

**DERMATOLOGY THERAPEUTICS**  
**ACNE, PSORIASIS & DRUG INDUCED SKIN DISORDERS**  
**TH 5001 Therapeutics III - Fall 2003**  
**Tricia M. Berry, Pharm.D., BCPS**  
**December 3, 2003**

**Required Readings:**

1. Patel NM, Elias SS, Cheigh NH. Acne and psoriasis. In: Dipiro JT, et al. *Pharmacotherapy: A Pathophysiologic Approach*. 5<sup>th</sup> edition. Elsevier, New York. 2002. pp 1689-1704.
2. Elias SS, Patel NM, Cheigh NH. Drug-induced skin reactions. In: Dipiro JT, et al. *Pharmacotherapy: A Pathophysiologic Approach*. 5<sup>th</sup> edition. Elsevier, New York. 2002. pp 1705-1715.

**Supplemental Readings:**

Lebwohl M. Psoriasis. *Lancet* 2003;361:1197-204.

**Ability Outcomes:**

The successful student will be able to:

1. Assess a patient's acne, psoriasis or drug-induced skin disorders.
2. Evaluate the appropriateness of patient-specific drug therapy for acne or psoriasis, and modify therapy as necessary.
3. Select/recommend appropriate therapy for acne, psoriasis, and drug-induced skin disorders.
4. Monitor for expected therapeutic outcomes and potential adverse effects associated with selected drug therapy for acne, psoriasis, and drug-induced skin disorders.
5. Educate patients and health care professionals regarding drug therapy for acne, psoriasis, and drug-induced skin disorders.

**Content Questions:**

The student is responsible for knowing the information from the content questions listed below. To answer the following questions, refer to the required readings and/or information in the handout. Many of the questions are dispersed throughout the study guide.

**ACNE VULGARIS**

- Define the following acne lesions: closed comedone, open comedone, papule, pustule, nodule and cyst.
- Categorize acne lesions as either non-inflammatory or inflammatory.
- List the four pathogenic factors associated with acne vulgaris and explain their role in the pathogenesis of acne lesions.
- Identify drugs and other factors that may exacerbate or precipitate acne lesions.
- Based on their mechanism of action, identify the pathogenic factor(s) affected by each of the following therapies: benzoyl peroxide, tretinoin, topical antibiotics, azelaic acid, adapalene, oral antibiotics, and isotretinoin.
- List the common side effects/precautions associated with the following acne therapies: benzoyl peroxide, tretinoin, oral antibacterial agents, and isotretinoin.
- List the conditions that must be met prior to using isotretinoin (Accutane<sup>®</sup>) therapy in females with child-bearing potential.
- Compare and contrast the clinical characteristics of acne rosacea and acne vulgaris.

**PSORIASIS**

- Describe the clinical presentation of plaque psoriasis, pustular psoriasis, and psoriatic arthritis.
- Identify adverse effects associated with the use of topical corticosteroids, methotrexate, etretinate, and cyclosporine.

**DRUG INDUCED SKIN DISORDERS**

- Identify medications which produce photosensitivity reactions.
- Identify medications which are associated with erythema multiforme and Stevens-Johnson Syndrome.
- Describe the clinical presentation of hyperpigmentation reactions associated with oral contraceptives and amiodarone.
- List the clinical characteristics of erythema multiforme and Stevens-Johnson Syndrome.
- Describe the clinical presentation of toxic epidermal necrolysis.

## DERMATOLOGY: ACNE, PSORIASIS & DRUG-INDUCED SKIN DISORDERS

### Definitions

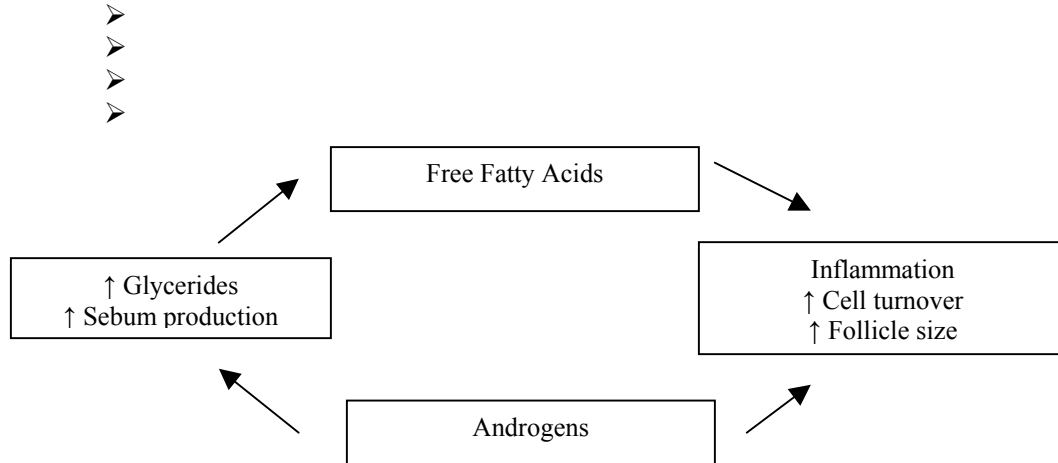
- ✧ **Acne conglobata** - Cystic acne; occurs after teenage years. Characterized by numerous double and triple large fused comedones, abscesses, cysts, and multiple inflammatory lesions. Marked scarring is common.
- ✧ **Acne vulgaris** - A common, self-limiting skin disease involving the pilosebaceous units of the skin. Earliest lesions appear on the face, but the chest, back, or upper arms may also be affected.
- ✧ **Bulla** - An elevated fluid-filled lesion greater than 1 cm. These large blisters may be tense or flaccid to palpation.
- ✧ **Closed comedone** – whitehead, non-inflammatory lesion
- ✧ **Cyst** – Similar to a nodule, but saclike, containing fluid or solid material
- ✧ **Fissure** - A linear break in the skin to the depth of the dermis.
- ✧ **Lichenification** - A raised flat-topped lesion, often with transverse ridges and leather like texture from long-term rubbing or scratching. Lichenification is a common sign in several forms of dermatitis.
- ✧ **Macule** - A flat lesion (in the plane of the skin) denoted by a change in normal skin color. Usually well circumscribed with distinct outline and no elevation or depression of skin.
- ✧ **Microcomedone** - The initial, clinically undetectable, acne lesion.
- ✧ **Nodule** – Inflammatory lesion > 5mm; may become suppurative or hemorrhagic, may involve > 1 follicle
- ✧ **Open comedone** – “blackhead”; non-inflammatory lesion
- ✧ **Papule** – Elevated, solid lesion; red, < 5mm diameter; inflammatory lesion
- ✧ **Plaque** - An elevated patch usually larger than 1 cm in diameter and with a flat top. Plaques may sometimes consist of many papules grouped together.
- ✧ **Propionibacterium acnes (P. acnes)** - Microaerophilic gram-positive diptheroid. Normal component of skin flora, but is higher in concentration in acne. Involved in immune-mediated inflammatory acne.
- ✧ **Plaque Psoriasis** - A chronic skin disorder characterized by sharply, demarcated, erythematous papules and plaques covered with silver white scales.
- ✧ **Psoriatic arthritis** - A distinct clinical entity in which both psoriatic lesions and inflammatory “arthritis” occurs.
- ✧ **Pustular psoriasis** - A type of psoriasis characterized by lesions with a mixture of brown and white non-infected pustules associated with erythema and scaling. It usually affects palms and soles symmetrically.
- ✧ **Pustule** – Similar to a papule, but has a visible core of purulent material; inflammatory
- ✧ **Scale** - Over accumulation of loose epidermal cells. Some may be white, yellow, or brown, shiny or dull, and dry or greasy.
- ✧ **Sebum** - Produced by the sebaceous glands. Consists of wax esters, glycerides, cholesterol, keratin and squalene. Converted to free fatty acids (resulting in inflammation) by P. acnes.
- ✧ **Vesicle** - An elevated lesion that is less than 1 cm in diameter, filled with clear, red, or yellow fluid, and well circumscribed. An example of a vesicle is a blister.
- ✧ **Wheal** - Similar to a plaque (elevated, round, or flat topped, red or pink) but edematous and pruritic. Urticaria (hives) is an example.

# ACNE VULGARIS

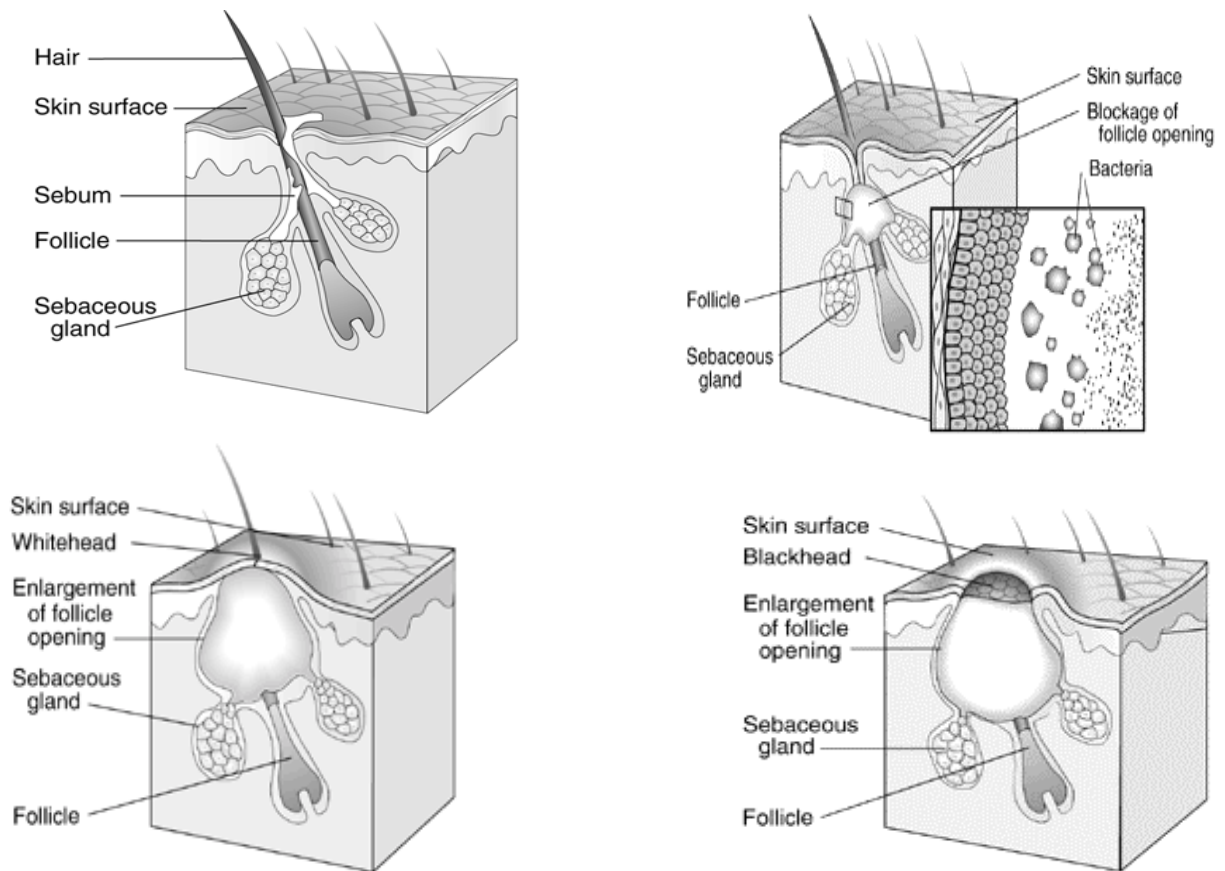
## I. Epidemiology

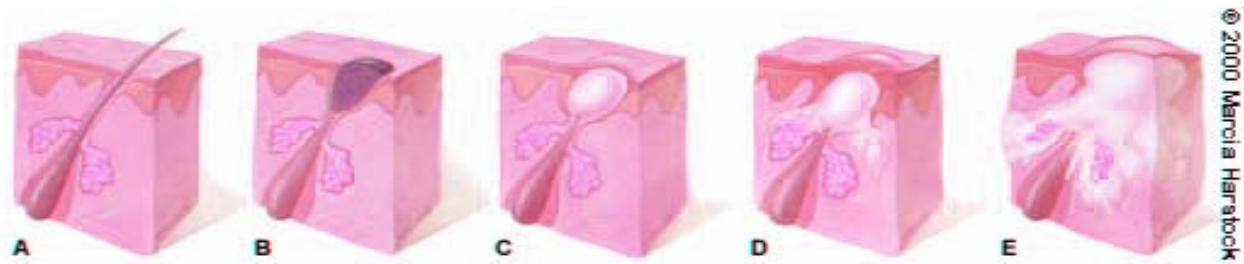
## II. Pathophysiology

### A. Pathogenic factors of acne vulgaris



### B. Pathogenesis of acne lesions





| Factors that can exacerbate or precipitate acne   |  |
|---|--|
| <b>Drugs</b><br>Corticosteroids<br>Oral contraceptives<br>Azathioprine<br>Haloperidol<br>Isoniazid<br>Lithium<br>Phenytoin<br>Thyroid hormone | <b>Other</b><br>Premenstrual<br>Humidity/prolonged sweating<br>Local irritation<br>Cosmetics (esp. oil-based)<br>Hair products<br>Occupational/environmental exposures<br>Manipulation of lesions<br>Scrubbing<br>Controversial - diet, stress |

**III. Classification of acne**

- ✓ No universally accepted method of assessing gradations of acne severity
- ✓ Non-inflammatory acne - comedonal acne
  - rarely severe, unless number, size, extent of such lesions are overwhelming
- ✓ Inflammatory acne - papulopustular, nodular, cystic

| Severity | Papules/Pustules     | Nodules       |
|----------|----------------------|---------------|
| Mild     | Few - several        | None          |
| Moderate | Several - many       | Few - several |
| Severe   | Numerous - extensive | Many          |

- ✓ Severe acne -
- ✓ Other factors involved in evaluating severity
  - location of lesions (limited to face vs. present on trunk)
  - psychosocial impact
  - failure to respond to therapy
  - scarring
  - presence of persistent purulent or serosanguinous drainage

### **In-class activity**

T.N., a white, 19 year old college student majoring in anthropology, presents to her physician complaining of “these darned zits”. Several of her friends take medications for acne and she also wants a “strong medicine” to make them go away. She began having acne at age 13 when her lesions appeared on her chin and forehead. Her acne has seemed to get progressively worse, especially in the summer, and she now has 6-8 lesions consistently. She works part-time on a local “dig site”, is on the College softball team (catcher), and enjoys playing the violin. She currently has several closed comedones distributed around the facial area, open comedones on her nose and forehead, 5 pustules across her forehead, and several papules covered with make-up on her cheeks and chin. Her back, chest and trunk are clear of any lesions.

*How would you assess TN’s acne?*

*What questions would you ask to complete the patient history for TN’s acne?*

#### **IV. Nonpharmacologic therapy**

#### **V. Drug therapy**

☞ There is NO CURE for acne, but treatment can reduce its severity

##### ***Goals of therapy***

- ✓ relieve discomfort
- ✓ improve skin appearance
- ✓ prevent pitting or scarring
- ✓ prevent psychological or social distress

| Product   | Mechanism/Efficacy   | Availability/Dosing   | Adverse Reactions  | Comments   |
|---|--|---|--|--|
| <b>Topical benzoyl peroxide</b><br>(generic)  | <i>MOA:</i> Comedolytic; antibacterial<br><br><i>Efficacy/use:</i><br>- Use in mild-mod acne (inflammatory or noninflammatory)<br>- Used in combo with other tx  | 2.5-10%<br>cream, gel, lotion, soaps<br><br>start at low concentration every other day; titrate to effect as tolerated  |  | - FDA is currently unable to state that it is generally recognized as safe; further studies are ongoing to assess the tumorigenic potential<br>- to minimize irritation apply to <u>dry</u> skin at least <u>30 min after</u> washing.   |
| <b>Topical antibiotics</b><br>Clindamycin<br>(generic)<br>Erythromycin<br>(generic)<br>Tetracycline<br>(Topicyclin <sup>®</sup> )<br>Sodium sulfacetamide<br>(Klaron <sup>®</sup> ) | <i>MOA:</i> antibacterial vs. <i>P. acnes</i><br><br><i>Efficacy/use:</i><br>- for mild-mod inflammatory acne<br>- clindamycin most effective<br>- Benzamycin <sup>®</sup> more effective than either ingredient alone; effective for mod-severe acne; DUAC more effective than either alone for inflammatory lesions, equally effective as BP for noninflammatory | Clinda: soln, lotion, gel<br>Emycin: 1.5%, 2% soln, powder, gel<br>TCN: 2.2% soln BID<br>Benzamycin <sup>®</sup> gel (QD-BID)<br>Klaron <sup>®</sup> 10% lotion (BID)<br>Benzaclin (BID)<br>DUAC (QD) | occasional stinging and burning;<br><u>TCN</u> : photo-oxidizes to produce visible yellow tinting;<br><u>Clinda</u> : diarrhea, pseudomembranous colitis | - do not affect existing lesions; reduces inflammatory lesions<br>- Benzamycin <sup>®</sup> must be refrigerated<br>- Klaron <sup>®</sup> - caution in pts w sulfa allergy<br>- other antibiotic-benzoyl peroxide products: BenzaClin <sup>®</sup> gel (clindamycin 1%, benzoyl peroxide 5%); DUAC <sup>®</sup> gel (clin 1%, benzoyl peroxide 5%)<br>- DUAC <sup>®</sup> : doesn't require reconstitution; refrigerate prior to dispensing. |
| <b>Topical tretinoin</b><br>(Retin-A <sup>®</sup> , Retin-A Micro <sup>®</sup> , Avita <sup>®</sup> )   | <i>MOA:</i> ↑ cellular turnover and ↓ cohesiveness of cells; extrusion of existing comedones and ↓ new comedones. (Comedolytic)<br><br><i>Efficacy/use:</i><br>- use in mild-mod comedonal acne<br>- substantial efficacy at 6 wks<br>- max improvement in 3-4 mo.   | 0.01 - 0.05%<br>gel, cream, liquid polymer, microsphere gel, solution<br><br>start with low conc cream 3x/wk and increase to QHS as tolerated (up to BID)   |  | - apparent worsening of acne may occur w/in first 3-6 weeks of tx followed by clinical clearing in 8-12 wks.<br>- to reduce irritation: 1) slowly titrate dose, 2) apply to <u>dry</u> skin about 30 min after washing<br>- benzoyl peroxide QAM and tretinoin at HS may ↑ efficacy and ↓ adv. effects<br>- generic now available  |

| Product   | Mechanism/Efficacy  | Availability/Dosing   | Adverse Reactions  | Comments   |
|---|---|---|--|--|
| <b>Topical azelaic acid</b><br>(Azelex <sup>®</sup> ,<br>Finevin <sup>®</sup> )                                     | <i>MOA:</i> antibacterial properties; normalizes keratinization (anticomedonal)<br><br><i>Efficacy/use:</i><br>- comparable response rates as other topical therapies in mild-mod inflammatory acne<br>- improvement in 4 weeks<br>- ↓ comedones and inflammatory lesions                       | 20% cream; 30 gm tube<br><br>apply BID (AM & HS)  | 1-5%: pruritis, burning, stinging, tingling<br><1%: erythema, dryness, rash, peeling, irritation | - avoid occlusive dressings<br>- pts with dark complexion, monitor and report skin color changes<br>- thin film should be gently but thoroughly massaged into the affected areas BID after skin is washed and patted dry<br>- Finevin cheaper, avail only in 20gm  |
| <b>Topical adapalene</b><br>(Differin <sup>®</sup> )  | <i>MOA:</i> normalizes the differentiation of follicular epithelial cells, ↓ microcomedone formation (comedolytic); anti-inflammatory properties<br><br><i>Efficacy/use:</i><br>- most improvement in 8-12 wks<br>- may be more effective than tretinoin 0.025% gel                             | 0.1% gel<br>15 gm, 45 gm tube<br><br>QD (HS)  | erythema, scaling, dryness, pruritis, burning  | - limit exposure to sunlight<br>- pregnancy category C<br>- adapalene 0.1% gel is suitable alternative to tretinoin 0.025% gel in patients with mild-mod acne, with the advantage of better skin tolerability<br>- acne may appear to worsen initially   |
| <b>Topical tazarotene</b><br>(Tazorac <sup>®</sup> )  | <i>MOA:</i> Mechanism has not been defined<br><br><i>Efficacy/use:</i><br>- mild - mod facial acne  | 0.1% gel<br>30gm, 100gm tubes<br><br>QD (QHS)   | peeling, burning, stinging, dryness, erythema, pruritis  | - pregnancy category X<br>- cover entire affected area with a thin film after washing/drying skin<br>- limit exposure to sunlight  |
| <b>Systemic antibiotics</b><br>Tetracycline<br>Erythromycin<br>Doxycycline<br>Minocycline<br>TMP/SMX<br>Clindamycin | <i>MOA:</i> antibacterial vs. P. acnes. Prevents inflammation by ↓ FFA released as a result of bacteria<br><br><i>Efficacy/use:</i><br>- use only for: 1) mod - severe inflammatory acne, 2) pts intolerant or unresponsive to topical agents, and 3) pts with acne on trunk, back or shoulders | <u>TCN</u> : 500mg BID;<br><u>Emycin</u> 500mg BID<br><u>Clinda</u> : 300-450mg/d<br><u>Doxycycline</u> : 50-100mg BID<br><u>Minocycline</u> : 100mg BID<br><br>- may increase dosage in severe or refractory cases<br>- once controlled, dosage can be tapered to a maintenance dose or discontinued | _TCN:<br><br>Emycin:<br><br>Clinda:<br><br>Minocycline:  | - reserve TMP/SMX for refractory cases to minimize the risk of resistance<br>- potential interaction with oral contraceptives (Ampicillin, TCN)<br>- TCN - drug/food interaction<br>- clindamycin use limited by diarrhea and pseudomembranous colitis<br>- in refractory cases, minocycline and doxycycline may be effective b/c of greater lipid solubility<br>- see Table 88-7 in text for add'l dosing |

| Product                                     | Mechanism/Efficacy  | Availability/Dosing  | Adverse Reactions | Comments  |
|---|---|--|-------------------|---|
| <b>Systemic isotretinoin</b><br>(Accutane®) | <p><i>MOA:</i> Reduces colonization of P. acnes, ↓ sebum production, normalizes keratinization, ↓ inflammation</p> <p><i>Efficacy/use:</i></p> <ul style="list-style-type: none"> <li>- indicated for 1) nodular or cystic acne,</li> <li>2) acne not responsive to other therapy,</li> <li>3) presence of scarring</li> <li>- takes several weeks for benefit</li> <li>- complete remission after 20 -24wks</li> </ul> | 10, 20 & 40mg caps<br>- 0.5-1mg/kg/d (40-80mg/d)<br>-If severe, may use up to 2mg/kg/d<br>- optimal results with cumulative does of 120-150mg/kg.<br>- give in 2 divided doses daily<br>- after 16 wk course, 70% success rate followed by a prolonged remission of more than 20 mos.<br>- may require 2nd course, only if off tx for ≥ 2 mos. |                   | <ul style="list-style-type: none"> <li>- pregnancy category X</li> <li>- <u>Monitor:</u> LFT's, lipid panel, CBC, pregnancy test at baseline and monthly</li> <li>- minimize alcohol intake</li> <li>- acne may initially (first 3-6 weeks) worsen</li> </ul> |

✓ Salicylic acid, resorcinol, and sulfur are keratolytic OTC agents that have limited efficacy, are inferior to other treatments, and have significant ADRS (odor, discoloration/staining)

✓ Cleansing products containing benzoyl peroxide are alone of little value because little residue remains after washing off

Isotretinoin (Accutane®) is contraindicated in females of child-bearing potential unless the patient meets the following criteria:

- The patient must be reliable, capable of understanding and carrying out instructions
- Must receive oral/written counseling on the benefits & risks of isotretinoin; including need for 2 forms of birth control and the hazards associated with taking isotretinoin while pregnant.
- Must have 2 negative urine/serum pregnancy tests; Additional pregnancy test each month during treatment
- Must have selected and committed to use 2 forms of effective contraception for 1 month before, during , and for 1 month after treatment
- Must have signed a patient information/consent

Requirements for dispensing:

Other treatments:

➤ Hormonal:

Oral contraceptives:

Anti-androgens and other hormonal therapy:

Spironolactone, flutamide, cyproterone

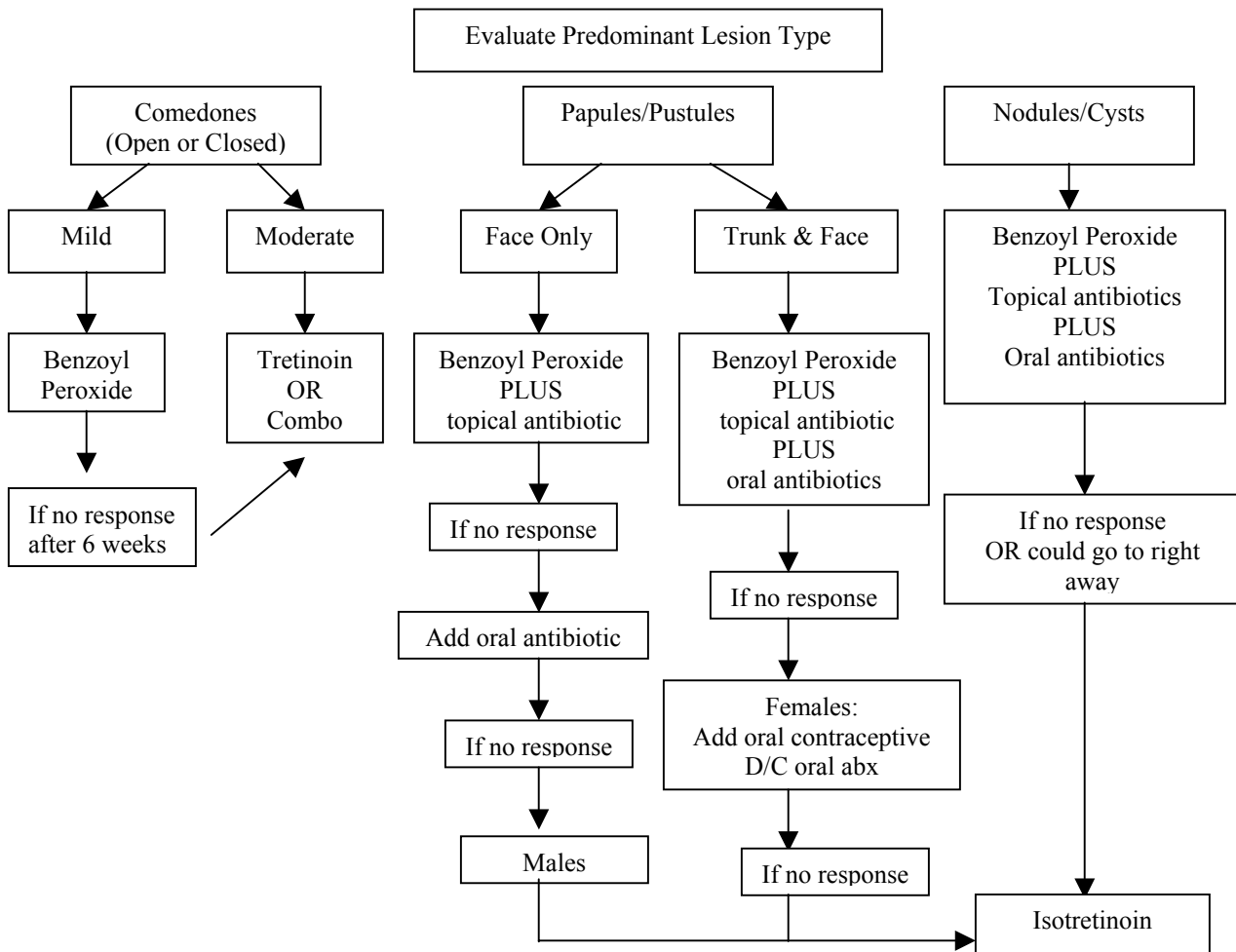
Gonadotropin releasing hormone agonists, 5-alpha-reductase inhibitors, corticosteroids

- Intra-lesional triamcinolone injection
  - Lesional therapy: Comedonal extraction, Superficial pustule/cyst drainage, Sinus tracts/cysts excision
  - Cryotherapy
  - Dermabrasion or surgical repair for scars
- ✓ Many drugs and drug combinations ultimately may be used, all therapies are based on treating one or more of the primary pathogenic factors.
- ✓ Lesions generally take 6-8 weeks to resolve; therefore an adequate trial of 6-8 weeks should be allowed before reassessing therapy

| Product                                    | Comedolytic | Anti-inflammatory | Antibacterial | ↓ sebum production |
|--|-------------|-------------------|---------------|--------------------|
| Topical benzoyl peroxide                   | Yes         | Yes               | Yes           | No                 |
| Topical antibiotics                        | No          | Yes               | Yes           | No                 |
| Topical tretinoin                          | Yes         | No                | No            | No                 |
| Topical azelaic acid                       | Yes         | Yes               | Yes           | No                 |
| Topical adapalene                          | Yes         | Yes               | No            | No                 |
| Topical tazarotene                         | Yes         | No                | No            | No                 |
| Systemic antibiotics                       | No          | Yes               | Yes           | No                 |
| Systemic isotretinoin                      | Yes         | Yes               | Yes           | Yes                |
| Oral contraceptives/<br>Hormonal therapies | No          | No                | No            | Yes                |

**General considerations in therapy selection:**

**Pharmacotherapy for acne:**



**In-class activity**

*Select/recommend initial pharmacologic therapy for T.N.*

**VI. Monitoring**

- ✧ Expected therapeutic response
- ✧ Adverse effects
- ✧ Compliance
  
- ✧ Isotretinoin

**VII. *Patient education is the key to compliance!***

**In-class activity**

*What important counseling points should you discuss with T.N.?*

**ACNE ROSACEA**

**I. Etiology**

**II. Clinical Presentation**

**III. Triggers**

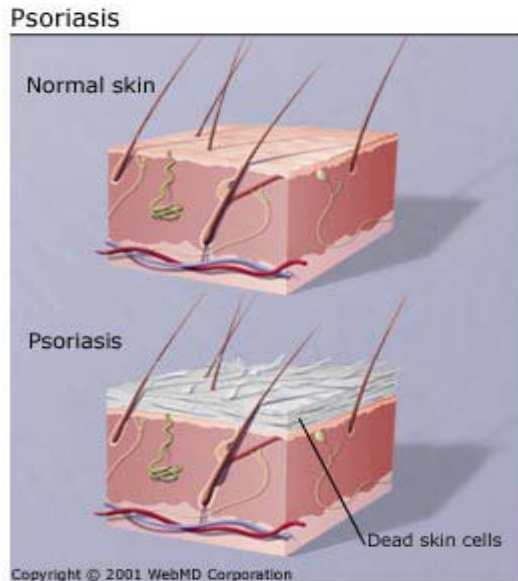
**IV. Treatment**

# PSORIASIS

## I. Incidence/epidemiology

## II. Pathophysiology

➤ The cause of psoriasis remains unclear; however, many hypothesis regarding the pathophysiologic mechanisms of psoriasis exist.



| Hypothesis   | Description   |
|--|---|
| Defects in epidermal cell cycle  | Psoriatic epidermal cells proliferate at a rate sevenfold faster than normal epidermal cells. The germinative cell population increases in psoriatic skin, and duration of the cell cycle is calculated at 37.5 hours (vs. 300 in normal skin).   |
| Disruption in arachidonic acid metabolism  | Arachidonic acid levels are 30 times normal, HETE levels are 80 times normal, and prostaglandin E2 are 50% higher. Glucocorticoids normalize levels of AA and HETE by inhibition of phospholipase A and those activities may be partly responsible for regression of psoriatic lesions  |
| Genetics   | Exact mode of inheritance is uncertain; about 36% of patients with psoriasis have at least one immediate relative with the disorder.  |
| Exogenous trigger factors  | <ul style="list-style-type: none"> <li>a) 90% report worsening in cold weather; warm seasons and sunlight reportedly improved in 80% of patients</li> <li>b) Stress worsened psoriasis in 30-40% of patients; exact role is uncertain</li> <li>c) Identified retrospectively</li> <li>d) May occur at a site of injury to normal-appearing skin (Koebner response); incidence is variable; length of time from injury to developing psoriasis is variable, but usually a few days to wks.</li> <li>e) Lithium, b-blockers, ACE-Inhibitors, Indomethacin, OCs</li> </ul> |
| <ul style="list-style-type: none"> <li>a) climate</li> <li>b) stress</li> <li>c) infection</li> <li>d) trauma</li> <li>e) drugs</li> </ul> |   |

Patient assessment

- onset and duration of psoriasis
- family history
- exacerbating factors
- previous history of antipsoriasis agents with efficacy/side effect data
- all current and recent topical and systemic medications
- environmental and occupational exposure to chemicals and toxins
- allergies (food, drug, environmental)

**III. Clinical manifestations**

| Type of psoriasis       | Clinical manifestations/characteristics   |
|-------------------------|---|
| Plaque psoriasis        |   |
| Pustular psoriasis      |   |
| Erythrodermia psoriasis | - diffuse erythema and scaling (> 90% of body surface area)<br>- fevers, chills, malaise, hypothermia and hypoalbuminemia may be present<br>- pneumonia and renal failure may occur<br>- high output heart failure may develop in patients with heart disease |
| Guttate psoriasis       | - small, scaly, erythematous spots of psoriasis<br>- classically following beta-hemolytic streptococcal pharyngitis   |
| Psoriatic arthritis     |   |

Severity: Mild - moderate: ≤ 20% body surface area involved; Severe: > 20% body surface area involved

**In-class activity**

M.M, a 35 year old male, presents to the Dermatology Clinic with a two-week history of small, erythematous, pruritic, well-demarcated papules covered with silver-white scales over his elbows, and upper arms that did not respond well to Vaseline Intensive Care lotion or calamine. The papules have spread to his upper back and have become progressively larger and scaler. He admits to scratching them, especially at night, which sometimes causes them to bleed. Patient has had no injury but states he has recently recovered from a severe sunburn on his recent trip to Hawaii. He swears that he caught a cold from the lady next to him (who made no effort to cover her mouth when coughing or sneezing) during the long flight back to the Midwest. He was “laid up” for several days and when he finally did get back to work, the place was an absolute zoo!!!

*List questions to ask MM to obtain a complete patient history.*

*Assess MM’s psoriasis.*

**IV. Treatment**

**Goals of therapy**

- ✓ Complete clearing of lesion
- ✓ Prevent recurrence for as long as possible
- ✓ Relieve discomfort
- ✓ Minimize the impact of disease on patient’s personal, social or professional life

| Product               | Mechanism/Efficacy   | Availability/Dosing   | Adverse effects  | Comments  |
|-----------------------|--|---|--|---|
| <b>Emollients</b>     | <p><i>MOA:</i> Hydrate stratum corneum, minimize evaporation of H<sub>2</sub>O. May have antipruritic activity, mild vasoconstrictor activity</p> <p><i>Efficacy/use:</i><br/> - useful with excess drying or dry skin<br/> - enhance efficacy of phototherapy</p> | <p>apply TID - QID</p>  | <p>folliculitis; contact dermatitis</p>  | <p>- 20 minute bath in warm water prior to application is beneficial<br/> - occlusion of nonmedicated emollients with cellophane may enhance effects</p>  |
| <b>Salicylic acid</b> | <p><i>MOA:</i> Keratolytic; removes scale, smooths the skin and decreases hyperkeratosis</p> <p><i>Efficacy/use:</i><br/> - used alone or w/ tar or topical steroids<br/> - no studies have documented efficacy as monotherapy</p>                                 | <p>2-10%</p> <p>gels, lotions, ointments</p> <p>apply BID-TID</p>   | <p>application to large areas may result in salicylism with symptoms of N/V, tinnitus, or hyperventilation</p> | <p>- may enhance penetration of some drugs<br/> - particularly helpful for thick, scaly plaques<br/> - do not use prior to phototherapy</p>   |
| <b>Coal Tar</b>       | <p><i>MOA:</i> antimitotic action</p> <p><i>Efficacy/use:</i><br/> - Place in therapy: 1) steroid-resistant psoriasis, 2) large area of involvement, 3) oral agents are contraindicated b/c of systemic illness</p>  | <p>1-48.5%</p> <p>- ointment, cream, lotion, solution, gel, soap, oil, liquid<br/> - start with lower conc and titrate upward<br/> - usually QD (at HS)</p>   | <p>unpleasant odor, stains skin and clothing, photosensitivity, carcinogenicity (w/ long term use)</p>         | <p>- resolution of mild-mod plaques<br/> - may also reduce redness and itching<br/> - use in combo w/ UVB may be no more effective than either used alone<br/> - tar creams are useful for psoriasis of the scalp and often are used overnight<br/> - limited by burdensome, time-consuming treatment with disadvantages (see ADRS)</p> |
| <b>Anthralin</b>      | <p><i>MOA:</i> Inhibits DNA synthesis yielding an antiproliferative effect</p> <p><i>Efficacy/use:</i><br/> - effective for widespread discrete psoriatic plaques; can be used alone, in combo w/ UVB, topical steroids, coal tar or PO tx</p>                     | <p>0.1%, 0.2%, 0.25%, 0.4%, 0.5%, 1%</p> <p>ointment, cream<br/> - titrate slowly from low conc to higher conc; QD<br/> - short-contact regimen preferred</p> | <p>irritation, staining, difficult to apply</p>  | <p>- <i>longer contact regimen:</i> apply QHS for 8-12hr; <i>shorter contact regimen:</i> apply BID for 20 minutes contact time<br/> - wear plastic gloves, plastic cap over tx scalp<br/> - do not apply to face, genitalia, or intertriginous skin</p>  |

| Product   | Mechanism/Efficacy  | Availability/Dosing   | Adverse effects   | Comments   |
|---|---|---|---|--|
| <b>Calcipotriene</b><br>(Dovonex <sup>®</sup> ) | <i>MOA:</i> topical vitamin D3 analogue; regulates cell differentiation and proliferation and suppresses lymphocyte activity<br><i>Efficacy/use:</i><br>- mild-mod plaque psoriasis<br>- improvement seen w/in 2 weeks<br>- 70% showing marked improvement within 8 weeks   | 0.005% (50mcg/g)<br>ointment, cream<br><br>- BID for 8 weeks<br>- do not exceed 100g/week<br>- maintenance therapy may be needed for long term control  | dry skin, peeling, rash, worsening of psoriasis, hypercalcemia (rare) | - decreases erythema, induration, and scaling<br>- effective in difficult to clear areas (elbows, knees, shins)<br>- do not use on the face  |
| <b>Tazarotene</b><br>(Tazorac <sup>®</sup> )    | <i>MOA:</i> Mechanism is not well-defined; thought to affect cell differentiation, proliferation and inflammation.<br><i>Efficacy/use:</i><br>- mild-mod plaque psoriasis (do not apply to more than 20% body surface area)<br>- use in combination with topical steroid was more effective than tazarotene alone | 0.05%, 0.1% gel<br><br>QD (PM) to psoriatic lesions   | peeling, burning, stinging, dryness, erythema, pruritis               | - pregnancy category X<br>- apply to <u>dry</u> skin<br>- apply only to affected areas; unaffected skin is more susceptible to irritation<br>- therapeutic effect may be maintained for up to 12 weeks after d/c in some patients  |
| <b>Topical Corticosteroids</b><br>(many)        | <i>MOA:</i> anti-inflammatory, antimetabolic, and antipruritic properties<br><br><i>Efficacy/use:</i><br>- most frequently used topical tx of psoriasis<br>- <b>adjunct</b> to other forms of topical therapy<br>- monotherapy only if isolated plaque(s) or small area<br>- intermittent                         | - variable conc, formulations, and potencies<br>- plaque psoriasis: high-potency BID until lesions improved, then least effective dose<br>- <i>acute, severe</i> psoriasis: pulse therapy: apply a high potency steroid Q2h for 24-48 hours followed by 3-4x/day<br>- <i>maintenance:</i> 1- 2 x/day<br>- intermittent use (1-2 weeks on and 1-2 weeks off) |   | - choice of steroid/vehicle dependent on severity & extent of involvement, area of the body to be treated, and anticipated duration<br>- ointments most clinically effective in psoriasis; not suited for axilla, groin or other intertriginous areas<br>- tachyphylaxis and rebound flare can occur after abrupt cessation of therapy; benefits do not persist for more than a few months<br>- combination with phototherapy is controversial; question of ↑ recurrence rate; if used, use with PUVA only |

## Phototherapy

### ➤ Photochemotherapy (PUVA)

- MOA: antiproliferative, anti-inflammatory and immunosuppressive effects
- Efficacy: Either treatment alone is ineffective
- ADRS (long-term PUVA): premature skin aging, cataracts, skin cancer

#### ✓ **Oral** PUVA therapy

- Methoxsalen 2 hours prior to UVA irradiation
- Typically 20 sessions are needed before lesions clear
- Common ADRS of oral psoralens: constipation, diarrhea, nausea, vomiting, pruritus, and delayed-onset erythema

#### ✓ **Topical** PUVA

- topical psoralen (cream, ointment, lotion, water-bath vehicle) plus UVA irradiation
- major advantage over oral = no GI adverse effects or cataract formation

#### ✓ **Comments:**

- Topical steroid therapy should be continued until psoriasis under control. If steroids discontinued at the start of PUVA, exacerbation of psoriasis usually occurs.
- Sunscreens, protective clothing need to be worn during exposure to sun; Most important during the eight hours immediately following PUVA therapy.
- Face, genitalia should be shielded during treatment.

### ➤ Rotational therapy

- Even if a particular regimen is working well for a patient, it is prudent to consider changing the treatment to avoid side effects
- Proposed regimen: patients receive one treatment for 1 to 2 years, then switch to another
- By following this regimen, it may take 4 or 5 years before it is necessary to return to the first treatment, thus minimizing cumulative toxicity
- In addition to rotational therapy, topical agents may be used sequentially or concomitantly with systemic agents and phototherapy. Retinoids or MTX can be combined with phototherapy



## General considerations in psoriasis treatment

### Step-wise approach to therapy:

#### Step 1: Topical therapies

- Topical corticosteroids
- Calcipotriene
- Tazarotene
- Coal tar/anthralin

#### Step 2: Phototherapies

- PUVA
- Combination of step 1 and phototherapy

#### Step 3: Systemic therapies

- Methotrexate
- Acitretin
- Cyclosporine
- “Newer therapies”
- Rotational and combination therapy

## DRUG-INDUCED SKIN DISORDERS

Important components of patient evaluation of drug-induced skin disorders:

Timing of drug reactions

- ✓ frequently within one week
- ✓ can occur at any time, depending on the drug (weeks after d/c semisynthetic penicillin; 6 months for beta-blocker induced psoriasis; 2 months - 5 yrs for drug-induced SLE)
- ✓ last several minutes - months, or may occur periodically throughout exposure period

| Type of reaction                 | Drugs implicated   | Clinical characteristics  | Management   |  |
|----------------------------------|--|---|--|--|
| <b>Maculopapular eruptions</b>   | <ul style="list-style-type: none"> <li>allopurinol</li> <li>barbiturates</li> <li>benzodiazepines</li> <li>captopril</li> <li>penicillin</li> <li>carbamazepine</li> <li>chloramphenicol</li> <li>ciprofloxacin</li> <li>erythromycin</li> <li>ethionamide</li> <li>hydantoin</li> <li>ibuprofen</li> <li>sulindac</li> <li>indomethacin</li> <li>isoniazid</li> <li>tolmetin</li> </ul> | <ul style="list-style-type: none"> <li>nitrofurantoin</li> <li>ofloxacin</li> <li>penicillinamine</li> <li>phenothiazines</li> <li>phenylbutazone</li> <li>piroxicam</li> <li>rifampin</li> <li>streptomycin</li> <li>sulfonamides</li> <li>tetracyclines</li> </ul>                | <ul style="list-style-type: none"> <li>- common skin reaction</li> <li>- often start on the trunk or in areas of pressure or trauma and are frequently symmetrical</li> <li>- flat or raised, reddened lesions, varying in size</li> <li>- involvement of mucous membranes or palms and soles is variable and infrequent; mild fever may accompany reaction</li> <li>- can be considered “early” (within 2-3 days) or “late” (approximately 9 days after drug exposure); can occur any time from first day of exposure to 2 weeks after therapy</li> </ul> | <ul style="list-style-type: none"> <li>- D/C offending agent</li> <li>- Lukewarm water baths/cool compresses</li> <li>- Oral antihistamines for itching</li> <li>- Systemic corticosteroids if severe rxn</li> </ul>   |
| <b>Urticaria and anaphylaxis</b> | <ul style="list-style-type: none"> <li>aspirin</li> <li>amitriptyline</li> <li>bisacodyl</li> <li>opiates</li> <li>cyclophosphamide</li> <li>gold</li> <li>heparin</li> <li>ibuprofen</li> <li>sulfonamides</li> <li>indomethacin</li> <li>insulin</li> <li>mannitol</li> <li>mesna</li> <li>iodinated radiocontrast dye</li> </ul>  | <ul style="list-style-type: none"> <li>naproxen</li> <li>nizatidine</li> <li>omeprazole</li> <li>penicillins</li> <li>sulindac</li> <li>senna</li> <li>tartrazine</li> <li>tolmetin</li> </ul>  | <ul style="list-style-type: none"> <li>- Urticaria: raised, pruritic erythematous wheals (hives) ranging in size from a few mm to lesions extending over the trunk or chest</li> <li>- Anaphylactic syndrome: acute onset of skin and mucosal lesions and progression to GI symptoms, peripheral vascular collapse, and shock.</li> </ul>  | <ul style="list-style-type: none"> <li>- D/C offending agent</li> <li>- Management depends on severity</li> <li>- Mild antipruritic agents (topical)</li> <li>- Topical antihistamines should be avoided due to contact sensitization</li> <li>- Doxepin - chronic urticaria</li> </ul>  |
| <b>Fixed drug reactions</b>      | <ul style="list-style-type: none"> <li>barbiturates</li> <li>dapsone</li> <li>digitalis</li> <li>diphenhydramine</li> <li>gold</li> <li>epinephrine</li> <li>erythromycin</li> <li>gold</li> <li>griseofulvin</li> <li>hydralazine</li> <li>hydroxyurea</li> </ul>   | <ul style="list-style-type: none"> <li>ibuprofen</li> <li>ipecac</li> <li>metronidazole</li> <li>quinidine</li> <li>phenolphthalein</li> <li>phenothiazines</li> <li>phenylbutazone</li> <li>sulfonamides</li> <li>sulindac</li> <li>tetracyclines</li> <li>trimethoprim</li> </ul> | <ul style="list-style-type: none"> <li>- erythematous round or oval lesion ranging from a few mm to 20 cm in diameter</li> <li>- with time, the color turns to a dusky-red or violaceous hue;</li> <li>- may complain of itching, but sensations of warmth and burning are more common</li> <li>- location: any part of skin or mucous membranes, lips and genitalia are more commonly affected.</li> <li>- reexposure results in recurrence of eruption in same location</li> </ul>   | <ul style="list-style-type: none"> <li>- D/C offending agent</li> <li>- Cool water compresses (acute)</li> <li>- Bleaching creams for hyperpigmented areas during chronic phases</li> <li>- Systemic corticosteroids</li> <li>- Systemic antihistamines</li> <li>- healing occurs within 7-10 days of discontinuation of drug and often leaves a dark, hyperpigmented patch</li> </ul> |
| <b>Photosensitivity</b>          | <ul style="list-style-type: none"> <li>amiodarone</li> <li>carbamazepine</li> <li>dacarbazine</li> <li>furosemide</li> <li>ketoprofen</li> <li>naproxen</li> <li>sulindac</li> <li>phenylbutazone</li> <li>thiazides</li> <li>phenothiazines</li> <li>oral contraceptives</li> </ul>   | <ul style="list-style-type: none"> <li>piroxicam</li> <li>propriptyline</li> <li>quinidine</li> <li>sulfonamides</li> <li>sulfonylureas</li> <li>tetracyclines</li> </ul>   | <ul style="list-style-type: none"> <li>- erythema, edema, papules, and plaque-like perhaps urticarial, lesions, sometimes with vesicle formation</li> <li>- hallmark is appearance on areas of skin receiving the greatest exposure to sunlight</li> <li>- in some situations, the eruption may extend to non-sun-exposed areas and generalize over the body</li> <li>- chronically, hyper- or hypo-pigmented, perhaps atrophic and w/ yellowish papules or telangiectasis</li> </ul>  | <ul style="list-style-type: none"> <li>- D/C offending agent</li> <li>- Avoid sunlight</li> <li>- Topical remedies (Cool wet dressings, soothing lotions, corticosteroids)</li> <li>- Topical or systemic antipruritic agents</li> <li>- PABA should be avoided in patients with allergies to “sulfa” drugs (see text)</li> </ul>  |

| Type of reaction                                    | Drugs implicated   | Clinical characteristics   | Management   |
|---|--|--|--|
| <b>Alopecia</b>                                     | carbamazepine    hydantoin<br>clofibrate isotretinoin<br>colchicine        propranolol<br>ethionamide      valproate Na<br>etretinate vit A (hi dose)  | - partial or total hair loss   | - D/C offending agent  |
| <b>Vasculitis</b>                                   | allopurinol        phenylbutazone<br>anticoagulants    phenytoin<br>cimetidine        piroxicam<br>fluoxetine        propylthiouracil<br>hydralazine        quinine<br>ibuprofen sulfonamides<br>indomethacin      thiazides<br>penicillins                            | - inflammation and damage of blood vessels that may affect various organ systems<br>- appears on lower extremities or pressure-dependent areas of the skin as red or purple lesions, ranging in size (pinpoint to several cm)<br>- may persist 1 - 4 weeks and become yellow to brown upon healing<br>- systemic symptoms may be present (burning, malaise, etc) | - D/C offending agent<br>- Bedrest and compression of lesion<br>- Oral corticosteroids   |
| <b>Hyperpigmentation</b>                            | amiodarone, antimalarial agents,<br>clofazimine, oral contraceptives,<br>phenothiazines, tetracyclines<br><u>heavy metals</u> - mercury, silver,<br>bismuth, arsenic, gold<br><u>chemotherapeutic agents</u> - busulfan,<br>bleomycin, doxorubicin,<br>mechlorethamine | Amiodarone:<br><br>Oral contraceptives:  | - D/C offending agent; not always reversible   |
| <b>Erythema multiforme/Stevens-Johnson Syndrome</b> | allopurinol        propranolol<br>carbamazepine    quinine<br>cephalosporins    salicylates<br>hydantoin         sulfonamides<br>ibuprofen sulfonamides<br>penicillins        sulindac<br>phenobarbital     thiazides<br>phenylbutazone   valproic acid                |  | D/C offending agent<br>If Mild:<br>- Blisters & necrosis: tap water compresses<br>- Pruritis: antihistamines<br>- Oral lesions: ½ strength hydrogen peroxide<br>- Use of systemic corticosteroids not clearly defined              |
| <b>Toxic epidermal necrolysis</b>                   | allopurinol        penicillins<br>barbiturates      phenylbutazone<br>chloramphenicol    quinine<br>hydantoin         sulfonamides<br>ibuprofen sulindac<br>indomethacin      tolmetin   |  | - D/C offending agent<br>- Fluid and electrolyte maintenance<br>- Treatment and prevention of infections or ocular complications<br>- Possible burn unit<br>- Systemic corticosteroids controversial (use only within 48-72 hours) |