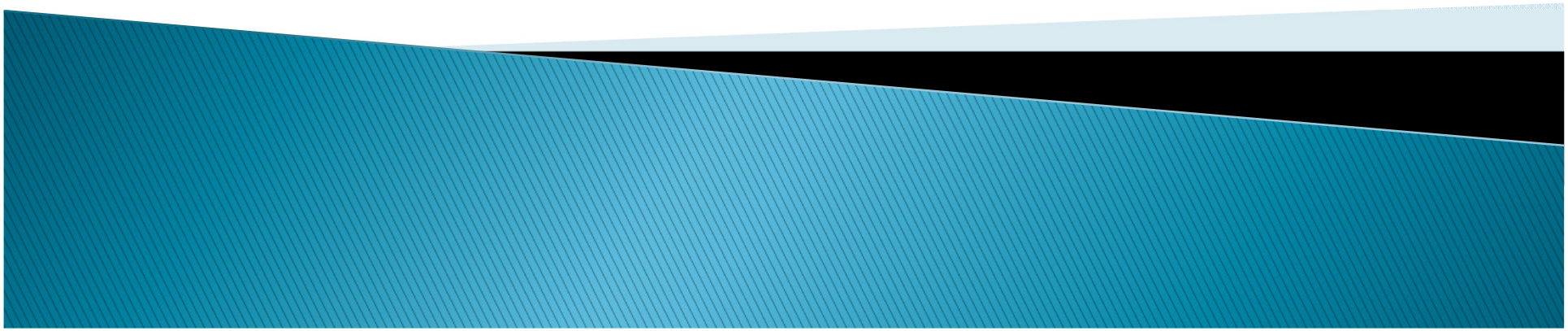
Skin conditions

Dr Noluthando Nematswerani
Department of Pharmacology

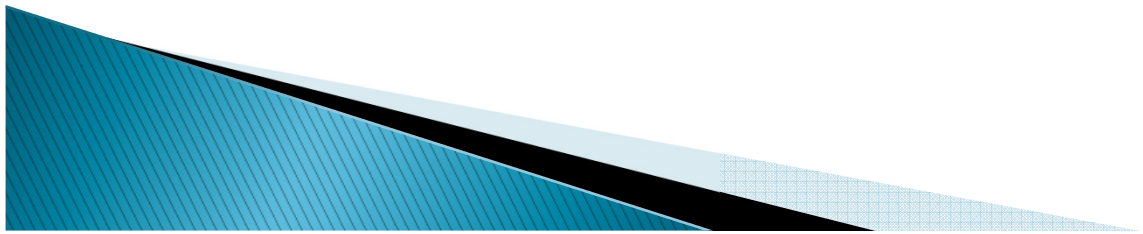


Skin conditions

- They account for 2% of consultations in GP
- Important to make correct diagnosis
- Adverse reactions to topical or systemic drugs produce a wide variety of skin lesions

Skin conditions

- Acne
- Alopecia and hirsutism
- Dermatitis (eczema)
- Psoriasis
- Urticaria
- Superficial bacterial skin infections
- Fungal and nail infections
- Viral skin infections
- Adverse drug reactions involving the skin



Acne

- Acne vulgaris is one of the most common skin disorders
- Affects 80–90% adolescents
- In approximately 60% of cases, acne is a self-limiting condition that can be managed with combination treatment followed by topical maintenance therapy
- Associated with *Propionibacterium acnes* infection of the sebaceous glands

Pathogenesis

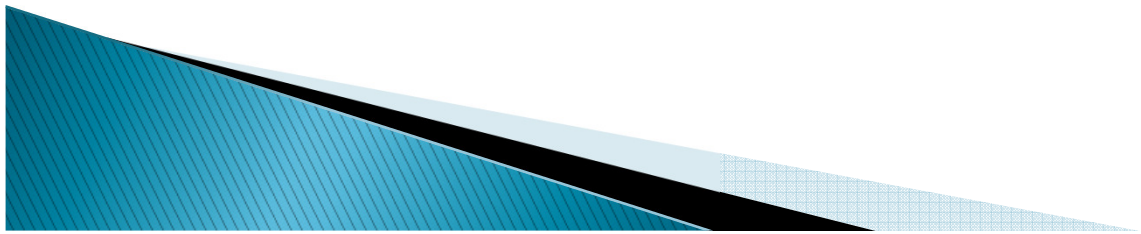
- Follicular epidermal hyperproliferation and subsequent plugging of the follicle
- Excess sebum production
- Presence and activity of *Propionibacterium acnes*
- Inflammation

Presentation

- Comedones
- Papules
- Pastules
- Nodules
- Cysts
- Scarring

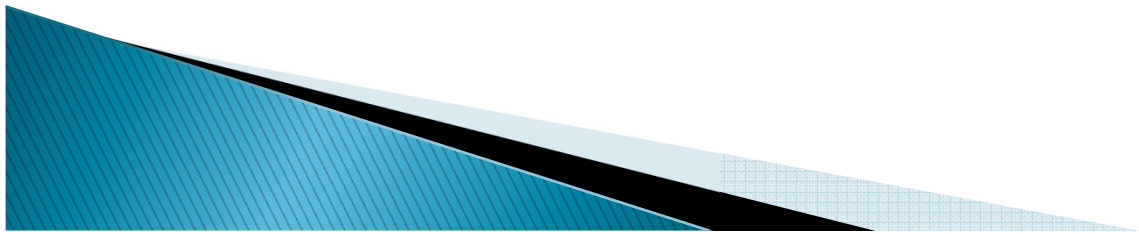
Areas involved

- Face, chest, back and arms

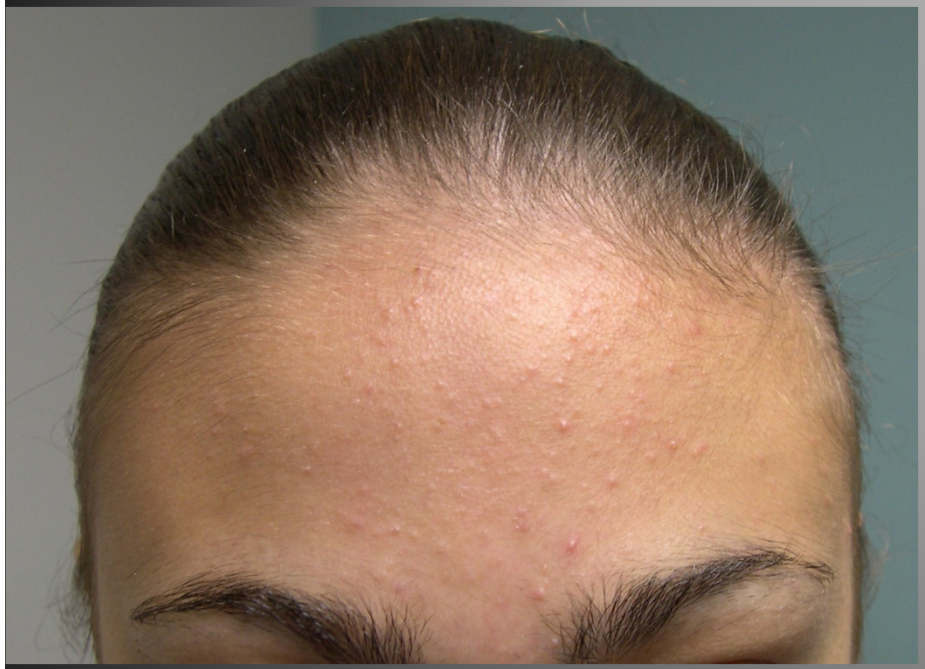


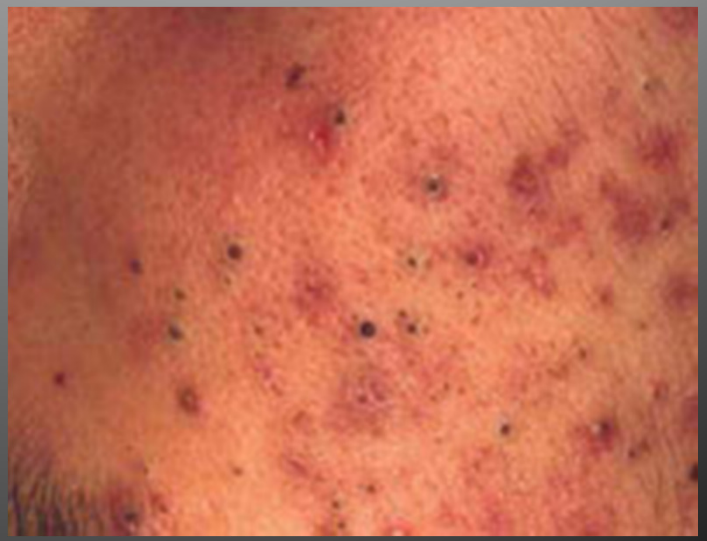
Types

- Comedonal
  - White heads and black heads
- Papulopastular
  - Papules and pustules
- Nodulocystic
  - Nodules and cysts

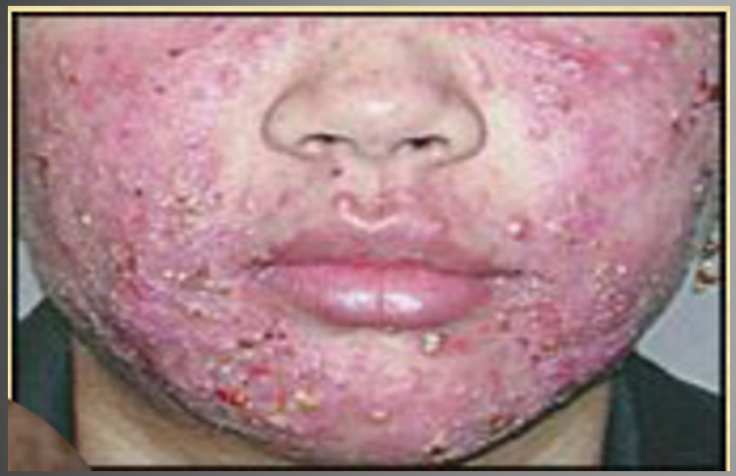


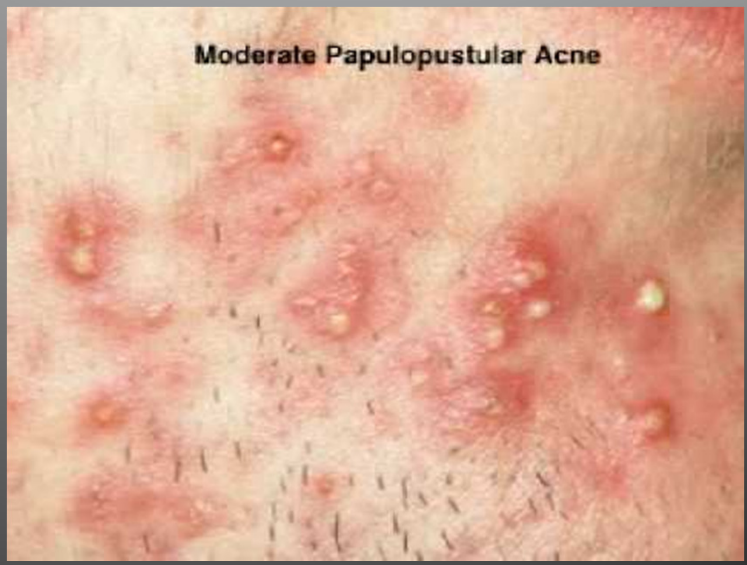
Comedonal



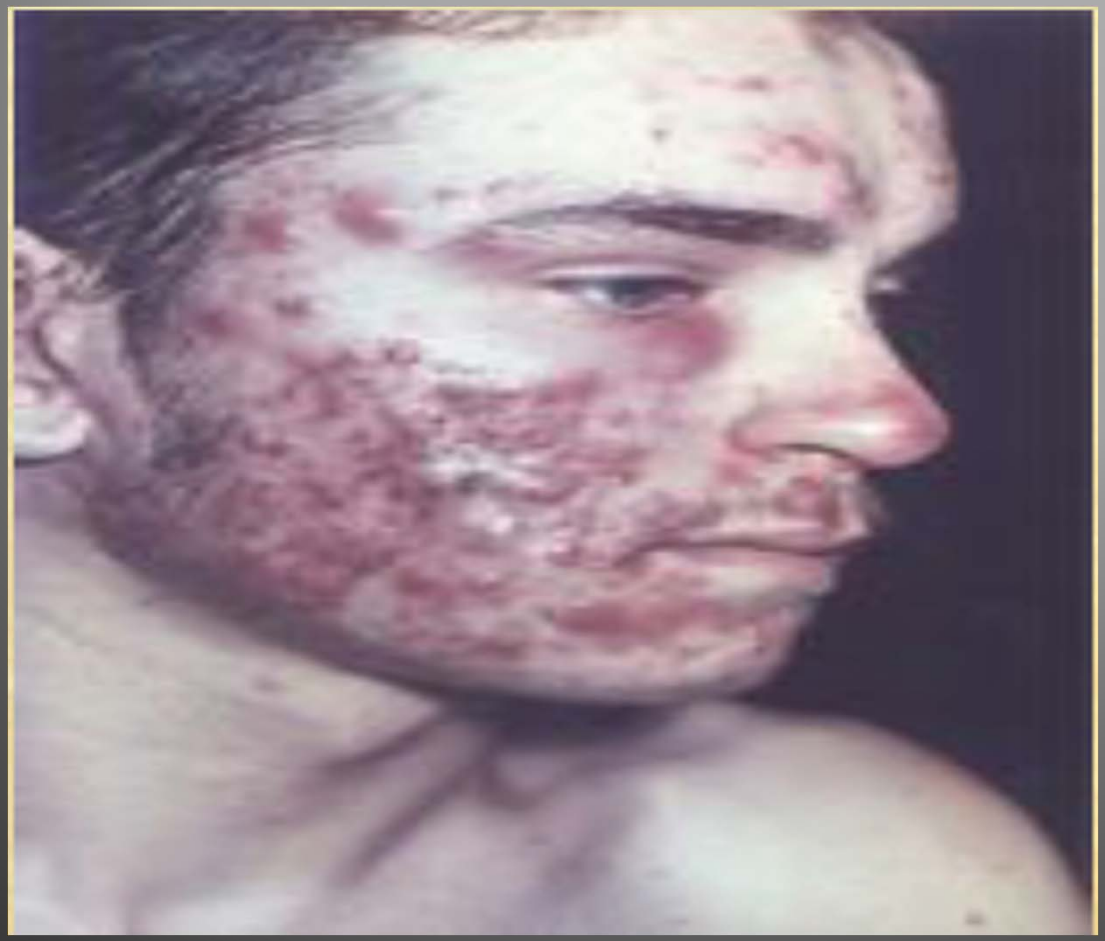


Papulopastular





Nodulocystic

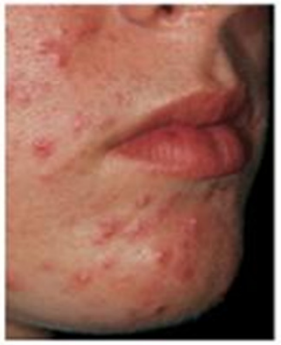


Acne Classification

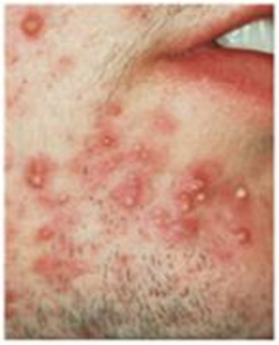
Mild acne: few to several papules/pustules (generally <10) and no nodules

Moderate acne: several to many papules/pustules (10 to 40) along with comedomes (10-40) and few to several nodules

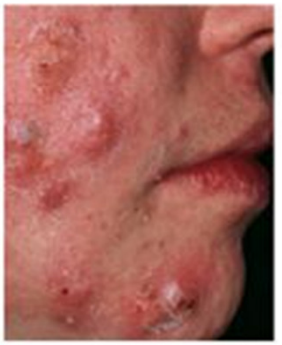
Severe acne: numerous or extensive papules/pustules and many nodules



MILD



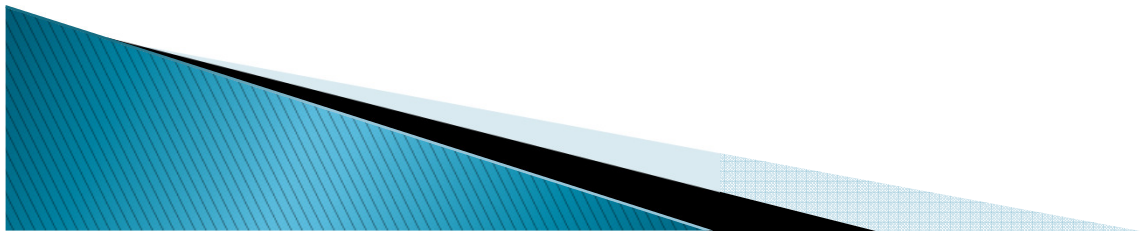
MODERATE



SEVERE

Goals of Treatment

- Correct the abnormal follicular keratinization
- Decrease sebaceous gland activity
- Decrease follicular bacteria
- Inhibit the production of extracellular inflammation



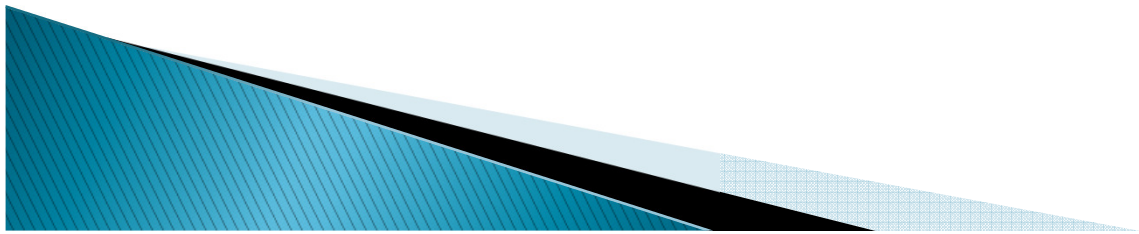
Drug therapy

Topical (mild-to-moderate acne)

- Benzoyl peroxide
- Antibiotics
- Retinoids
- Azelaic acid

Systemic (moderate-to- severe acne)

- Antibiotics
- Isotretinoin
- Hormonal therapy
- Spironolactone



Benzoyl peroxide

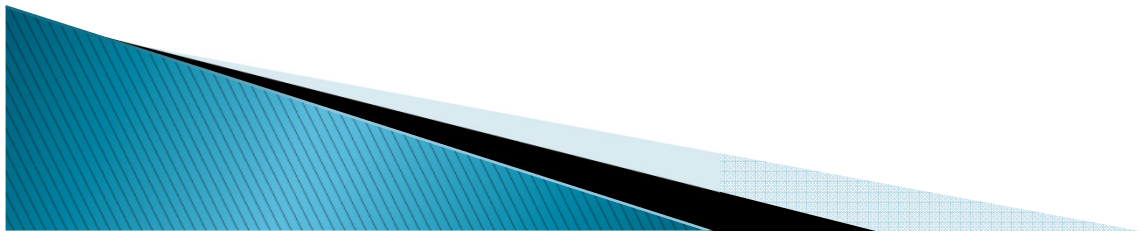
- Keratolytic, anti-inflmammatory
- Antimicrobial agent destroying surface and ductal bacteria
- Reduses follicular hyperkeratosis- mused on non-inflammatory lesions
- It is lipophillic- penetrates pilosebaceous duct
- Efficacy is largely against superficial inflammatory lesions
- No effect on sebum production
- Used in combination with other agents e.g. topical retinoids, topical antibiotics
- Resistance develops when used as monotherapy
- Formulations (2.5, 4, 5 and 10%), available over the counter
- Unwanted effects: Irritant dermatitis -reduce freqeuncy of applications, subsides as treatment continues.
- Can bleach hair and clothing

Topical Antibiotics

- Examples: Clindamycin, erythromycin, tetracycline
- Reduce inflammatory lesions
  - Antioxidant effect on leukocyte chemotaxis
  - Suppress proinflammatory free fatty acids and surface lipids
- Some effect on non-inflammatory lesions- reduce perifollicular lymphocytes involved in comedogenesis
- Topical clinda and erythro as effective as benzoyl peroxide
- Topical Tetracycline least effective
- Increasing worldwide emergence of bacterial resistance to *P. acnes* – erythro (47%), clinda (41%), tetra(18%)

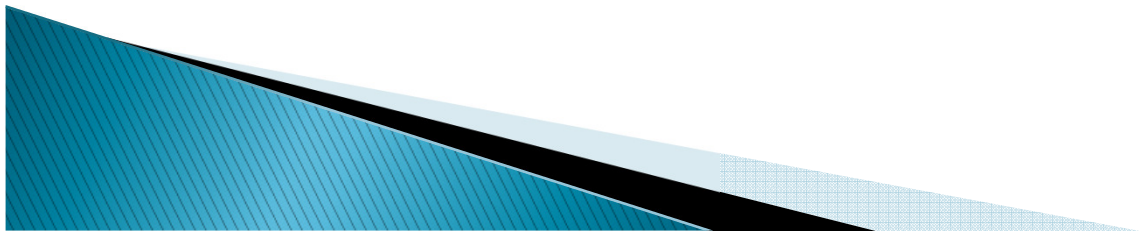
Topical Retinoids

- Examples: Retin A cream and gel, Adapalene (Differin gel)
- Keratolytic and anti-inflammatory
- Retinoinds reduce abnormal growth and and development of keratinocytes within the pilosebaceous unit
- Reverse hypercornification within the follicular canal
- Induction of accelerated proliferation of the follicular epithelium helps to unplug the follicle
- Can produce irritant dermatitis (dryness, scaling, erythema, burning, irritation) and photosensitivity
- Are applied at night



Azelaic Acid

- 20% cream
- Antiinflammatory
- Treats postinflammatory hyperpigmentation caused by deep-seated nodular inflammatoey lesions
- No effect on sebum production
- Well tolerated but can cause mild cutaneous irritation

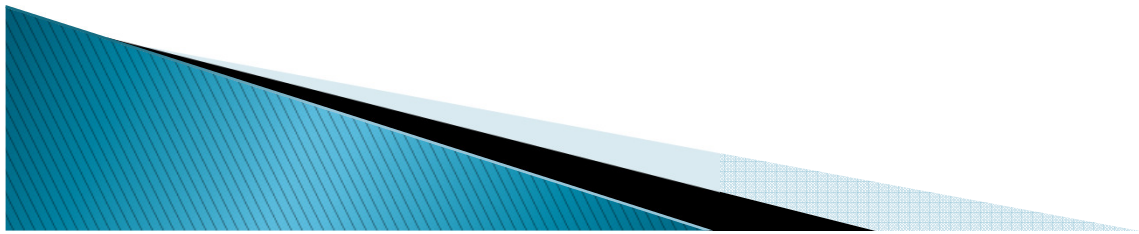


Combination Topical Therapy

- Offer superior clinical imporvement, reduce development of resistance to *P.acnes*
  - Topical retinoid + topical or oral antibiotic
  - Topical antibiotic plus zinc or 5% benzoyl peroxide

Systemic antibiotics

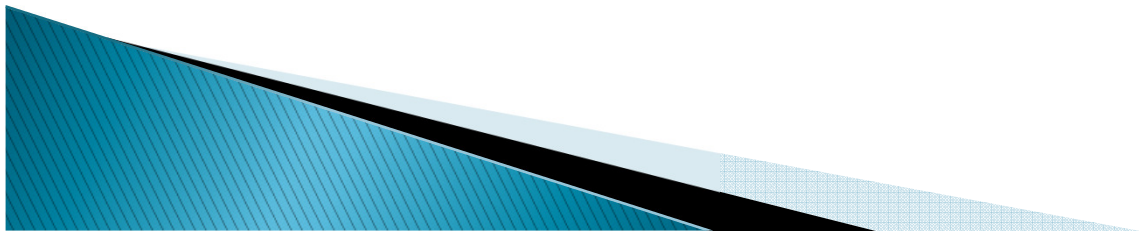
- Indicated for severe inflammatory acne, extensive truncal acne and moderate facial acne not responding to topical therapies
- Response is variable (favourable response for females with facial acne compared to males with marked seborrhoea and truncal acne)
- They exert effects that are independent of their antibacterial actions, mainly anti-inflammatory.
- They reduce numbers of *P.acnes, staph epidermis,* and pro-inflammatory mediators
- Should be prescribed in an adequate dosage and the frequency and duration only continued for as long as they are deemed to be working



Systemic antibiotics

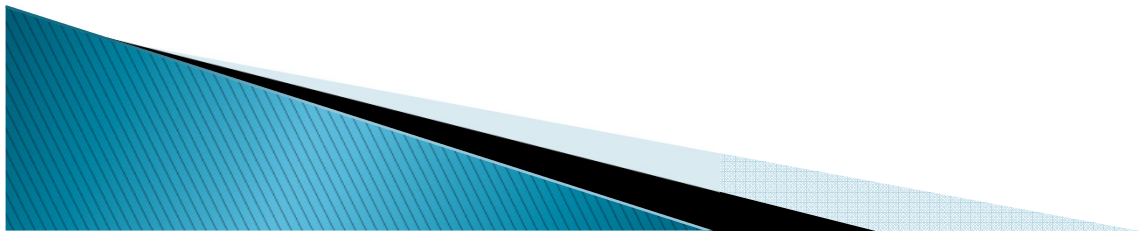
- Examples:
  - Cyclines (1st line)
    - Oxytetracycline (poor compliance)

    Second generation
    - Lymecycline
    - Doxycycline
    - Minocycline (poor side effect profile)
  - Trimetroprim (no licence) –third line
  - Clindamycin (diarrhoea is a problem) – psuedomembranoeous colitis



Hormonal Therapies

- Increased sebum production owing to androgens acting at the sebaceous follicle is a prerequisite for acne in all patients
- Hormone therapies are most effective in adult females with persistent facial inflammatory papules and nodules.
- They act by opposing the effects of androgens on the sebaceous gland, and, to a lesser extent, the follicular keratinocyte
- Examples:
  - Combined oral contraceptives (COC)
  - Androgen receptor blockers (cyproterone acetate – Diane 35)
  - Gonadotrphin –releasing agonist



Isotretinoin

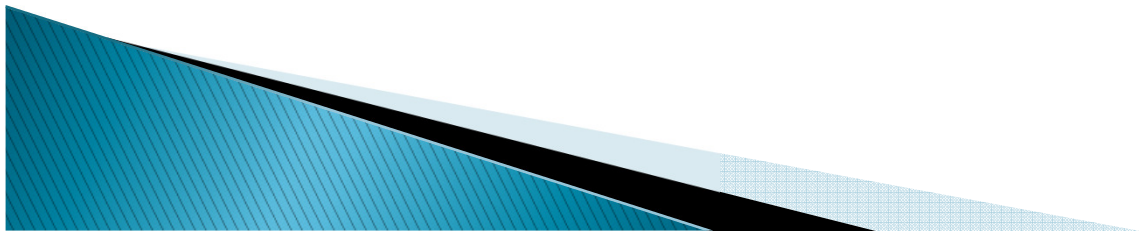
- Synthetic Vitamin A analog
- For moderate or severe recalcitrant acne
- The only treatment that has an effect on all 4 major pathogenic factors.
  - Decreases the size and secretion of the sebaceous gland
  - Normalises follicular keratinization & prevents comedogenesis
  - Inhibits growth of surface and ductal *P.acnes*
  - Has anti-inflammatory effects
- Most clinically effective anti-acne therapy available.
- Produces long-term remission or significant improvements in many patients
- 85% of patients who receive a dose of 0.5-1.0 mg/kg/day are virtually clear of all of their acne by 16 weeks

Isotretinoin

- Metabolized by P450 enzyme system
- Oral tetracyclines should be avoided with isotretinoin as both can cause raised intracranial pressure
- Approximately 6% of patients will experience a moderate-to-severe flare in their acne during the first few weeks of treatment.
- Most significant adverse event associated with the administration of isotretinoin is teratogenicity (no pregnancy a month before starting, during therapy and a month after stopping treatment)

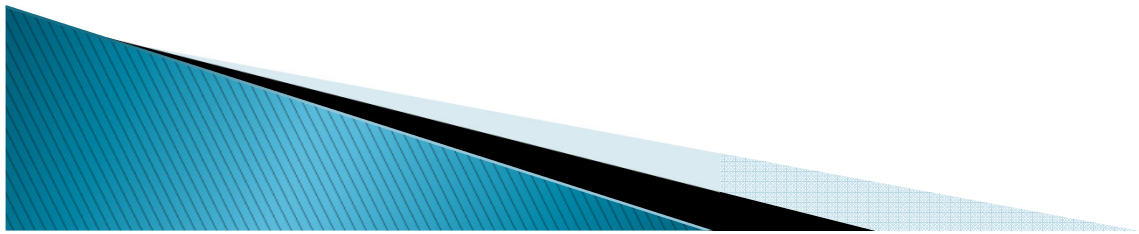
Adverse effects

- Mucocutaneous dryness is the most common problem, including chelitis, facial and irritant dermatitis, vestibulitis and blepharoconjunctivitis
- Adverse psychiatric events including mood changes, depression and suicidal ideation have been reported in acne patients taking isotretinoin
- Elevations in lipids and liver function tests are observed in almost all patients and rapidly return to pretreatment levels after therapy has stopped.A baseline assessment is essential



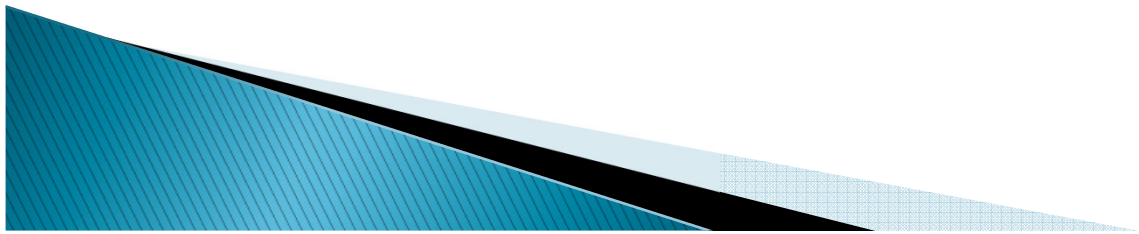
Alopecia and hirsutism

- Androgenic baldness
  - Minoxidil sulphate (acive metabolite of minoxidil)
  - Has a mitogenic effect on hair follicles
  - Adverse effects : local itching and dermatitis
  - In women: cypreterone acetate combined with ethinylestradiol prevent progression of androgenic alopecia



Dermatitis

- Atopic dermatitis / Atopic Eczema
- Seborrhoeic dermatitis
- Contact dermatitis



Atopic Eczema

- Atopic dermatitis can have a significant impact on morbidity and quality of life.
- Children may be affected by itching and associated sleep disturbance, the social stigma of a visible skin condition, and the need for frequent application of topical medications and physician visits.
- Children with atopic dermatitis lose an average of 1.9 hours of sleep per night, and
- Their parents lose an average of 2.1 hours per night.

Atopic eczema

- Frequent problems:
  - irritability,
  - daytime tiredness,
  - dependence,
  - fearfulness,
  - and mood changes

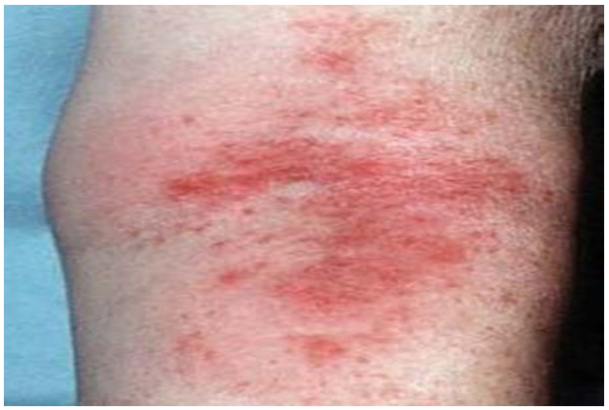


TABLE 1
Clinical Features of Atopic Dermatitis

Essential features*

Pruritus

Eczema (acute, subacute, chronic)

- Typical morphology and age-specific patterns (i.e., facial, neck, and extensor involvement in children; current or previous flexural lesions in any age group; sparing of groin and axillary regions)
- Chronic or relapsing history

Important features†

Onset at early age

Atopy

- Personal or family history
- Immunoglobulin E reactivity

Xerosis

Associated features‡

Atypical vascular responses (e.g., facial pallor, white dermatographism, delayed blanch response)

Keratosis pilaris, hyperlinear palms, and ichthyoses

Ocular or periorbital changes

Other regional findings (e.g., perioral changes, periauricular lesions)

Perifollicular accentuation, lichenification, and prurigo lesions

NOTE: *An atopic dermatitis diagnosis depends on excluding conditions such as scabies, seborrheic dermatitis, allergic contact dermatitis, ichthyosis, cutaneous lymphoma, psoriasis, and immunodeficiency disorders.*

*—*Essential features must be present for an atopic dermatitis diagnosis.*

†—*Important features are seen in most patients, supporting the diagnosis.*

‡—*Clinical associations help to suggest the diagnosis but are too nonspecific to define or detect atopic dermatitis in research or epidemiologic studies.*

Adapted with permission from Eichenfield LF, Hanifin JM, Luger TA, Stevens SR, Pride HB. Consensus conference on pediatric atopic dermatitis. J Am Acad Dermatol 2003;49:1088.

Atopic eczema

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Emollients are the mainstay of maintenance therapy for atopic dermatitis.	B	3, 4, 10
Topical corticosteroids should be first-line treatments for patients with atopic dermatitis flare-ups.	A	3, 4, 11
Sedating antihistamines are indicated for the treatment of atopic dermatitis when patients have sleep disturbances and concomitant allergic conditions.	A	11, 13
Antibiotics should be reserved for the treatment of acutely infected lesions associated with atopic dermatitis.	A	4
Topical calcineurin inhibitors should be second-line treatments for atopic dermatitis flare-ups and maintenance.	A	25

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 453 or http://www.aafp.org/afpsort.xml.

TABLE 4

Appropriate Quantity of Topical Corticosteroids for the Treatment of Atopic Dermatitis

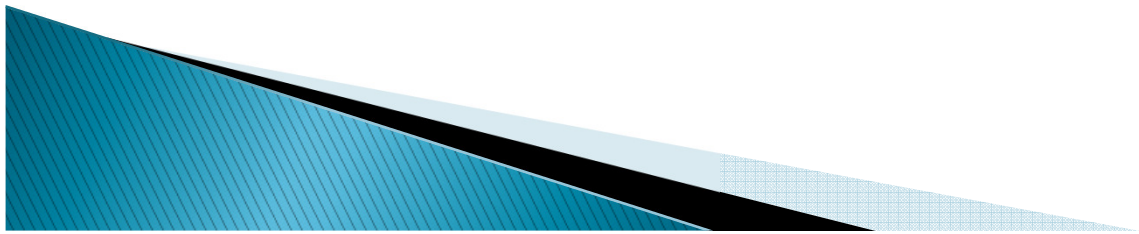
	Amount of topical corticosteroid required (g)		
Anatomic site	*Infants*	*Children*	*Adults*
Face and neck	10	15	30
Hand	5	7.5	15
Arm	10	15	30
Leg	20	30	60
Body	100	150	300

NOTE: *These quantities represent the amount of cream needed for a 10-day treatment course with twice-daily application.*

Information from references 14 through 16.

Emollients

- Emollients are the mainstay of maintenance therapy for atopic dermatitis.
- Should be applied once or twice daily to prevent skin dryness and irritation
- Liberal amounts of a lubricant or emollient cream should be applied to the skin immediately after bathing.



Topical Steroids

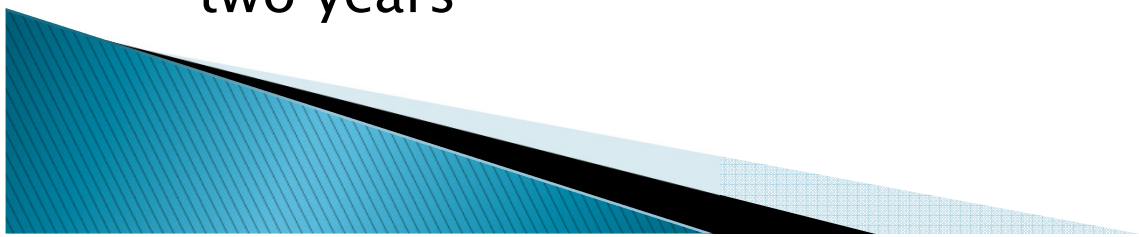
- Topical steroids are currently the mainstay of treatment. In association with moisturization, responses have been excellent.
- Ointments generally are more potent than creams but may have a greasy appearance.
- Ointments should be avoided on open or oozing lesions and in intertriginous folds.

  They also should not be used in hot, moist climates.
- Creams may contain preservatives that can precipitate

  contact dermatitis.
- Lotions generally lack the hydrating properties necessary for treating atopic dermatitis

Topical calcineurin Inhibitors

- Calcineurin inhibitors (e.g. tacrolimus) are immunosuppressant agents originally developed for systemic administration to prevent allogeneic transplant rejection.
- They inhibit calcineurin in the skin, which blocks early T-cell activation and the release of cytokines.
- A meta-analysis demonstrated that tacrolimus 0.1%is as effective as potent corticosteroids and more effective than mild topical corticosteroids in the treatment of atopic dermatitis.
- The most common local adverse effects are skin burning and irritation.
- Patients should be on adequate sun protection
- Risk of malignancy, should avoid longterm use in all patient populations and limits use to children older than two years

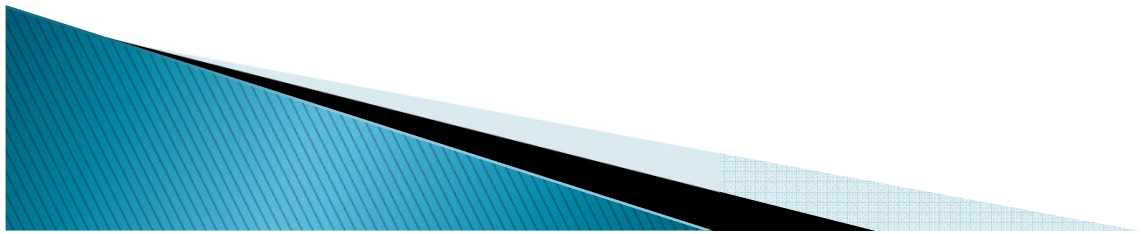


Systemic Therapy

- Rarely indicated
- Systemic corticosteroids are effective at acutely controlling atopic dermatitis in adults, but their use should be restricted to the short term.
- Agents such as cyclosporine (Sandimmune) and interferon gamma-1b (Actimmune) may be effective for severe atopic dermatitis
- Data on the use of mycophenolate mofetil (Cellcept), azathioprine (Imuran), and intravenous immune globulin (human; Baygam) are conflicting, and there is no evidence to support the use of leukotriene inhibitors, methotrexate, desensitization injections, theophylline, or oral pimecrolimus

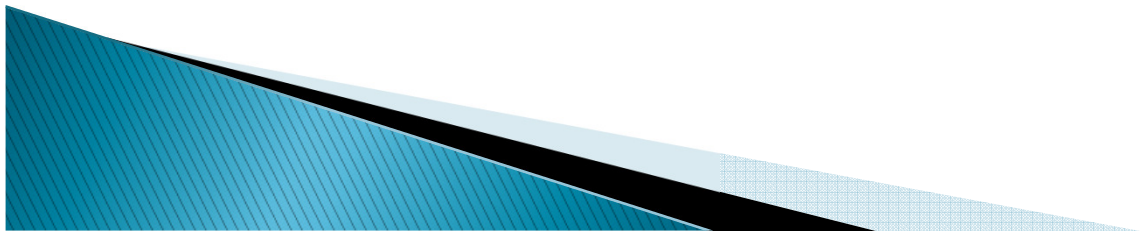
Other therapies

- Ultraviolet (UV) phototherapy using UVB, narrow-band UVB, UVA, or psoralen plus UVA may be beneficial for the treatment of severe disease if it is used appropriately, depending on the patient's age



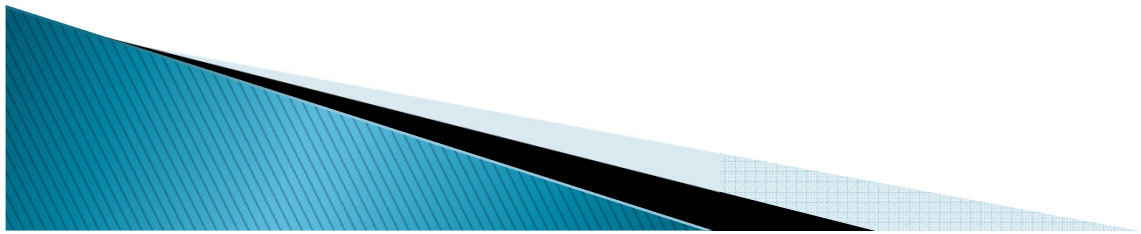
Antihistamines

- The use of sedating and nonsedating antihistamines to treat pruritus associated with atopic dermatitis has been shown to be ineffective when compared with placebo



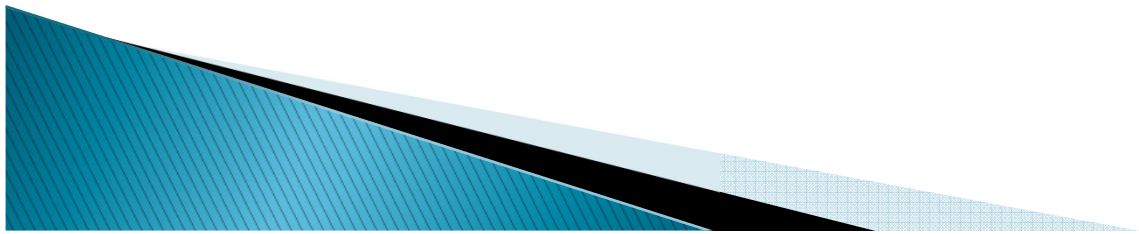
Psoriasis

- Psoriasis is a common, chronic, inflammatory, multisystem disease with predominantly skin and joint manifestations
- Approximately 80% of patients with psoriasis have mild to moderate disease,whereas20% have moderate to severe disease



Presentation

- Traditional plaques are by far the commonest presentation
- Inverse psoriasis affects intertriginous areas such as the breasts, groin, axillae, and intergluteal clefts

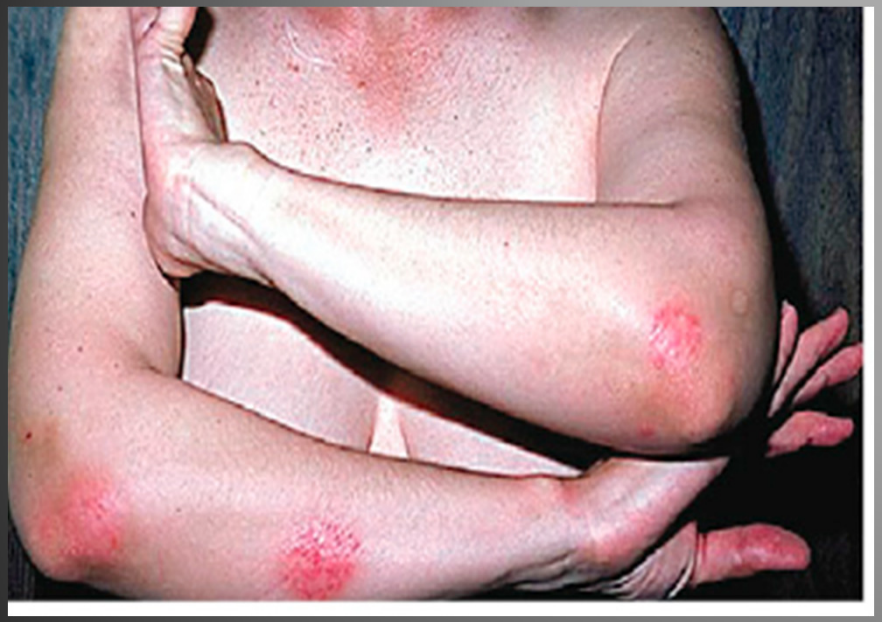


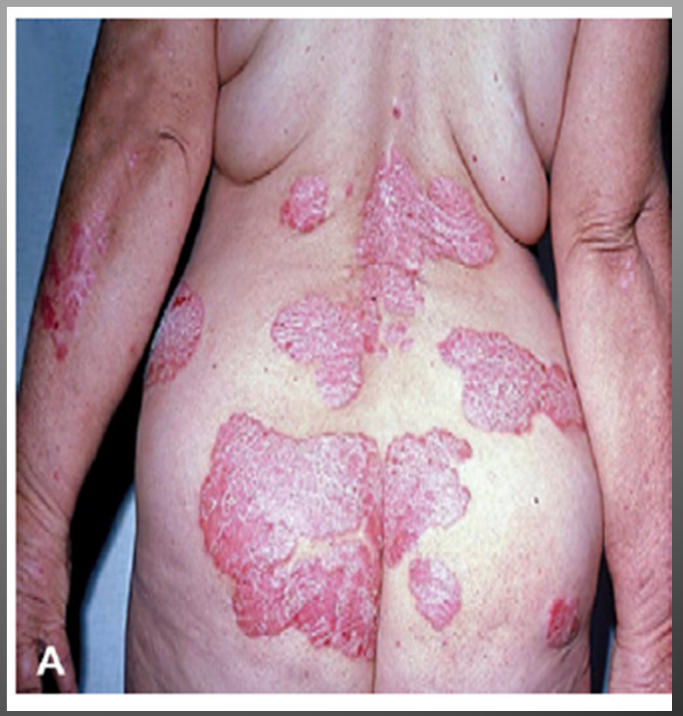
Severity

- The severity of psoriasis is defined not only by extent of body surface area (BSA) involvement
  - <5% being considered mild,
  - ≥5% but<10% moderate,
  - and ≥10% severe),

But also by involvement of the hands, feet, facial, or genital regions, by which, despite involvement of a smaller BSA, the disease may interfere significantly with activities of daily life

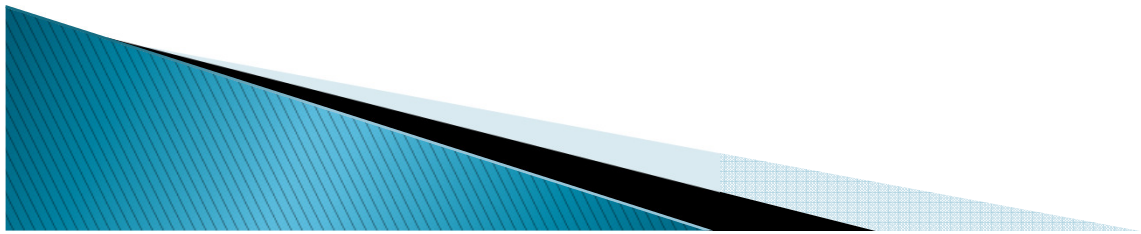
Psoriasis





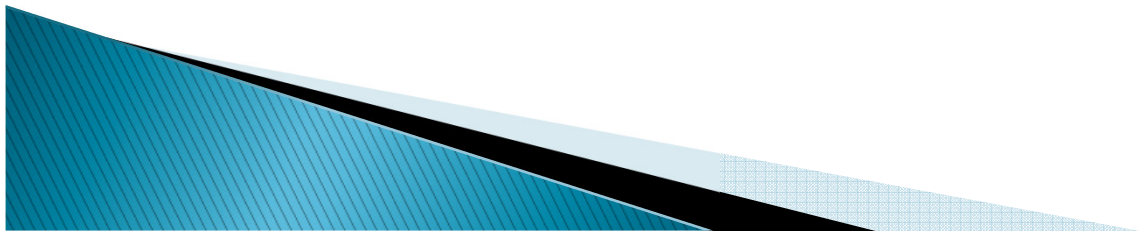
Topical treatment

- Topical corticosteroids (first-line treatment for limited psoriasis)
- The vitamin D analogs, calcipotriene, calcipotriol,and calcitriol, are other first-line topical agents with proven efficacy in the treatment of psoriasis
- Topical tazarotene, a retinoid, is an additional corticosteroid-sparing agent
- Topical tacrolimus may also be considered a firstline of therapy for intertriginous psoriasis.
- Emollients and ointments are widely used in the treatment of psoriasis but there is limited evidence that they are beneficial.



Vit D analogs

- They inhibit keratinocyte proliferation and enhance keratinocyte differentiation.
- These agents are less effective than class 1 topical corticosteroids, they are often used in combination with topical corticosteroids to enhance efficacy and reduce the risk of atrophy

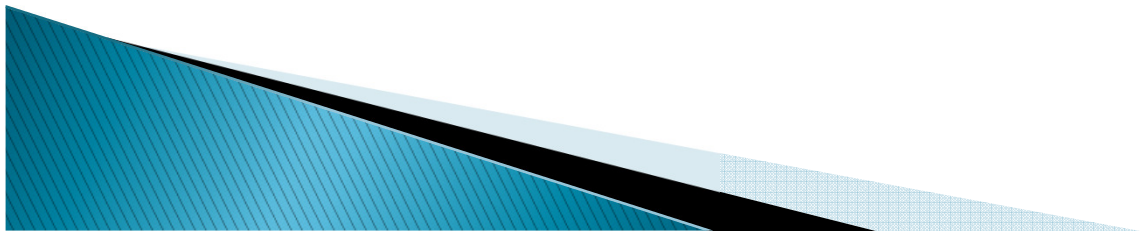


Acitretin

- Retinoid, active carboxylated metabolite of etretinate
- Given orally
- For severe resistant or complicated psoriasis
- Therapeutic effect after 2–4 weeks, maximal benefit after 6 weeks
- Highly teratogenic, adequate contraception one month prior to and during therapy and for 2 years after stopping the drug.

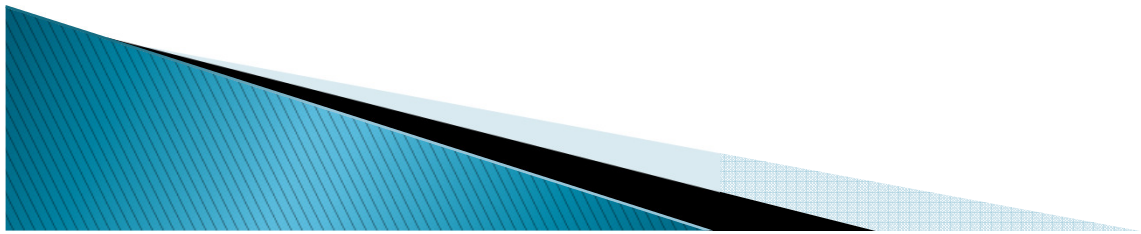
Systemic treatments

- Cyclosporine
  - cyclosporine is traditionally used as a‘‘rescue’’ medication in psoriasis and rarely used as a maintenance therapy (nephrotoxic)
- Methotrexate
  - most commonly used systemic agent worldwide for moderate to severe psoriasis,
- Biologics (TNF-alfa antagonist)
  - Etanercept, Adalimumab



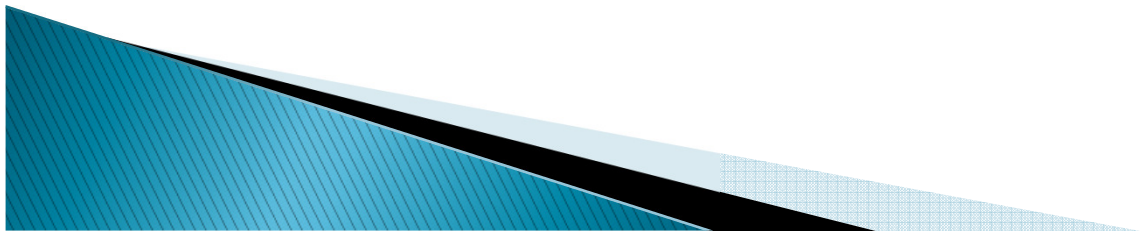
PUVA

- Psoralen – ultraviolet A (PUVA)
- Psoralen is a photosesnitiser that is ingested prior to light exposure
- PUVA can result in long remissions
- Low efficacy for nail psoriasis
- Adverse effects:
  - Conjunctival hyperaemia and dry eyes



UVB (Ultraviolet B)

- Narrow band UVB
- Low efficacy for nail psoriasis
- Less effective than PUVA
- Recommended in combination with other topical or systemic agents
- Decrease T-cells, dendritic cells and interleukins with responsive plaques



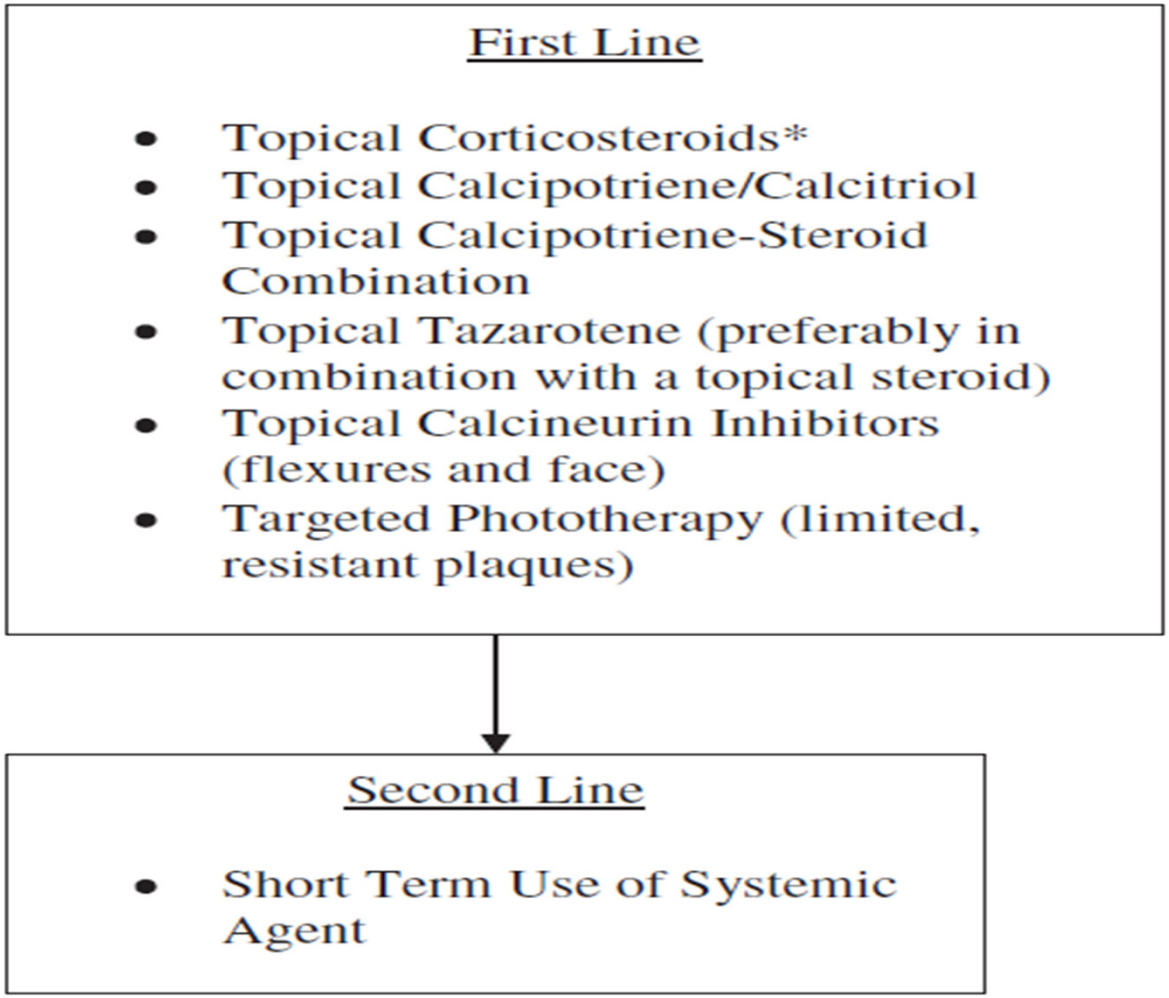


Fig 2. Algorithm for treatment of patients with limited disease. *Note the use of more potent topical corticosteroids must be limited to the short term, ie, <4 weeks, with gradual weaning to 1-2 times a week usage once adequate control is obtained, and the introduction of a secondary agent, eg, vitamin D_3 preparations, should be used for long term safe control.

ADULTS WITH PALMOPLANTAR PSORIASIS, W/O PSORIATIC ARTHRITIS (MALES OR FEMALES NOT OF CHILDBEARING POTENTIAL)

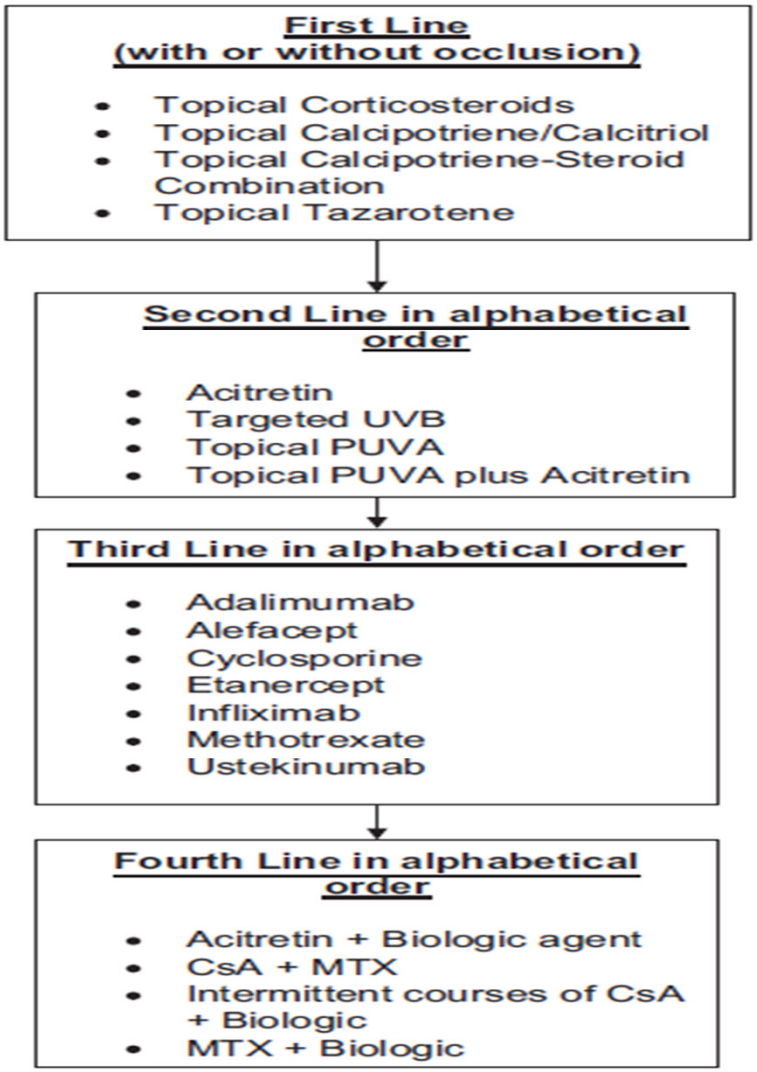


Fig 7. Algorithm for treatment of patients with palmoplantar disease. *CsA*, Cyclosporine; *MTX*, methotrexate; *PUVA*, psoralen plus ultraviolet A; *UV*, ultraviolet.

PEDIATRIC PSORIASIS PATIENTS (<18 YRS) WITH >5% BSA, W/O PSORIATIC ARTHRITIS

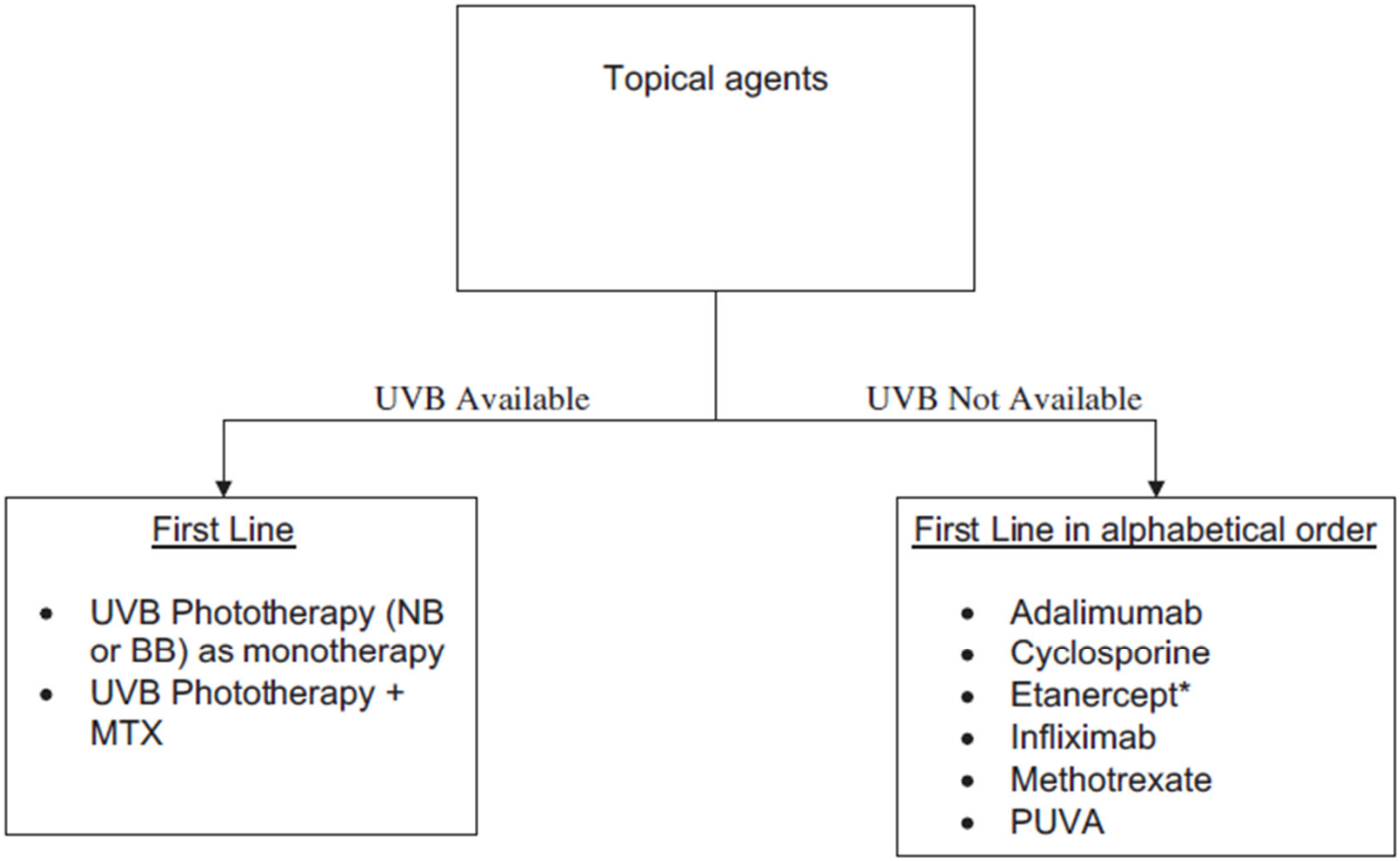


Fig 11. Algorithm for treatment of pediatric psoriasis involving greater than 5% body surface area. *BB*, Broadband; *MTX*, methotrexate; *NB*, narrowband; *PUVA*, psoralen plus ultraviolet A; *UV*, ultraviolet. *Etanercept is the only medication that has level 1 evidence to support this recommendation.

WOMEN TRYING TO CONCEIVE WITH CHRONIC PLAQUE PSORIASIS (>5% BSA), W/O PSORIATIC ARTHRITIS

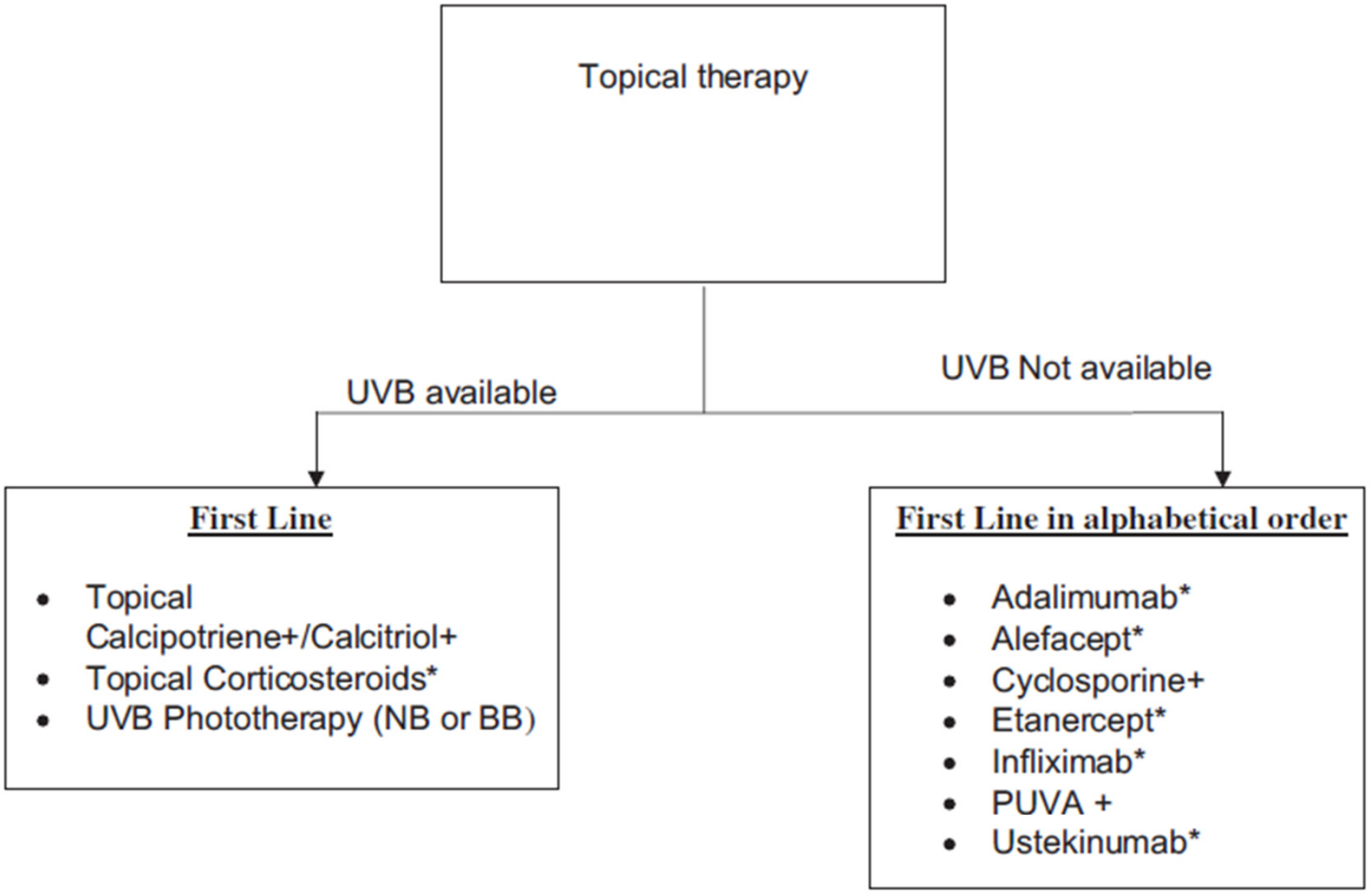


Fig 14. Algorithm for treatment of women trying to conceive with chronic plaque psoriasis involving greater than 5% body surface area without psoriatic arthritis. *BB*, Broadband; *FDA*, Food and Drug Administration; *NB*, narrowband; *PUVA*, psoralen plus ultraviolet A; *UV*, ultraviolet. *These medications are FDA pregnancy category B. +These medications (including psoralen) are FDA pregnancy category C.

Urticaria

- Hives = pale red , raised, itchy bumps.
- Well circumscribed areas of erythema and oedema involving the dermis and epidermis
- Acute < 6 weeks, chronic > 6 weeks
- Attributed to allergic or non allergic reactions caused by viral infections, medications and foods.
- Pathogenesis:
- Mast cell degranulation causes vasodilation and leakage of plasma in the superficial dermis
- Treatment:
  - Antihistamines(1st line) e.g. second generation, loratidine,cetirizine, fexofenadine etc
  - 2nd line – systemic steroids to control severe generalised urticaria or unricarial vasculitis

Fungal and nail infections

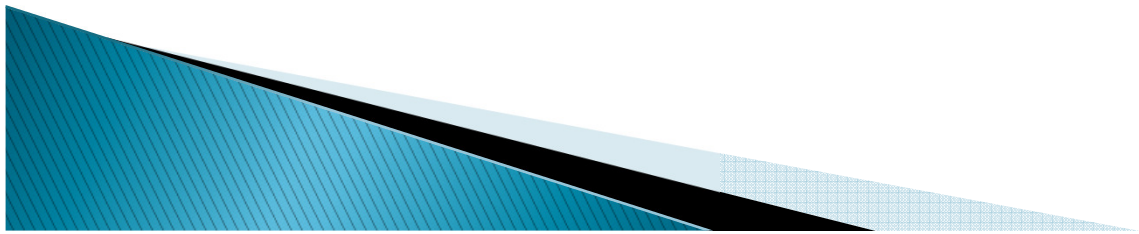
Fungal skin infection	Drug therapy
Candida skin infection, vulvovaginitis or balanitis	Topica nyastatin cream or ketoconazole, clotrimazole or miconazole
Fungal nail infections	Griesofulvin or fluconazole, terbinafine
Pityriasis capitis, seborrhoeic dermatitis (dandruff)	Topical steroids (clobetasol propionate 0.05%), betamethasone valerate. May add ketoconazole
Tinea capitis	Sytemic therapy with fluconazole, itraconazole, miconazole or clotrimazole, terbinafine
Tinea corporis	Topical ketoconazole 2% or clotrimazole 1%, terbinafine
Tinea pedis	As for tinea corporis

Superficial bacterial skin infections

- Commonly due to staph or strep
  - Impetigo
    - Mupirocin or fucidic ointment
  - Echthyma
    - IV antibiotics – aminoglycosides (genta/ amikacin), antipseudomonal agents –ceftazidime, piperacillin, quinolones
  - Erysipelas
    - Oral cloxacillin – (clarithromycin in penicillin-allergic patients)
  - Cellulitis
    - Oral cloxacillin – (clarithromycin in penicillin-allergic patients)
  - Furuncles and carbuncles
    - Mupirocin for localised lesions
    - Cloxacilin for carbuncles
  - Staphylococcal scalded syndrome
    - IV cloxacillin or cephalosporin

Viral skin infections

- Local:
  - Herpes simplex
    - Topical 5% aciclovir, systemic acyclovir for buccal and vaginal herpes simplex
  - Herpes zoster
    - Oral antiviral (aciclovir) – within 72 hours of rash
    - Analgesia
  - Molluscum contagiosum
    - Topical tretinoin cream, imiquimod
    - Surgical: cryotherapy, scraping the lesions with a curette
  - Warts
    - Imiquimod, podophyllin, salicylic acid, cryosurgery, surgical curettage, laser treatment



Drug eruptions

- They are common
- Present with a rash (macules, papules, urticarial, tiny red spots etc)
- Maybe life threatening (e.g. Stephen Johnsons)
- Discontinue offending medication
- Treatment:
  - Antihistamines
  - Emollients
  - Steroids
  - Severe reactions- hospitalisations