PHARMACOTHERAPY OF DERMATOLOGICAL DISORDERS

By Fasil B.

Acne Vulgaris

- Acne is a common, usually self-limiting disease involving inflammation of the sebaceous follicles of the face, back, upper chest, & shoulders.
- It usually begins in the prepubertal period and progresses as androgen production and sebaceous gland activity increase with gonad development.
- Circulating androgens cause sebaceous glands to increase their size and activity.

EPIDEMIOLOGY AND ETIOLOGY

- Acne is more likely to occur in males during adolescence and females during adulthood.
- Individuals with a positive family history of acne have been shown to develop more severe cases of acne at an earlier age.
- Prevalence of acne among ethnic groups is similar
- there is evidence to suggest that high glycemic load diets may exacerbate acne.
- Local irritation from occlusive clothing or athletic equipment,
- oil-based cosmetics or beauty products, prolonged sweating

Pathophysiology

- Major etiologic factors…
  - increased sebum production, due to hormonal influences
- increased follicular keratinization (open comedo or "blackhead)
  - bacterial colonization of the duct with Propionibacterium acnes (closed comedo or whitehead)
  - production of inflammation in acne sites

Clinical Presentation and Diagnosis of Acne

Acne lesions are most often seen on the face, but can also present on the chest, back, neck, and shoulders and are described as either noninflammatory or inflammatory. Severe inflammatory lesions may lead to scarring and hyperpigmentation.

Noninflammatory Lesions

Open comedo or "blackhead": A plugged follicle of sebum, keratinocytes, and bacteria that protrudes from the surface of the skin and appears black or brown in color. Although dark in color, blackheads do not indicate the presence of dirt, but rather, an accumulation of melanin.

Closed comedo or "whitehead": A plugged follicle of sebum, keratinocytes, and bacteria that remains beneath the surface of the skin. Closed comedos usually appear as small white bumps about 1 to 2 mm in diameter.

Inflammatory Lesions

Papules: Solid, elevated lesion less than 0.5 cm in diameter

Pustules: Vesicles filled with purulent fluid less than 0.5 cm in diameter

Nodules: Lesions greater than 0.5 cm in both width and depth

Cysts: Nodules filled with a fluid or semisolid that can be expressed

Scars

Inflammatory acne can result in permanent scarring that ranges from small depressed pits to large elevated blemishes.

Hyperpigmentation

Inflammatory acne may result in hyperpigmentation of the skin that can last for weeks to months.

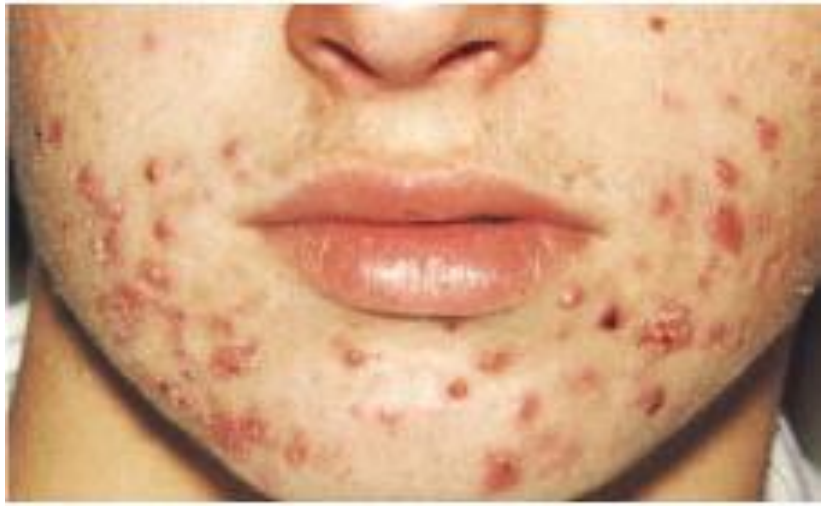
Diagnosis

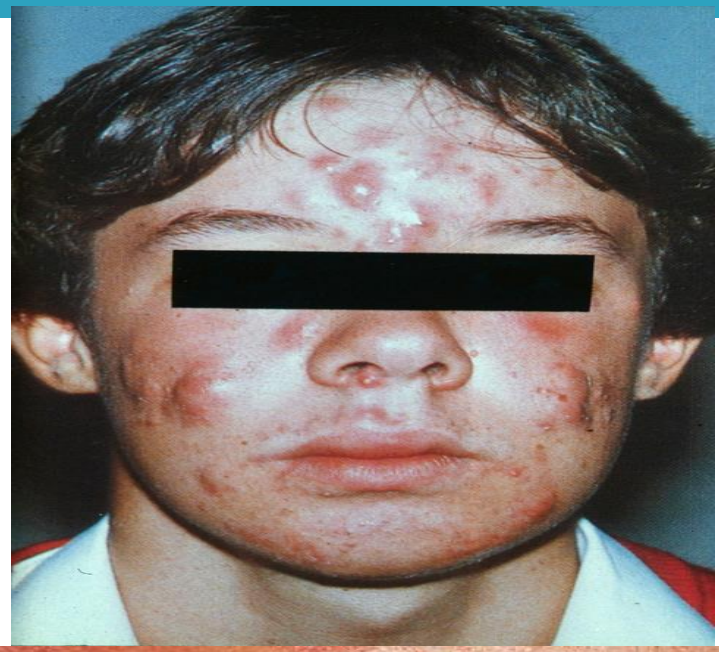
The diagnosis of acne vulgaris is clinical. Lesion cultures may be warranted when treatment regimens fail to rule out other skin infections.

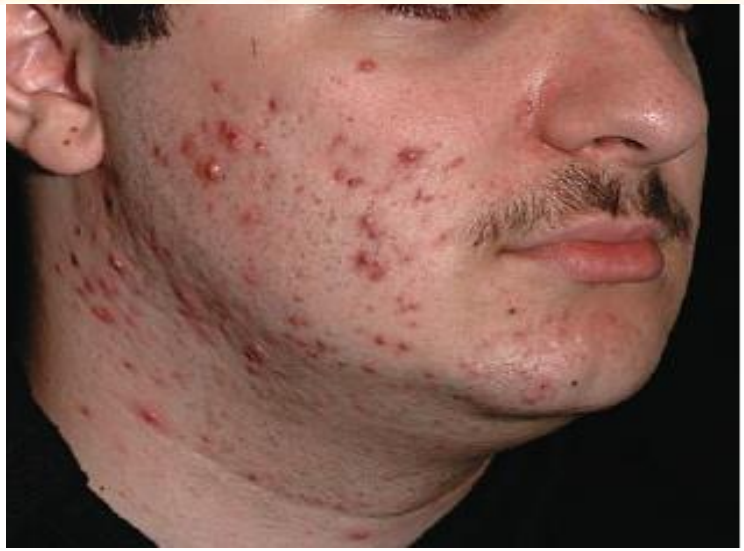
Assessment

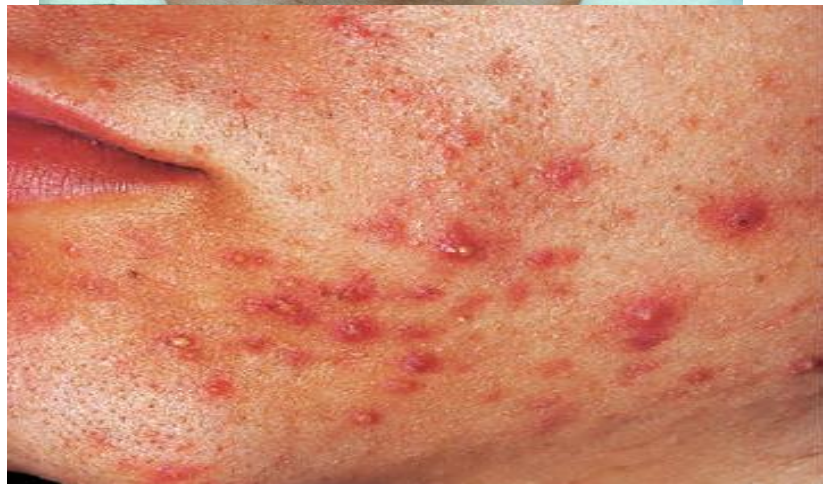
No standard acne grading scale has been identified. While several grading scale exist,[7,8,9] most clinicians describe acne as mild (few noninflammatory lesions), moderate (many inflammatory lesions) or severe (numerous severe inflammatory lesions and evidence of scarring).

Inflammation form…

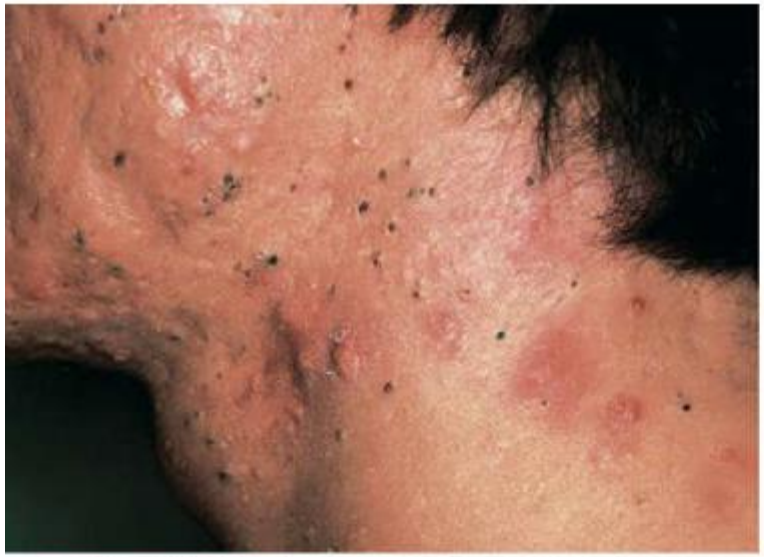


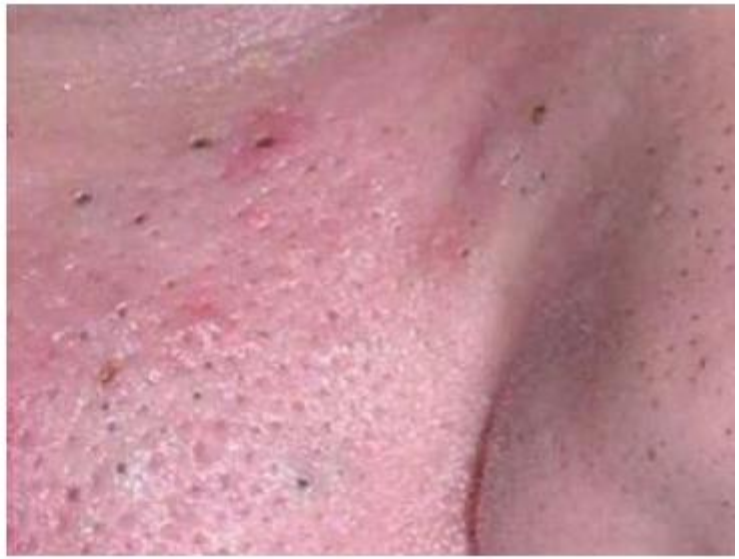


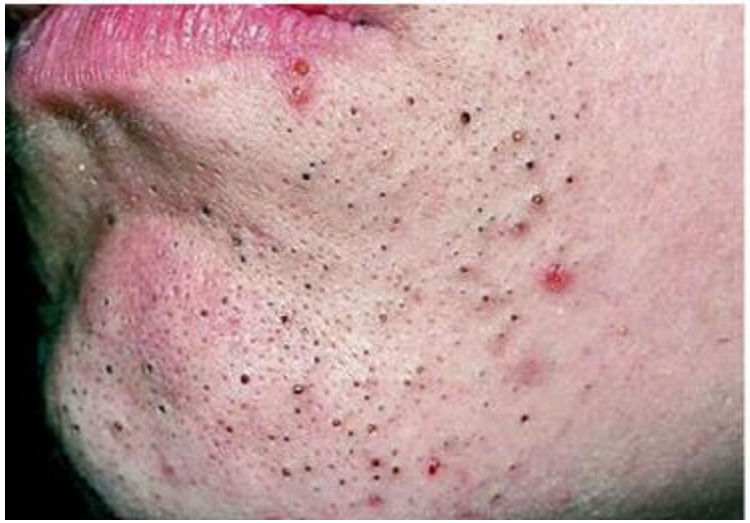


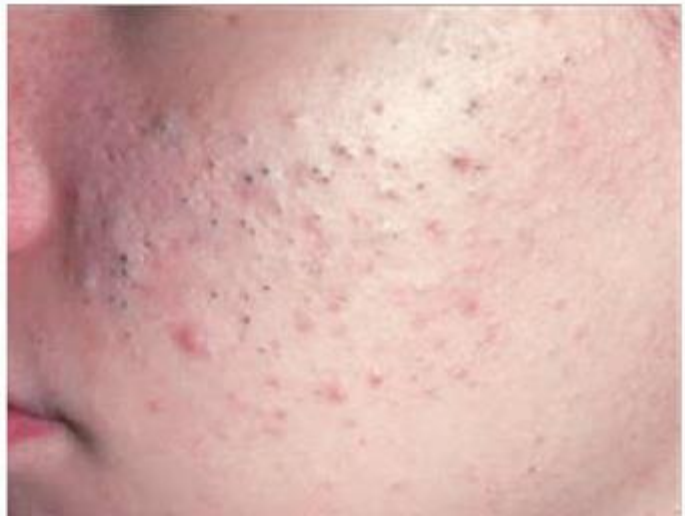


Non. Inflammation acne..







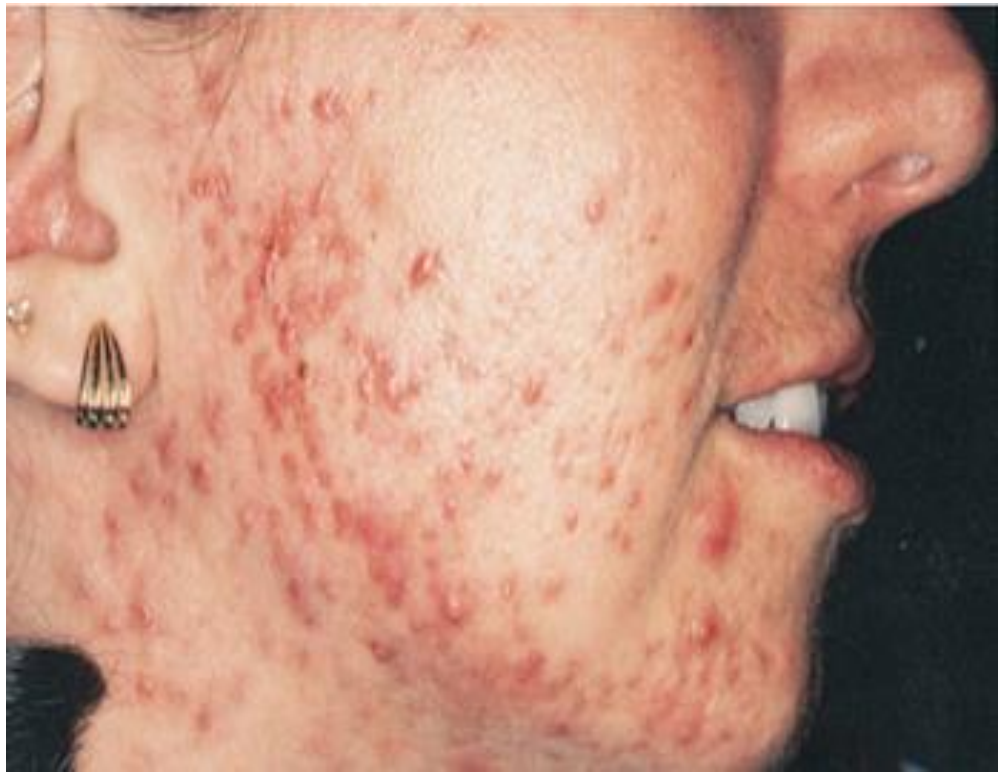


Acne Vulgaris …

- Severity varies from a mild comedonal form to severe inflammatory acne.
- It can be described as ….
  - mild acne (few lesions, little or no inflammation)
  - moderate (many lesions, significant inflammation)
  - severe (numerous lesions, extreme inflammation and/or nodules, significant scarring)
- Lesions may take months to heal completely, and fibrosis associated with healing may lead to permanent scarring.

Acne Vulgaris …

- Acne vulgaris with inflammatory papules, pustules, and comedones.



Treatment/Acne Vulgaris

- Goals of treatment:
  - reduce the number and severity of lesions
  - slow disease progression
  - limit disease duration
  - prevent formation of new lesions
  - prevent scarring and hyperpigmentation

General Approach to Treatment

- *Acne treatment regimens should be based on acne severity and type of acne lesion. Other factors such as response to*
  - *previous treatment,*
  - *patient preference,*
  - *cost and adherence should also be considered.*
- Topical therapy is considered first line for mild acne with oral therapies added to topical therapy in moderate to severe acne.
- Improvement of symptoms following induction therapy occurs gradually, sometimes taking 6 to 8 weeks for results to be physically apparent.
- Maintenance therapy should begin after 12 weeks of induction therapy and continues for 3 to 4 months.

Nonpharmacologic Therapy

- Patients should be counseled to avoid aggressive skin washing and to use a mild, noncomedogenic facial soap twice daily.
- Furthermore, discourage the use of abrasive cleansers and manipulating or squeezinglesions to minimize scarring.
- Use of an oil-free,
- non comedogenic moisturizer may improve the tolerability of topical drug therapy.
  - Comedone extraction
    - has an immediate cosmetic improvement
    - but has not been widely tested in clinical trials

Pharmacologic therapy

- Comedonal noninflammatory acne
- Topical retinoids (tretinoin, adapalene, azarotene. and especially adapalene) ….drugs of choice
  - Consider benzoyl peroxide
- Mild to moderate papulopustular inflammatory acne
  - First choice therapy …. fixed-dose combination of …
    - adapalene and benzoyl peroxide, or
    - topical clindamycin and benzoyl peroxide
  - Alternatives: a different topical retinoid used with a different topical antimicrobial agent, with/without benzoyl peroxide.

Treatment/Acne Vulgaris ….

- Moderate papulopustular acne
  - combination of a systemic antibiotic with adapalene … DOC
  - Alternative: fixed-dose combination of isotretinoin and erythromycin

Treatment/Acne Vulgaris ….

- Severe papulopustular OR moderate nodular acne
  - Oral isotretinoin monotherapy …first choice
- Alternatives
  - combination of systemic antibiotics and adapalene
  - combination of systemic antibiotics and benzoyl peroxide
  - combination of adapalene and benzoyl peroxide
  - combination of oral antiandrogens and oral antibiotics

Exfoliants

- Exfoliants (peeling agents)
  - induce continuous mild drying and peeling by irritation, damaging superficial skin layers and inciting inflammation.
  - stimulates mitosis, thickening the epidermis and increasing horny cells, scaling, and erythema.
  - Decreased sweating results in a dry, less oily surface and may resolve pustular lesions.

Exfoliants ….

- Salicylic acid ….. keratolytic
  - has mild antibacterial activity against P. acnes
  - offers slight anti-inflammatory activity at conc up to 5%
  - may be less potent than benzoyl peroxide or topical retinoids
  - used as 1st-line therapy for mild acne
  - used as alternative when patients are intolerant to skin irritation of topical retinoids

Exfoliants ….

- Sulfur ….
  - keratolytic
  - has antibacterial activity
  - It can quickly resolve pustules and papules, mask lesions, and produce irritation that leads to skin peeling.
  - used in the precipitated or colloidal form in conc of 2% to 10%
  - combined with salicylic acid or resorcinol to increase effect
    - offensive odor …. limit its use

Exfoliants ….

- Resorcinol …. keratolytic, but less than salicylic acid
  - irritant and sensitizer …..should not be applied to large areas or on broken skin
  - may produce dark brown scale [reversible] on some individuals
  - not recognized as safe and effective, when used alone
  - Safe and effective ….when used in combination with sulfur
  - Eg, combination of resorcinol 2% and resorcinol monoacetate 3% and sulfur 3% to 8%

Topical Retinoids

- Retinoids ….
  - reduce obstruction within the follicle
    - stimulate epithelial cell turnover and aid in unclogging blocked pores.
  - Inhibit useful for both comedonal and inflammatory acne
  - microcomedone formation, decreasing the number of mature comedones and inflammatory lesions
  - are active keratolytics

Topical Retinoids …

- Topical retinoids
  - safe, effective, and economical …. for treating acne
- For moderate acne;
  - initially used alone or in combination with antibiotics and benzoyl peroxide
  - used alone for maintenance therapy ……once adequate results are achieved
- Side effects: erythema, dry skin, burning, peeling

Topical Retinoids …

- Retinoids …..should be applied at night, a half hour after cleansing, starting with every other night for 1 to 2 weeks to adjust to irritation.
- Tretinoin (retinoic acid and vitamin A acid)
  - available as 0.05% solution (most irritating)
  - 0.01% and 0.025% gels
  - 0.025%, 0.05%, and 0.1% creams (least irritating)
  - should not be used in pregnancy …risk to the fetus

Topical Retinoids …

- Adapalene
  - the topical retinoid of first choice ….for both treatment and maintenance therapy
  - it is as effective but less irritating than other topical retinoids
  - available as 0.1% gel, cream, alcoholic solution, and as a 0.3% gel formulation

Topical Retinoids …

- Tazarotene
  - as effective as adapalene in reducing noninflammatory and inflammatory lesion counts
  - as effective as tretinoin for comedonal and more effective for inflammatory lesions
  - available as a 0.05% and 0.1% gel or cream

Topical Antibacterial Agents

- Benzoyl peroxide
  - Bactericidal and comedolytic
  - useful for both noninflammatory and inflammatory acne
    - increases the rate of epithelial cell turnover and helps to unclog blocked pores
  - has rapid onset ….may decrease the number of inflamed lesions within 5 days
  - standard of care for…. mild to moderate papulopustular acne
    - alone or in combination [with topical retinoids, or an antimicrobial]
  - available as soaps, lotions, creams, washes, and gels in conc of 1% to 10%

Topical Antibacterial Agents …

- Benzoyl peroxide ….
  - gel formulations …. most potent
  - lotions, creams, and soaps ….. weaker potency
  - alcohol-based preparations ….cause more dryness and irritation
  - initiate therapy with the weakest concentration (2.5%) in a water-based formulation
  - Once tolerance is achieved, the strength may be increased

Topical Antibacterial Agents …

- Benzoyl peroxide ….
  - Wash the product off in the morning
  - Apply a sunscreen during the day
  - no more than two times a day.
  - Side effects:
    - dryness, irritation
    - allergic contact dermatitis (rare)
    - may bleach hair and clothing

Topical Antibacterial Agents …

- Topical erythromycin and clindamycin
  - less effective …..due to resistance by P. acnes
- Combination with benzoyl peroxide or topical retinoids is more effective than antibiotic monotherapy
  - Use in Mild to moderate inflammatory acne
- Clindamycin ….. preferred
  - more potent and lack systemic absorption
  - available alone or in combination with benzoyl peroxide
- Erythromycin
  - available alone & in comb with retinoic acid or benzoyl peroxide

Topical Antibacterial Agents …

- Dapsone 5% topical gel
  - has anti-inflammatory and antibacterial properties that improve both inflammatory and noninflammatory acne.
  - useful for patients with intolerance to conventional antiacne agents
  - used alone or in combination with adapalene or benzoyl peroxide
    - but, more irritating than other topical agents

Topical…

Azelaic Acid

- With antibacterial and anti-inflammatory properties, and
- the ability to stabilize keratinization,

- an effective alternative in the treatment of mild to moderate acne in patients who cannot tolerate benzoyl peroxide or topical retinoids.
- It can also even out skin tone and may prove effective in patients who are prone to postinflammatory hyperpigmentation resulting from acne.
- Azelaic acid 20% cream should be applied twice daily, with improvement of symptoms seen in 4 week

Oral Antibacterials

- Systemic antibiotics ….standard therapy for ….
  - moderate and severe acne
  - treatment-resistant inflammatory acne
- Patients with less severe forms
  - should not be treated with oral antibiotics,
  - duration of therapy should be limited (eg, 6-8 wks), if possible
    - increasing bacterial resistance

Oral Antibacterials ….

- Minocycline and doxycycline …used as systemic agents
  - have antibacterial and anti-inflammatory effects
- Minocycline ….
  - stronger response than doxycycline …due to greater lipophilicity
  - cause pigment deposition in the skin, mucous membranes, and teeth
  - may cause dose-related dizziness, urticaria, hypersensitivity syndrome, autoimmune hepatitis, serum sickness–like reactions.
- Doxycycline …. photosensitizer at higher doses

Oral Antibacterials …

- Erythromycin ….
  - its use should be limited to patients who cannot use a TTC derivative (eg, pregnant women and children <8 years old).
    - bacterial resistance ….higher than TTCs
- Ciprofloxacin, cotrimoxazole, and trimethoprim alone
  - effective ….where other antibiotics cannot be used or are ineffective

Antisebum Agents

- Isotretinoin
  - decreases sebum production, inhibits P. acnes growth, reduces inflammation
  - approved for treatment of severe nodular acne
  - the only drug for acne that produces prolonged remission
  - Dose: 0.5 to 2 mg/kg/day, given over a 20 week course
  - Drug absorption is greater when taken with food

Antisebum Agents …

- Adverse effects of Isotretinoin
  - are often dose related
  - mucocutaneous effects; drying of the mouth, nose, and eyes; cracking of the skin of the lips
- Systemic effects ….
  - transient increases in serum cholesterol and triglycerides,
  - hyperglycemia, photosensitivity, abnormal liver tests, bone abnormalities, muscle stiffness, headache, teratogenicity.

Antisebum Agents …

- Oral contraceptives containing estrogen …. useful for acne in some women
  - Combination oral contraceptive use reduced inflammatory and noninflammatory facial lesion
- Cyproterone acetate …..an antiandrogen
  - combined with ethinyl estradiol (in the form of OC)…. effective for acne in females
- Spironolactone …. antiandrogenic in higher doses
  - doses of 50 to 200 mg …effective in acne
- Oral corticosteroids in high doses
  - used for short courses in severe inflammatory acne

Treatment algorism ....

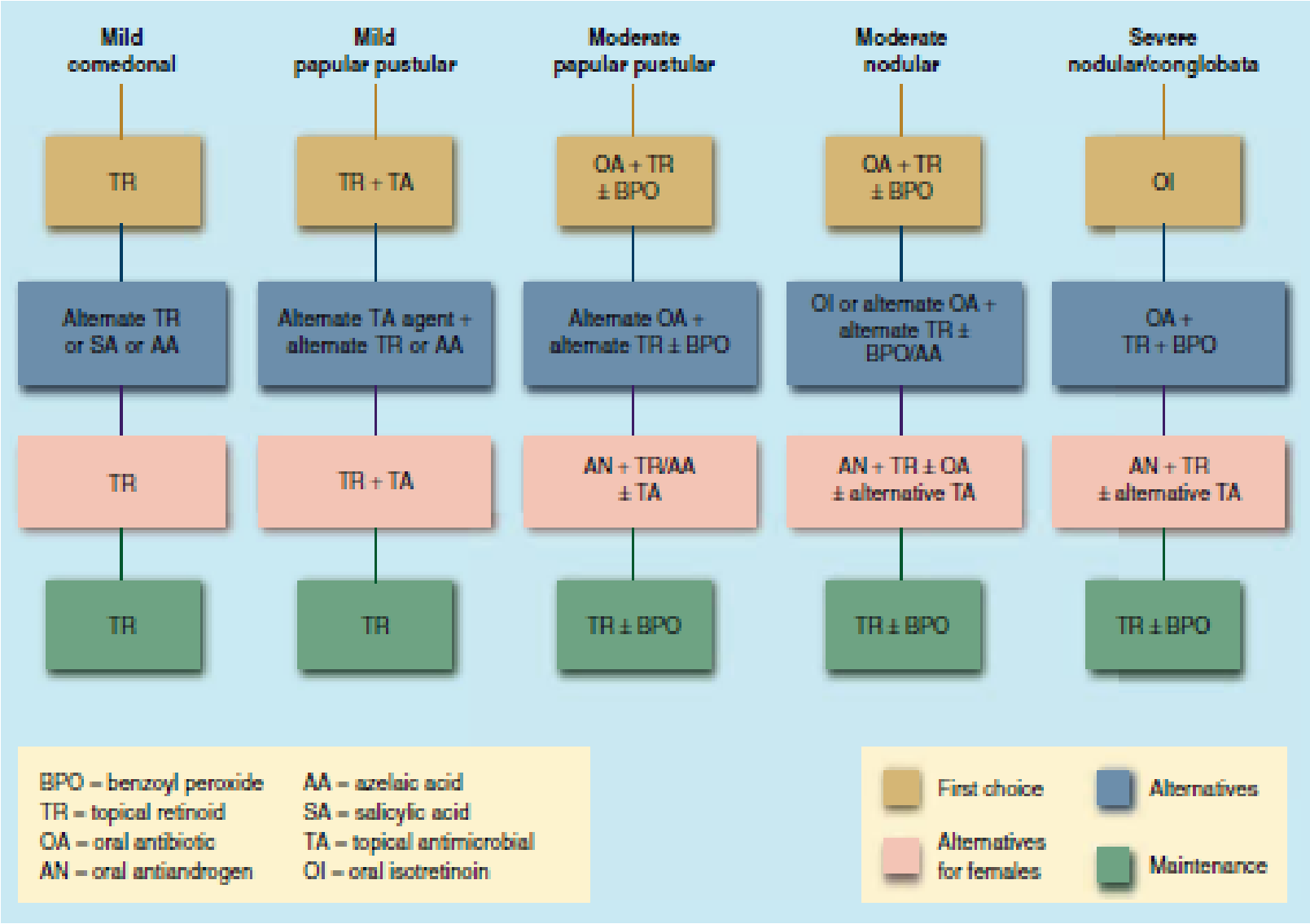


Table 65–1

Topical Agents Used in the Treatment of Acne

Drug	Brand	Dosage Form	Adverse Reactions	Comments
Retinoids				
Tretinoin	Atralin	0.05% gel	Erythema, dryness, scaling, stinging/burning, pruritus, initially may worsen acne	Local adverse reactions most likely occur in first 2 to 4 weeks of use and will usually lessen with continued use.
		0.025% cream; 0.025% gel		
	Avita	0.025%, 0.05%, 0.1% cream		
	Retin-A	0.01%, 0.025% gel	Possibly teratogenic	Category C. Use cautiously in pregnancy.
	Retin-A Micro	0.04%, 0.1% gel		
	Tretin-X	0.038%, 0.075% cream	Photosensitivity	Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended.
Tazarotene	Tazorac	0.05%, 0.1% cream	Erythema, dryness, scaling, stinging/burning, pruritus, initially may worsen acne	Local adverse reactions most likely occur in first 2 to 4 weeks of use and will usually lessen with continued use.
		0.05%, 0.1% gel		
	Fabior	0.1% foam		
			Teratogenic	Category X. Use in pregnancy is contraindicated.
			Photosensitivity	Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended.
Adapalene	Differin	0.1% cream	Erythema, dryness, scaling, stinging/burning, pruritus, initially may worsen acne	Local adverse reactions most likely occur in first 2 to 4 weeks of use and will usually lessen with continued use
		0.1%, 0.3% gel		
		0.1% lotion		Less irritation compared to other retinoids.
			Photosensitivity	Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended.

Topical Agents Used in the Treatment of Acne

Drug	Brand	Dosage Form	Adverse Reactions	Comments
Other topical Agents				
Benzoyl peroxide	1%–10%, Various over the counter and prescription products	Lotion, gel, foam, pads	Excessive drying, peeling, erythema, allergic contact sensitization/ dermatitis Bleaching of hair and colored fabric. Photosensitivity	Local reactions are dose dependent. Gradually increase dose as tolerance develops. Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended. Pregnancy Category C
Azelaic Acid	Azelex	20% cream	Erythema, skin irritation	Alternative to benzoyl peroxide. Pregnancy Category B
Clindamycin	Cleocin T Clindagel ClindaMax Evoclin BenzaClin Duac	1% solution, lotion, gel 1% gel 1% gel, lotion 1% foam 1%–5% benzoyl peroxide combination gel 1.2%–5% benzoyl peroxide combination gel	Burning, itching, dryness, erythema, peeling Diarrhea, colitis (pseudomembranous colitis)	Rare cases of colitis have been observed with topical use. Discontinue immediately and seek medical attention if diarrhea occurs. Should be combined with topical benzoyl peroxide.
Erythromycin	ERYGEL Ery Benzamycin	2% gel 2% pad 5%–3% benzoyl peroxide combination gel	Burning, peeling, dryness, pruritus, erythema	Should be combined with topical benzoyl peroxide.
Dapsone	Aczone	5% gel	Dryness, erythema, oiliness, and peeling	Does not have a risk of phototoxicity.

Data from (1) Lexicomp [Internet]. Hudson (OH): Wolters Kluwer Health, Inc.1978-2014 [cited 2014 July 25]. http://online.lexi.com/lco/action/home/switch. (2) Facts & Comparisons eAnswers. St. Louis (MO) 2014: Wolters Kluwer health, Inc. 2014 [cited 2014 July 25]. http://online.factsandcomparisons.com/index.aspx

Oral Agents Used in the Treatment of Acne

Drug	Dosage form (mg)	Dosing Regimen	Adverse Reactions	Comments
Oral Antibiotics				
Tetracycline	250, 500 capsule	250–500 mg twice daily	GI upset, headache, blurry vision, vaginal candidiasis, possible teratogenic risk, tooth discoloration in children Photosensitivity Drug–food interactions	Avoid use in in children < 8 years. Pregnancy Category D. Avoid use in pregnancy. Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended. Take 1 hour before or 2 hours after dairy products, antacids, vitamins, or iron supplements.
Doxycycline	50, 75, 100 tablets and capsules 200 delayed-release tablet	Immediate release: 50–100 mg once or twice daily Extended release: 200 mg once daily	GI upset, headache, blurry vision, possible teratogenic risk, tooth discoloration in children Photosensitivity Drug–food interactions	Avoid use in in children < 8 years. Pregnancy Category D. Avoid use in pregnancy. Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended. Take 1 hour before or 2 hours after dairy products, antacids, vitamins, or iron supplements.
Minocycline	50, 75, 100 immediate-release tablets 45, 55, 65, 80, 90, 105, 115, 135 extended-release tablets 50, 75, 100 immediate release capsules	Immediate release: 50–100 mg twice daily. Extended release: 1 mg/kg daily for 12 weeks.	GI upset, headache, blurry vision, lupus-like syndrome, hepatitis, exfoliative dermatitis, possible teratogenic risk, tooth discoloration in children Photosensitivity Drug–food interactions	Avoid use in in children < 8 years. Pregnancy Category D. Avoid use in pregnancy. Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended. Take 1 hour before or 2 hours after dairy products, antacids, vitamins, or iron supplements.
Erythromycin	250, 500 tablets	250–500 mg twice daily	GI upset, rash, hearing loss, hypersensitivity reactions	Highest incidence of GI intolerance and increasing bacterial resistance. Possible drug interactions: CYP3A4 substrate and P-glycoprotein inhibitor Alternative to tetracyclines. Drug of choice in pregnant women and children < 8 years.
Azithromycin	500 tablet	500 mg per dose 2 to 4 days a week	GI upset, rash, headache, drowsiness	Alternative if other antibiotics cannot be used.
Clindamycin	75, 150, 300 capsules	150–300 mg daily	GI upset, pruritus, rash, vaginitis, pseudomembranous colitis	Alternative if other antibiotics cannot be used. Discontinue immediately and seek medical attention if diarrhea occurs.
Sulfamethoxazole + trimethoprim	400/80, 800/160 tablet	400–800/80–160 mg one to two times daily	GI upset, allergic rash, urticaria, Stevens-Johnson syndrome, possible teratogenicity Photosensitivity	Alternative if other antibiotics cannot be used. Pregnancy Category D. Avoid use in pregnancy. Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended.
Hormonal Agents				

Oral Agents Used in the Treatment of Acne (*Continued*)

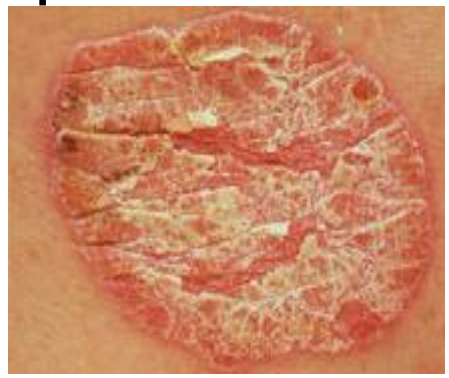
Drug	Dosage form (mg)	Dosing Regimen	Adverse Reactions	Comments
Hormonal Agents				
Oral Contraceptives	Norgestimate/ethinyl estradiol (Ortho Tri-Cyclen) Norethindrone acetate/ethinyl estradiol (Estrostep)	One tablet daily	Nausea, headache, weight gain, breast tenderness, break through bleeding, venous thromboembolism	Not for treatment of acne in men. Use only in females ≥ 15 years of age. Increased risk of venous thromboembolism in women who use tobacco products.
				(Continued)
Spironolactone	25, 50, 100	50–200 mg daily	Menstrual irregularities, breast tenderness, nausea, dizziness, headache, transient diuretic effect, hyperkalemia	Not recommended for treatment of acne in men. Monitor serum creatinine and potassium.
Oral Retinoid				
Isotretinoin	10, 20, 30, 40 tablets	0.5–1 mg/kg/day in two divided doses	Cheilitis, dryness of the nose, eyes, and mouth, peeling, pruritus, and drying of the face and skin, alopecia, acne flair up at start of therapy Teratogenicity Depression/suicidality Musculoskeletal pain Increased serum lipids, creatine phosphokinase, and blood glucose Photosensitivity	Nasal sprays, lip moisturizers, and hard candy may help to reduce drying of mucous membranes. Apply oil-free moisturizers to face to relieve drying of skin. Category X. Contraindicated in pregnancy. Monitor patient closely for changes in mood May use nonsteroidal anti-inflammatory drugs to relieve pain Monitor lipid panel, liver function tests, and blood glucose Minimize exposure to sun light and sun lamps. Sunscreen use and protective clothing recommended.

Monitoring

- Lesion counts should decrease
  - by 10% to 15% within 4 to 8 weeks, or
  - by >50% within 2 to 4 months
- Inflammatory lesions should resolve within a few weeks, and comedones should resolve by 3 to 4 months.
- Monitor for adverse drug effects, if intolerable ….
  - appropriate dose reduction
  - alternative treatments
  - drug discontinuation

Psoriasis

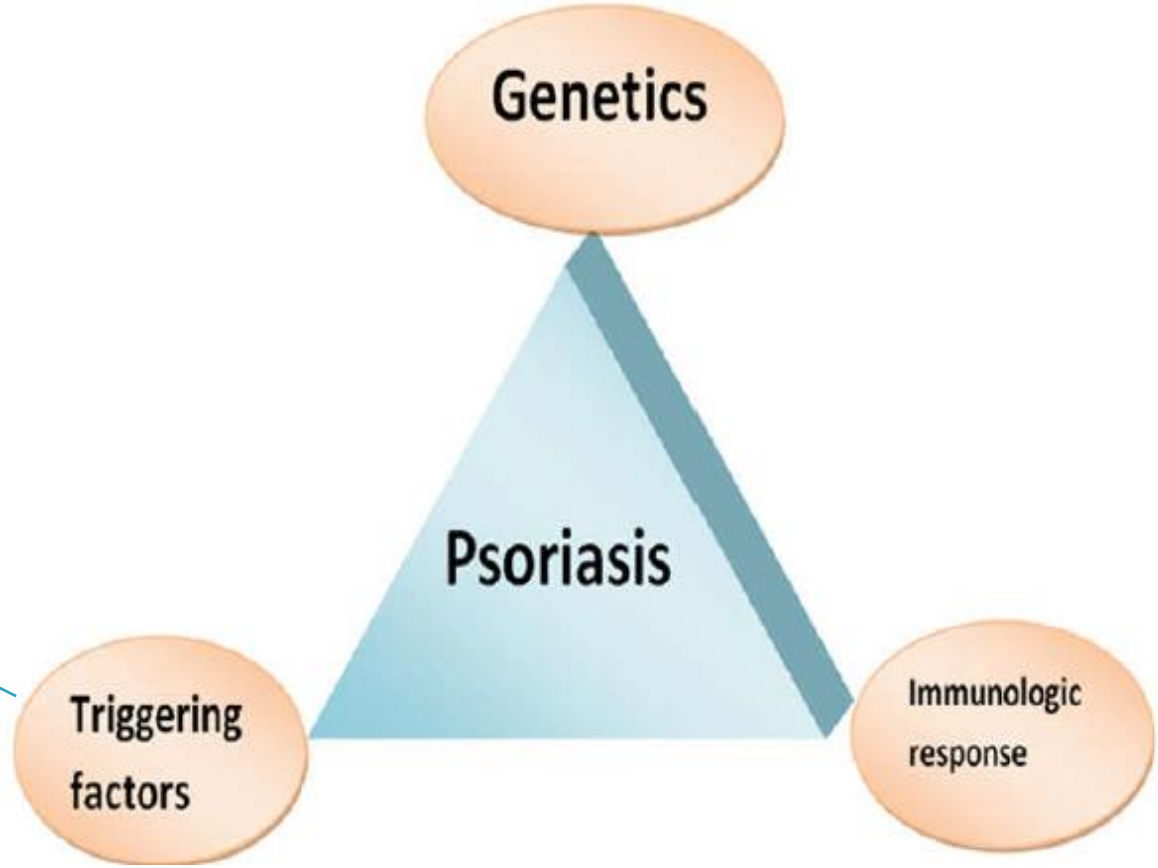
- Psoriasis is a chronic inflammatory skin disorder characterized by thickened, erythematous, sharply demarcated papules and scaling plaques.
- Elbows, knees, and scalp, distal interphalangeal joints and adjacent nails …. commonly involved
- Pruritus may be severe and require treatment
  - to minimize excoriations from frequent scratching



- Chronic relapsing inflammatory dermatoses of polygenic predisposition characterized by sharply demarcated red scaly lesion and disabling joint involvement

Etiology and pathogenesis

- Trauma
- Infections
- Sun light
- Drugs
  - Lithium, Antimalarials, NSAID
    Rapid tapering of steroids
- Endocrine
  - Pregnancy
  - Hypocalcaemia
- Psychogenic (Stress)
- Obesity, alcohol & smoking



Psoriasis ….

- Cytokines, T cells, and keratinocytes are central to the inflammatory process associated with psoriasis
- when keratinocytes are perturbed, the release of antimicrobial peptide LL-37 takes place
  - This peptide binds with DNA and RNA.
- This complex potentially leads to the activation of dendritic cells.
- These activated dendritic cells secrete interleukin IL-12 and IL-13.
- The production of these two interleukins eventually results in IL-17 and T helper cell type 1 differentiation
  - entire process then leads to alteration of the immune system and chronic inflammation that manifests in the skin causing vascular changes and formation of psoriatic lesions

Clinical presentation

Clinical Presentation and Diagnosis of Plaque Psoriasis

General characteristics

Small, discrete lesions to generalized confluent lesions over a large BSA.

Symptoms

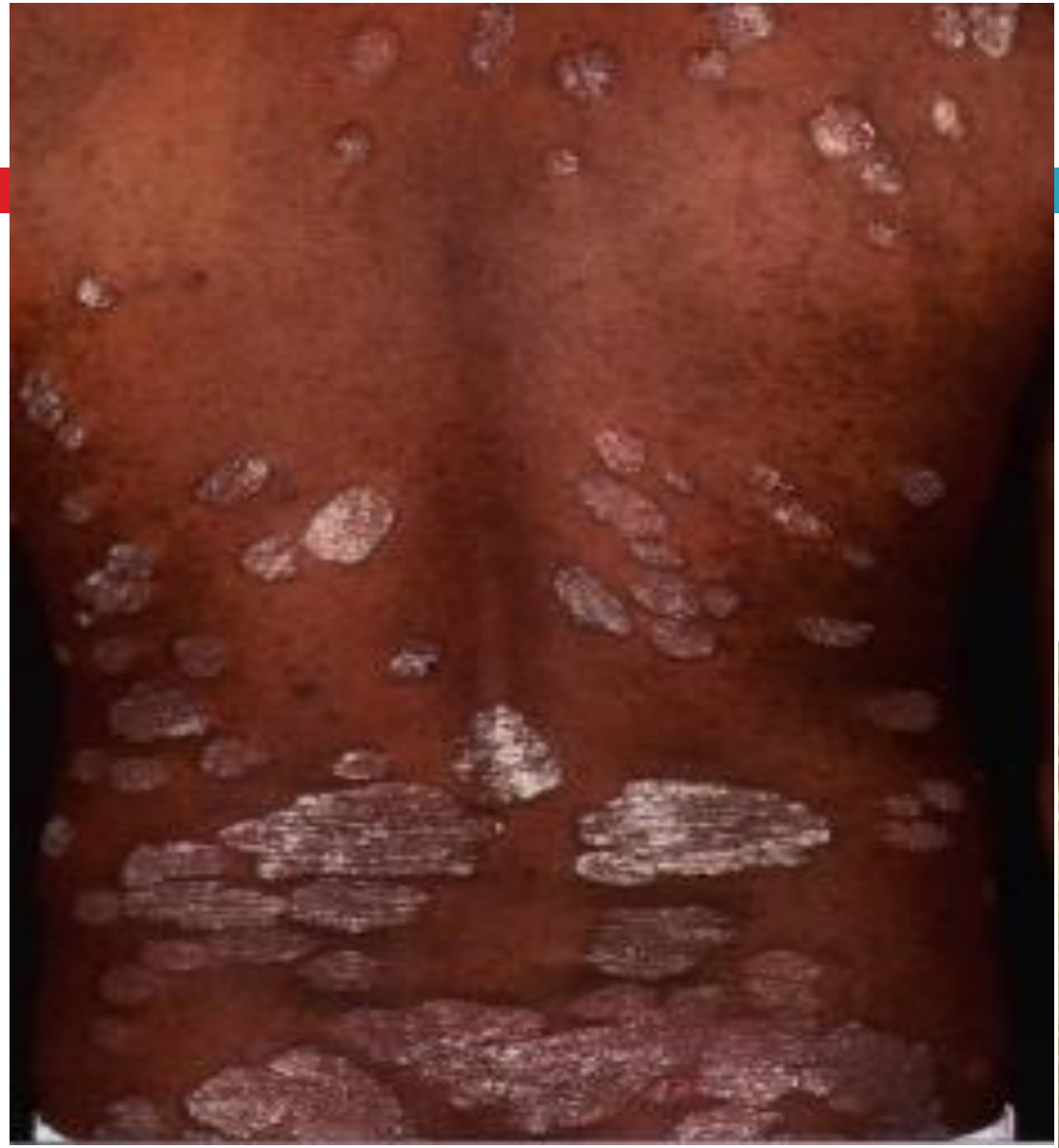
Severe itching.

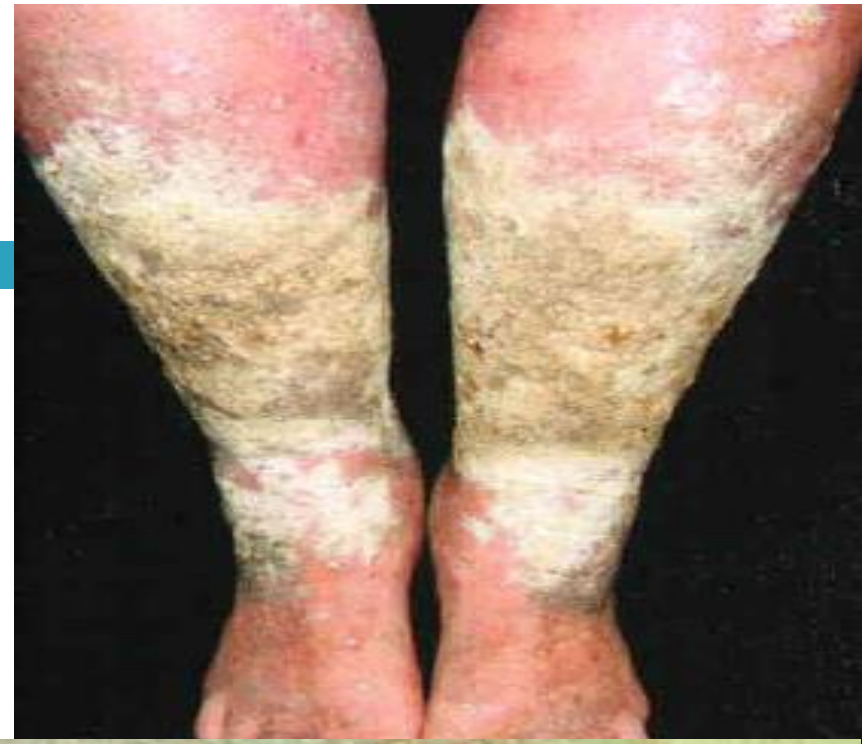
Signs

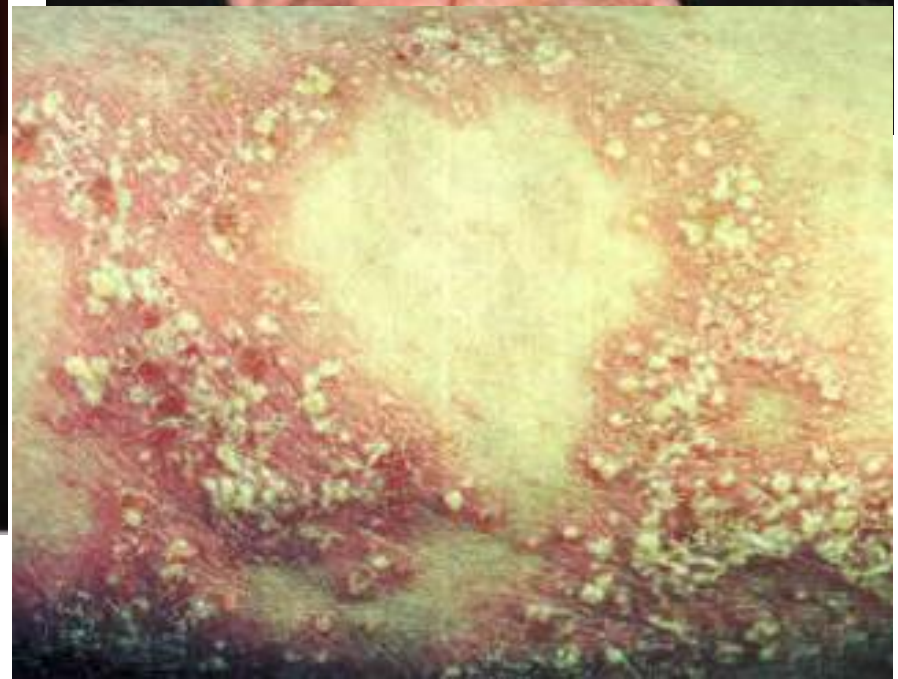
- Raised lesion red to violet or silvery in color (commonly known as plaques).
- Sharply demarcated borders lesions, except where confluent.
- Lesions are loosely covered with silvery-white scales, which if lifted off, show small pinpoints of bleeding (Auspitz sign).
- Plaques show on the elbows, knees, scalp, umbilicus, and lumbar areas, and often extend to involve the trunk, arms, legs, face, ears, palms, soles, and nails.
- Nail involvement presents as pitting, discoloration ("oil spots"), crumbling, splinter hemorrhages, growth arrest lines, or tissue buildup around the nails.

Clinical Presentation and Diagnosis of Other Types of Psoriasis

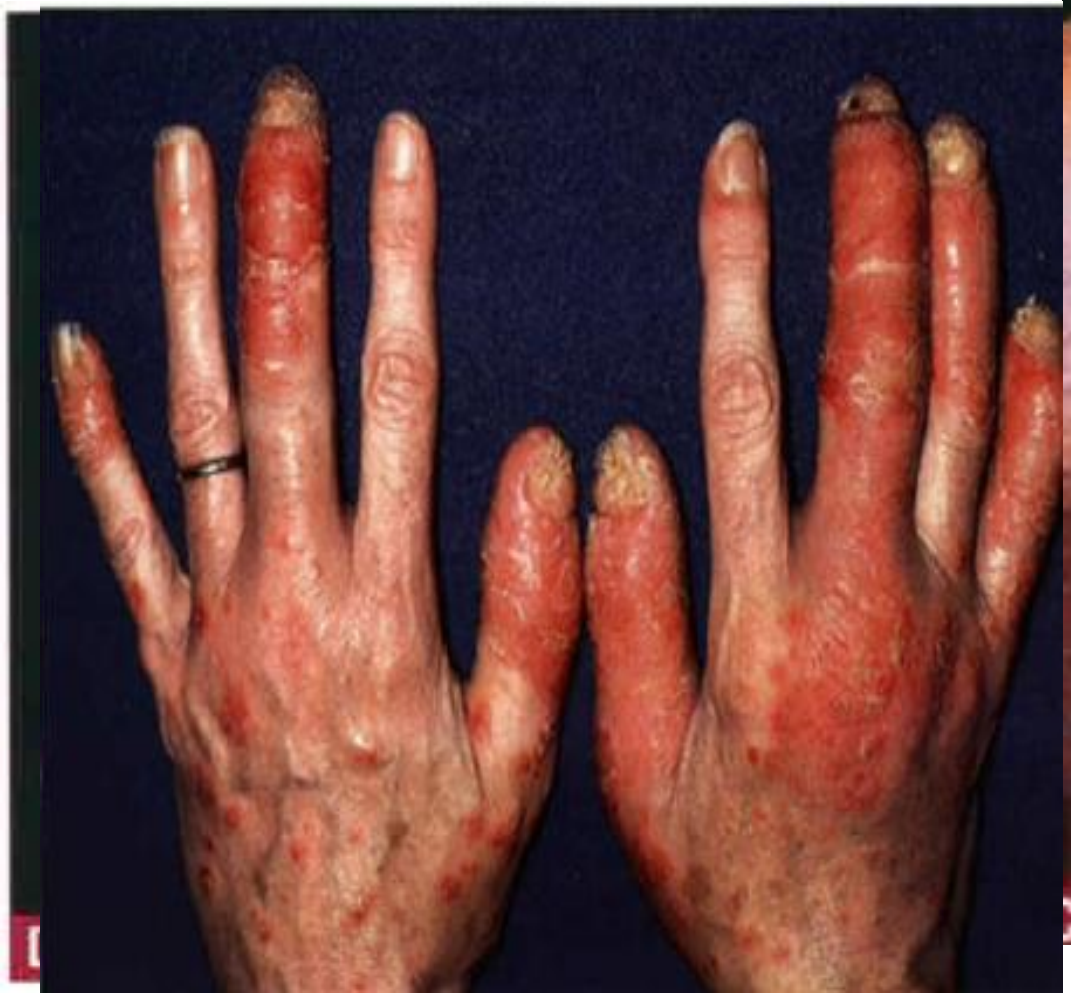
- Flexural psoriasis:
  - Appears in intertriginous area
  - Scaling is minimal
- Guttate psoriasis:
  - Sudden eruption of small, disseminated erythematosquamous papules and plaques
  - Often preceded by a streptococcal infection 2 to 3 weeks prior
- Pustular psoriasis:
  - May be localized or generalized
  - May be an acute emergency requiring systemic therapy. The others are given physical descriptions, but this one is not
- Generalized pustular psoriasis:
  - Disseminated deep-red erythematous areas and pustules
  - May merge to become "lakes of pus"
- Erythrodermic psoriasis: generalized, life-threatening condition
  - Erythema, desquamation, and edema
  - May require life support measures as well as systemic therapy

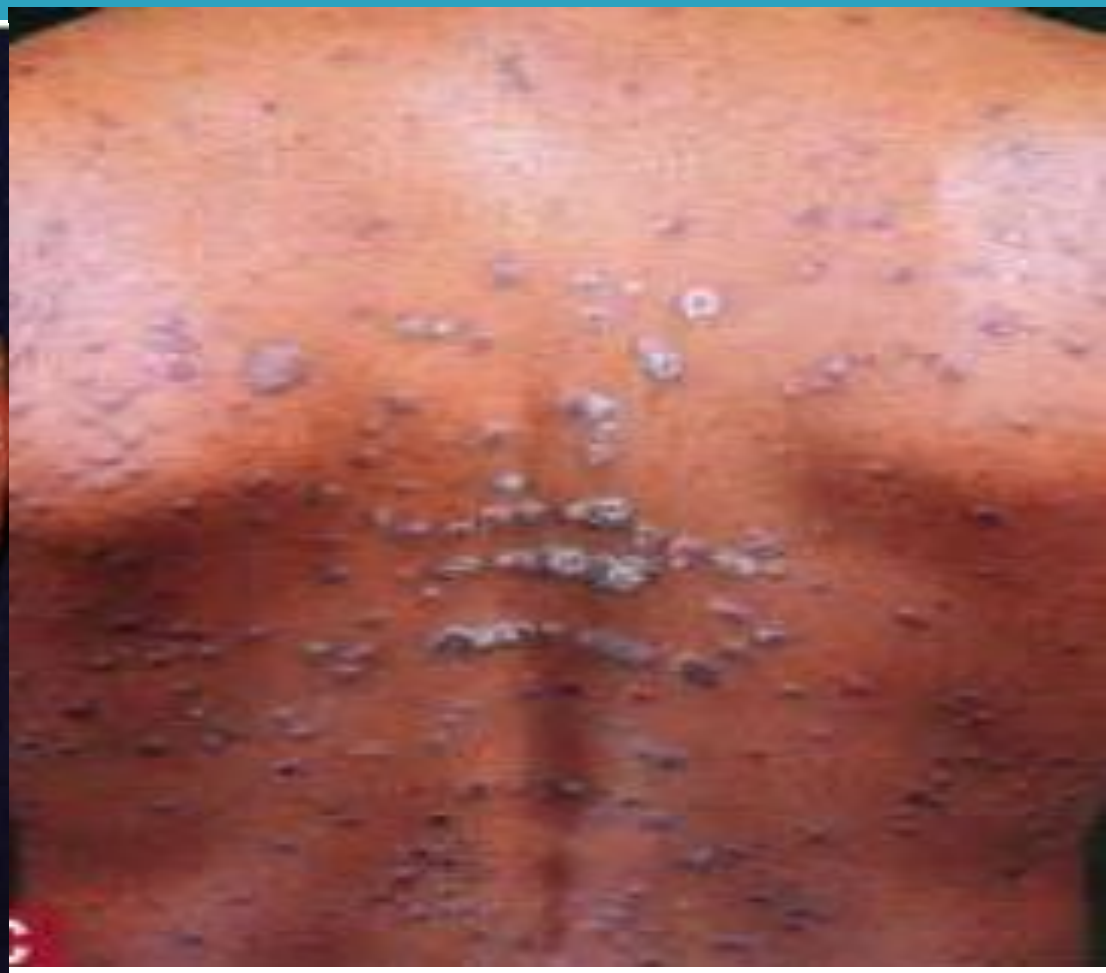






Presentation…





DX

- *Diagnosis of psoriasis is usually based on recognition of the characteristic*
  - *plaque lesion and*
  - *based on lab tests (biopsy).*

Disease Severity Classification[15,18]

Mild or limited disease	Less than or equal to 5% BSA involvement
Moderate disease	PASI greater than or equal to 8 (higher in trials of biologics)
Severe disease	The Rule of Tens: PASI greater than or equal to 10 or DLQI greater than or equal to 10 or BSA greater than or equal to 10% (in some phototherapy trials, BSA greater than or equal to 20% is used as the lower limit

Psoriasis Area and Severity Index (PASI)

Treatment

- Goals of treatment ….
  - Minimize or eliminate skin lesions, reduce frequency of flare-ups
  - alleviate pruritus
  - treat comorbid conditions
  - avoid adverse drug effects
  - provide appropriate counseling (eg, stress reduction)

Treatment ….

- Nonpharmacologic therapy
  - Stress reduction
  - Nonmedicated moisturizers (*Aloe vera*)
    - to maintain skin moisture, reduce skin shedding, control scaling, reduce pruritus
  - Cleansing with moderately warm water, with odor-free cleansers
  - Avoid harsh soaps and detergents
  - Sunscreens

Pharmacologic/Topical therapies

- Corticosteroids
  - have anti-inflammatory, anti-proliferative, immunosuppressive, and vasoconstrictive effects
- Lower-potency products ….
  - for infants
  - for lesions on the face, intertriginous areas, and areas with thin skin.

Topical therapies ….

- Mid to high-potency agents
  - as initial therapy for other areas of the body in adults
- Highest potency corticosteroids
  - for very thick plaques, such as plaques on the palms and soles
- Potency class I CSs …
  - to be used for only 2 to 4 weeks

Topical therapies ….

- Topical corticosteroid potency [class 1-7]
- Class 1: Superpotent
  - Betamethasone dipropionate 0.05% ointment
  - Clobetasone propionate 0.05% cream and ointment
- Class 7: Least Potent
  - Hydrocortisone 0.5%, 1%, 2%, 2.5% cream, lotion, spray, ointment
- Ointments ….the most occlusive & most potent formulations
  - enhanced penetration into the dermis

Topical retinoid

- Tazarotene
  - a topical retinoid that normalizes keratinocyte differentiation, diminishes keratinocyte hyper proliferation, and clears the inflammatory infiltrate in psoriatic plaques.
  - available as a 0.05% or 0.1% gel and cream
  - applied once daily (usually in the evening)

Topical therapies ….

- Adverse effects of tazarotene
  - dose-dependent irritation at application sites, resulting in burning, stinging, and erythema
  - Irritation may be reduced by using;
    - cream formulation
    - lower concentration
    - alternate-day applications
  - It is pregnancy category X

Topical therapies ….

- Calcipotriene
  - a synthetic vitamin D3 analogue, binds to vitamin D receptors
  - inhibits keratinocyte proliferation and enhances keratinocyte differentiation. It also inhibit T-lymphocyte activity
  - Used for mild psoriasis
  - Adverse effects:
    - mild irritant contact dermatitis, burning, pruritus, edema, peeling, dryness, and erythema.
    - It is pregnancy category C

Topical therapies ….

- Coal tar …keratolytic
  - have anti-proliferative and anti-inflammatory effects
  - Formulations … ointments, creams, and shampoos
  - used infrequently due to limited efficacy and poor patient adherence and acceptance.
    - has an unpleasant odor, and stains clothing
  - Adverse effects: folliculitis, acne, local irritation, phototoxicity
  - Low risk of teratogenicity

Topical therapies ….

- Salicylic acid ……keratolytic
  - used in shampoos or bath oils for scalp psoriasis
  - It enhances penetration of topical CSs, thereby increases CS efficacy
  - Systemic absorption and toxicity can occur, ….when applied to greater than 20% BSA
  - should not be used in children
  - may be used for limited & localized plaque psoriasis in pregnancy

Systemic therapies

- Acitretin
  - a retinoic acid derivative and the active metabolite of etretinate
- Retinoids may be less effective than MTX or cyclosporine when used as monotherapy
  - commonly used in combination with topical calcipotriene or phototherapy.
  - Initial dose: 25 or 50 mg
  - better tolerated when taken with meals
  - All retinoids are pregnancy category X ….. teratogenic

Systemic therapies ….

- Cyclosporine
  - a systemic calcineurin inhibitor
  - effective for inducing remission and for maintenance therapy of moderate to severe plaque psoriasis.
  - also effective for pustular, erythrodermic, and nail psoriasis
  - has similar or slightly better efficacy than methotrexate
  - Dose: 2.5 - 5 mg/kg/day given in two divided doses
- Adverse effects
  - nephrotoxicity, hypertension, hypomagnesemia, hyperkalemia, hypertriglyceridemia, gingival hyperplasia

Systemic Therapies ….

- Methotrexate
  - has antiinflammatory effects due to its effects on T-cell gene expression and also has cytostatic effects.
  - more effective than acitretin
  - has similar or slightly less efficacy than cyclosporine
  - Initial dose: 7.5 to 15 mg once weekly, increased incrementally by 2.5 mg every 2 to 4 weeks until response [max dose: 25 mg weekly]

Systemic therapies ….

- Adverse effects of methotrexate…
  - nausea, vomiting, stomatitis, macrocytic anemia, hepatic and pulmonary toxicity
  - Nausea and macrocytic anemia may be reduced by giving oral folic acid 1 to 5 mg daily.
  - pregnancy category X

Systemic therapy with **Biologic Response Modifiers** (BRMs)

- BRMs: used for moderate to severe psoriasis when other systemic agents are inadequate or contraindicated.
- Adalimumab: a monoclonal TNF-α antibody
  - provides rapid control of psoriasis
  - psoriatic arthritis [dose: 40 mg SC every other week]
  - mod-to-severe chronic plaque psoriasis [dose: initially 80 mg, followed by 40 mg every other week starting 1 week after the initial dose]
  - Most common adverse reactions: infections (eg, upper respiratory and sinusitis), injection site reactions, headache, and rash.

BRMs: Biologic response modifiers

Systemic therapy with BRMs ….

- Etanercept
  - a fusion protein that binds TNF-α, competitively interfering with its interaction with cell-bound receptors.
  - It is fully humanized, minimizing the risk of immunogenicity.
- Etanercept is indicated for….
  - psoriatic arthritis [Dose: 50 mg SC once per week]
  - adults with chronic moderate to severe plaque psoriasis.
    - Dose: 50 mg SC twice weekly for 3 months, followed by a maintenance dose of 50 mg once weekly.

Systemic therapy with BRMs ….

- Adverse effects of etanercept ….
  - Local reactions at the injection site
  - Respiratory tract and GI infections
  - Abdominal pain, nausea and vomiting
  - Headaches
  - Rash

Systemic therapy with BRMs ….

- Infliximab
  - a chimeric monoclonal antibody directed against TNF-α
  - indicated for psoriatic arthritis and chronic severe plaque psoriasis
  - Dose: 5 mg/kg as an IV infusion at weeks 0, 2, and 6, then every 8 weeks thereafter
- Adverse effects of infliximab….
  - headaches, fever, chills, fatigue, diarrhea, pharyngitis, and upper respiratory and urinary tract infections.
  - Hypersensitivity reactions (urticaria, dyspnea, and hypotension)

Alternatives

- Mycophenolate mofetil
  - inhibits DNA and RNA synthesis and may have a lymphocyte anti-proliferative effect.
  - oral products …used in moderate to severe plaque psoriasis
    - Dose: 500 mg orally four times daily, up to a maxof 4 g daily
- Hydroxyurea
  - inhibits cell synthesis in the S phase of the DNA cycle
  - sometimes used in refractory severe psoriasis
  - Dose: 1g daily, with a gradual increase to 2g daily as needed and as tolerated

Topical Medications [2,16,17,23,24]

Drug Class	Dosing and Application	Administration Guidelines	Cautions and Side Effects
Corticosteroid	• Mostly once or twice daily • Every other day or weekends only application may be suitable for chronic conditions • Treatment is recommended for 2–3 weeks • Low and intermediate potency can be used up to 3 months	• Intermediate and low potency agents are indicated for acute and mild lesions and tapering is recommended with the lowest dose when the condition improves • Low potency agents are suitable for lesions in infants due to large body surface area and elderly for the sensitive and thin layer of the skin • High and very high potency agents are indicated for chronic and severe lesions • Palms and soles of the skin require high and very high potency agents to maximize absorption and penetration due to the thickness of the skin	• Skin irritation • Dryness • Withdrawal effects
Vitamin D analogues	Mostly once or twice daily for a maximum of 2 months for effective result	• Recommended to be used with topical steroids to speed up the healing process • Considered less toxic than topical steroids • Combination therapy with steroids has shown to be more effective than the single agent • Onset of action is slow • Avoid calcipotriene use with salicylic acid due to instability of calcipotriene	• Pruritus • Skin irritation on facial area and skin folds • Skin irritation is less with Calcitriol • Skin Rashes • Burning • Changes in systemic vitamin D levels
Retinoids	Preferred as once daily at bedtime	• Best used to achieve better efficacy results with high potent steroids or UVB phototherapy	• Skin irritation • Pruritus • Dryness • Photosensitivity
Calcineurin inhibitors	Mostly once or twice daily depending on the product until effective result is observed	• Comparison data to other agents or in combination is lacking • Use with salicylic acid for 8 weeks showed efficacy improvement in facial lesions	• Skin irritation • Pruritus • Photosensitivity • Risk of malignancy
Other agents **Salicylic acid** **Coal tar** **Anthralin**	As directed	• Decreases the scaling of the skin lesion to allow application of other agents • Infrequent use of Tars and anthralins due to irritation and stain	• Skin irritation • Potential salicylic acid toxicity through nausea and ringing in ears

Systemic Agents[17,28,41]

Drug	Mechanism of Action	Doses and Administration	Dosage Forms	Adverse Effects	Therapeutic Efficacy on PASI 75	Therapeutic Application	Therapeutic Monitoring
Immunosuppressants							
Cyclosporine	An immunosuppressive agent that specifically inhibits helper T cell and keratinocyte activation and proliferation	2.5 mg/kg/day in two divided doses for at least 4 weeks This dose may be subsequently titrated and increased by 0.5 mg/kg/day every 2 weeks until there is control of plaques	Oral and IV solution	Nephrotoxicity, lowering of seizure threshold, tremor, gingival hyperplasia, hypertension, squamous cell carcinoma (cutaneous)	~41%–71%	First-line agent	-LFTs (Baseline and routine) -SCR, BUN -CBC -Uric acid -Blood pressure -Drug interaction with cytochrome P-450 substrate and inhibitors -pregnancy
Methotrexate	Folic acid antagonist Act by interfering with purine synthesis, thus inhibit DNA synthesis and cell replication	-7.5 to 10 mg weekly -2.5 mg Q12 hours times 3 doses	Oral and Injectable	Nausea, vomiting, stomatitis, fatigue, hepatotoxicity, bone marrow suppression, pulmonary fibrosis	24%–60%	First-line agent	-CBC -SCR, BUN -LFTs (baseline and Q 4 weeks) -Pregnancy category X
Oral Retinoids							
Acitretin	Stimulates differentiation and normalizes epidermal cell proliferation	10–50 mg/day	Oral capsule	Myalgia, hair loss, hepatotoxicity, pancreatitis	70%–75%	Second-line agent	Lipids -CBC -SCR, BUN (baseline and every 3 months) -Pregnancy category X

thanks ...