. applied topically to living tissue

b. destroy micro-organisms or inhibit their reproduction or metabolic activities

c. applied prophylactically by health care professionals

d. antimicrobial soap decreases skin bacteria for deodorant effect

e. skin cleansers and protectants for laity which contain antiseptics to

f. minimize potential for infection are of limited value - only adjuncts to removal of dirt and organic matter.

2 Drugs

a. Alcohols

i. ethanol, isopropanol

ii. bactericidal due to rapid coagulation of proteins

iii. 70% aqueous solution better than absolute - 70% kills 90% of cutaneous bacteria in 2 min.

iv. isopropyl alcohol slightly greater bactericidal

v. activity - full strength or 70% aqueous

vi. both are potent virucidal agents

- vii. not effective as fungicides or sporicides
- b. Triclocarban - COASTR, DIALR, ZESTR
  - i. used in deodorant soaps only
  - ii. antibacterial and antifungal actions
  - iii. limited to 1.5% concentration
- c. Hydrogen Peroxide
  - i. decomposes to oxygen and water in wounds and on mucous membranes - no effect on intact skin
  - ii. oxygen has little bactericidal effect but loosens masses of infected detritus in wounds
- d. Chlorhexidine Gluconate - HIBICLENS , HIBISTAT
  - i. broad spectrum of antimicrobial activity
  - ii. most effective against gram-positive and gram-negative bacteria
  - iii. rapid acting, considerable skin substantivity, low potential for contact sensitivity and poorly absorbed
- e. Chlorine compounds, chlorophors
  - i. sodium hypochlorite, oxychlorosene
  - ii. bactericidal, sporicidal, fungicidal, protozoacidal, virucidal
  - iii. antiseptic, disinfectant, sterilant
  - iv. 0.45 to 0.5% NaClO for surgical purposes
- f. Iodine, Iodophors - BETADINER, PHARMADINER, others
  - i. iodine is bactericidal, sporicidal, fungicidal, protozoacidal, cysticidal and virucidal
  - ii. valuable due to efficacy, economy and low toxicity
  - iii. iodine tincture - 2% elemental iodine, 2.4% sodium iodine in water and 44-50% alcohol

iv. povidone - iodine

( ) free iodine released in solution

g. Phenolic Compounds - PHISOHEX , LIFEBOUY , IRISH SPRING  
(with triclocarban)

i. hexachlorophene (PHISOHEX ) - bacteriostatic - most effective  
against Gram-positive, little activity against gram-negative or spores

ii. triclosan (deodorant soaps)

iii. irritant and cutaneous absorption - some toxicity

#### D. TOPICAL ANTIBIOTICS

##### 1 Principles

- a. Group A beta-hemolytic Streptococcus and Staphylococcus aureus most common organisms
- b. local cleansing with warm moist compress or soaks are useful; surgical incision and drainage or excision may be necessary
- c. poorly absorbed topical antibiotics (bacitracin, gramicidin, neomycin and polymixin B) especially useful in limited pyodermas.
- d. resistance by selecting out mutants
- e. cultures inappropriate, Gram stain helpful

##### 2 Bacitracin - generic, BACIGUENT , mixtures

- a. bactericidal against gram-positive
- b. inactive against gram-negative
- c. effective in primary pyodermas (superficial folliculitis, limited ecthyma, impetigo) and limited secondary pyodermas
- d. used with systemic antibiotics
- e. severe hypersensitivity reactions rare

- f. may be used in pregnancy or lactation
- 3 Neomycin - generic, MYCIGUENTR, mixtures
  - a. aminoglycoside
  - b. too toxic for parenteral use, poorly absorbed orally
  - c. especially effective against staphylococci
  - d. used with systemic antibiotics
  - e. hypersensitivity reactions, especially in individual with contact dermatitis or chronically damaged skin
- 4 Polymyxin B
  - a. not available alone - spectrum of action limited to gram-negative organisms including Pseudomonas
  - b. combined with other poorly absorbed antibiotic or corticosteroids
  - c. hypersensitivity most common adverse reaction although rare
- 5 Topical Antibiotics with Systemic Use
  - a. resistance after topical application
  - b. tetracycline, chlortetracycline, oxytetracyclin (with polymyxin B)
  - c. gentamicin - useful in Pseudomonas infections unresponsive to other topical antibiotics
  - d. erythromycin, tetracycline and clindamycin for acnes vulgaris

## E. ANTIFUNGALS

- 1 Principles
  - a. mycoses classified as superficial, deep or systemic
- 2 Dermatophytosis (tinea) infections most common - involve skin, hair and nails caused by Epidermophyton, Trichophyton, and Microsporum
- 3 resistant fungi or involvement of hair or nails requires prolonged oral griseofulvin or ketoconazole

- 4 mild to moderate tinea - miconazole (14-28 days) or tioconazole - tolnaftate, compound undecylenic acid
  - a. also salicylic acid effective due to keratolytic effect
  - b. haloprogin when OTC medications inadequate moderately severe infections
  - c. topical clotrimazole, econazole, miconazole, sulconazole or ciclopirox
  - d. infections of palms, soles, and fingernails may require oral griseofulvin
- 5 tinea versicolor
  - a. selenium sulfide suspension - 15-30 min. daily for 7 to 14 days
  - b. sodium thiosulfate 25% with salicylic acid 1% also effective
  - c. zinc pyrithone shampoo

#### F. Superficial Candidiasis

- 1 responds to topical preparations of polyene antibiotics (amphotericin B, nystatin)
- 2 imidazoles (clotrimazole, econazole, miconazole)

#### G. Imidazoles

- 1 clotrimazole - LOTRIMIN , GYNE-LOTRIMIN , MYCELEX , MYCELEX-G
- 2 miconazole - MICATIN , MONISTAT-DERM , MONISTAT 7 , MONISTAT 3
- 3 ketoconazole - NIZORAL
- 4 interferes with biosynthesis of ergosterol
  - a. clotrimazole
    - i. useful for tinea versicolor, cutaneous candidiasis and candidal infections of mucous membranes and mucocutaneous junctions
    - ii. two weeks to one month treatment

- iii. adverse reactions - erythema, stinging, blistering, peeling of skin, pruritis and uticaria
  - iv. troche - nausea, vomiting, abdominal cramping, diarrhea
  - v. not contraindicated in pregnancy for vulvovaginal infections
- b. miconazole
- i. effective topically in dermatophytic infections and tinea versicolor, superficial cutaneous and vaginal candidal infections
  - ii. side effects - irritation, burning or maceration
- c. ketoconazole
- i. adequate oral absorption
  - ii. oral reserved for superficial cutaneous infections non-responsive to topical drugs or oral griseofulvin

#### H. Griseofulvin

- 1 derived from Penicillium
- 2 fungicidal to actively growing organisms, inhibits fungal mitosis orally active for tinea infections except tinea versicolor, drug of choice for tinea barbae and tinea capitis
- 3 minor reactions - headache most common, dryness of mouth, G.I.disturbance - occasionally blurred vision, syncope, photosensitivity, rash, insomnia
- 4 serious reactions - leukopenia, granulocytopenia, hepatotoxicity

#### I. Tolnaftate - AFTATER, TINACTINR, ZEASORB-AFR

- 1 used topically in treatment of tinea infections including tinea versicolor
- 2 well tolerated, sensitization rare

#### J. Compound Undecylenic Acid

- 1 effective topically for tinea infections except tinea versicolor

- 2 most extensively used for tinea pedis (athlete's foot)

#### K. Polyene Antibiotics

- 1 amphotericin B - FUNGIZONER
  - a. topical application limited to treatment of cutaneous and some acute mucocutaneous candidal infections
  - b. not effective for tinea infections
  - c. local irritation reported
- 2 nystatin - MYCOSTATINR, NILSTATR, O-V STATINR
  - a. administered orally, vaginally or topically
  - b. not absorbed by GI tract
  - c. limited to infections of skin and mucous membranes caused by Candida
  - d. side effects infrequent, transitory - nausea, vomiting, diarrhea after oral administration

### VIII. TOPICAL CORTICOSTEROIDS

#### A. ACTIONS

- 1 vasoconstriction decreases extravasation of serum, inhibits swelling
- 2 inhibits release of cytotoxic chemical that cause pain and pruritus
- 3 suppression of mitotic activity diminishes epidermal hyperplasia, may lead to atrophy with excessive use
- 4 limit inflammation and immune response

#### B. FACTORS IN CHOOSING DRUGS

- 1 inherent potency - high, intermediate or low
  - a. more potent fluorinated steroids necessary for less permeable areas
  - b. less potent steroids for more permeable areas and in maintenance therapy

- c. hydrocortisone is steroid of choice in responsive conditions due to low expense and application to extensive areas for prolonged periods relatively safe
- 2 formulation and method of application affect degree of absorption - also character of lesion (acute, subacute, or chronic) - see lecture on Bases and Vehicles
- 3 age - young, especially infants, and elderly with atrophic skin may be more sensitive to steroids

### C. ADVERSE REACTIONS

- 1 Related to inherent potency, concentration of drug, volume applied, skin condition, duration of use, site and area of application, use of occlusive vehicles or wraps
- 2 Local effects
  - a. epidermal and dermal atrophy resulting in thinning of the skin, striae, telangiectasia, and senile-type purpura are most common in highly absorptive areas
  - b. less common - rosacea-like dermatoses, perioral dermatitis, acne, folliculitis and nonhealing leg ulcers - hypopigmentation
  - c. hypertrichosis with more potent steroids
  - d. rebound erythroderma or pustulation may occur on all body surfaces after more potent steroids are discontinued.
- 3 System toxicity
  - a. usually after high-potency corticosteroids applied to extensive areas under occlusive dressing for long periods