Topical Treatment

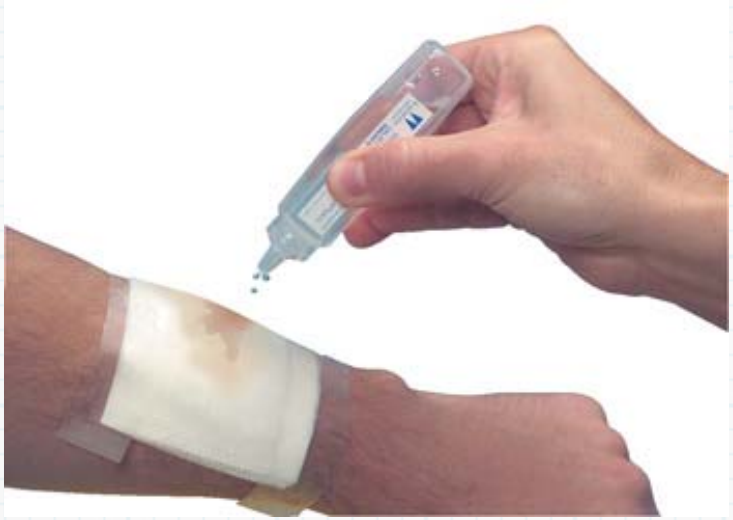
Chayada Chaiyabutr, MD.

Scope of Talk

- General principles
- Topical steroids
- Topical anti-fungals
- Topical therapy for psoriasis

Genral principles

- Formulations
- Quantity of application



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CLASSIFICATION OF EXTERNAL PREPARATIONS

LIQUID

- Monophasic solutions
  - Pure aqueous: lotions, gels
  - Alcoholic, alcoholic-aqueous: paints
  - Oily: oils
- Emulsions
  - Oil in water (O/W; can be washed off with water)
  - Water in oil (W/O; cannot be washed off with water)
- Suspensions
- Aerosols (solutions with pressurized gaseous propellants)
  - Foam
  - Spray

SEMISOLID

- Water-free: ointments
- Water-containing
  - Monophasic: hydrogels
  - Multiphasic: emulsions, creams (O/W or W/O)
- Highly concentrated suspensions: pastes

SOLID

- Powders (e.g. zinc oxide, titanium dioxide, talc)

FACTORS IN THE CHOICE OF FORMULATION AND VEHICLE FOR TOPICAL MEDICATIONS

NATURE OF THE DERMATOSIS

- Wet dermatoses (e.g. oozing) – water-based formulations, drying pastes
- Dry dermatoses (e.g. scaling) – ointments and other oil-based formulations
- Highly inflamed or crusted dermatoses – ointment or cream following or combined with wet compresses (e.g. open wet dressings, wet wraps) or soaks
- Fissured or eroded skin – avoid formulations containing alcohol or salicylates, which can lead to stinging and burning

LOCATION OF THE DERMATOSIS

- Glabrous skin – ointment, cream or emulsion
- Skin folds – lotion or O/W cream; avoid occlusive ointments and W/O formulations
- Hairy areas – lotion, gel, foam or oil

FACTORS THAT AFFECT PERCUTANEOUS ABSORPTION

CHARACTERISTICS OF THE PATIENT/SKIN

- Patient age
  - Suboptimal skin barrier function in neonates, especially if premature (see Table 129.7)
- Diseases, physical injuries or chemical exposures that disrupt skin barrier function (e.g. Netherton syndrome)
- A thicker stratum corneum decreases absorption
- Skin hydration and/or occlusion increase absorption (e.g. in a skin fold)
- Anatomic location (approximate ratio of absorption compared to the forearm)
  - *Higher absorption:* scrotum (40), face (10), axilla (4), scalp (3)
  - *Intermediate absorption*: trunk (1.5), arm (1)
  - *Lower absorption*: palm (0.8), ankle (0.4), sole (0.1)

PROPERTIES OF THE MEDICATION/ITS APPLICATION

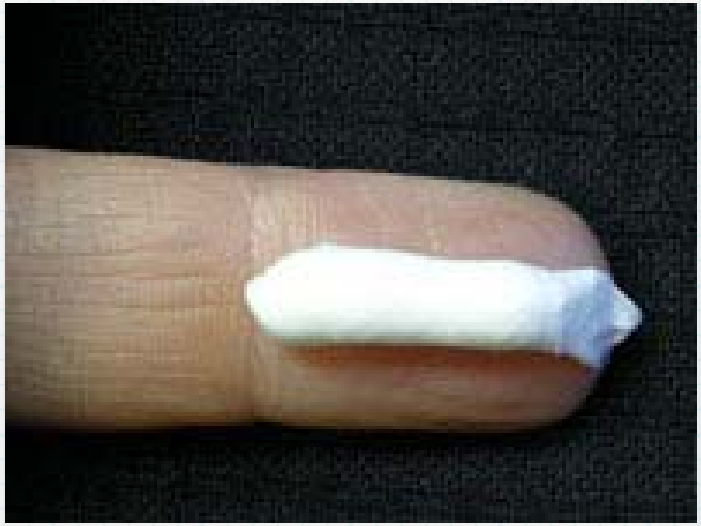
- Drug/prodrug properties that increase absorption
  - Smaller molecular size and/or lower frictional coefficient
  - Increased lipophilicity
  - Increased concentration and/or solubility
- Vehicle composition
- Application under occlusion increases absorption (e.g. ointment, occlusive dressing)

Quantity of application

- 0.05 to 0.1 mm in thickness
- Thicker layer does not result in additional therapeutic benefit

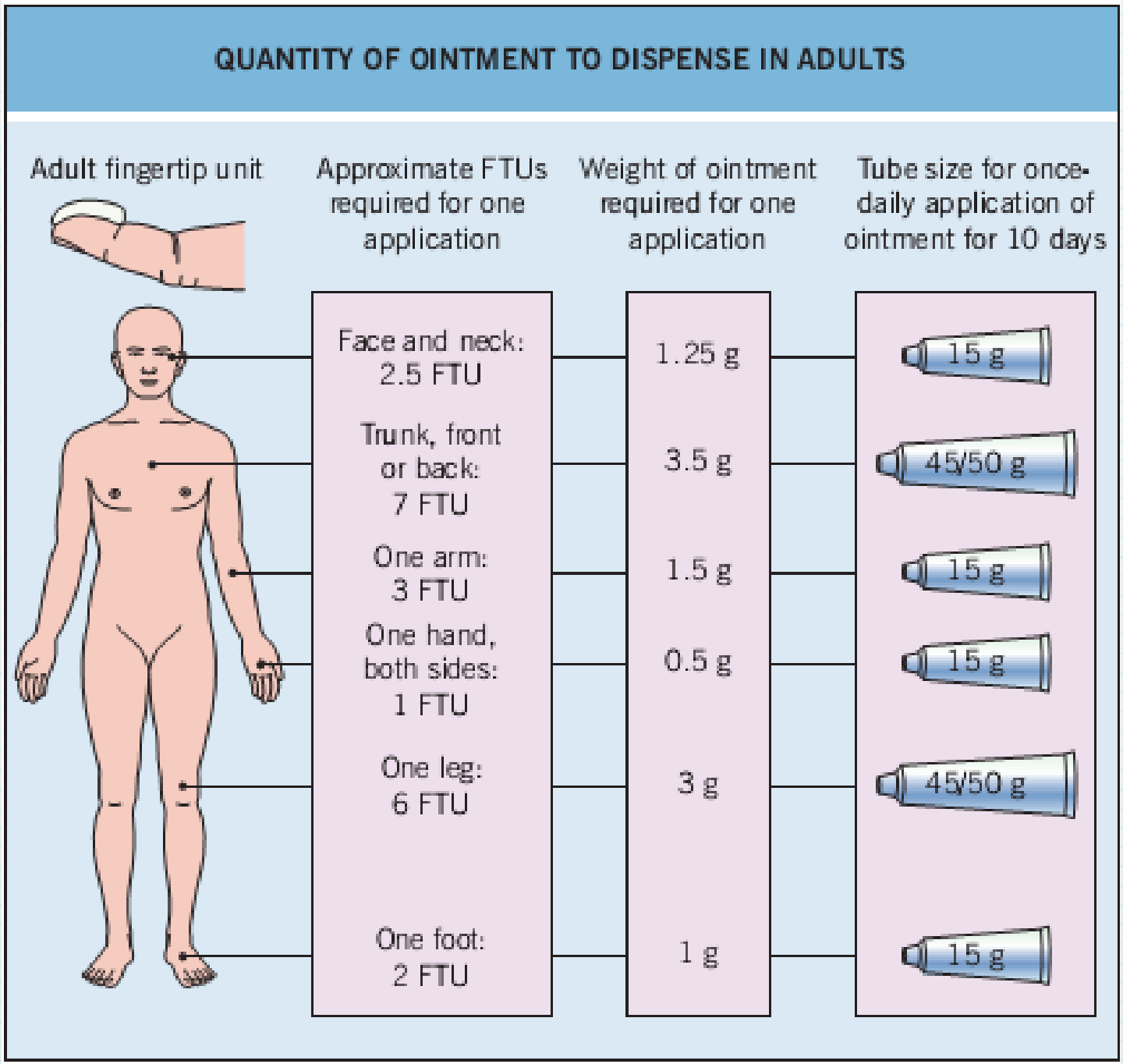
Quantity of application

- 1 FTU (fintertip unit) ~ 0.5 g
- 0.5 FTU (0.25 g) for 1 flat hand area



5 mm

QUANTITY OF OINTMENT TO DISPENSE IN ADULTS



Topical steroids

- How to choose it ???

Topical steroids

* Indication

TABLE 216-2
Responsiveness of Dermatoses to Topical Application of Corticosteroids

HIGHLY RESPONSIVE	MODERATELY RESPONSIVE	LEAST RESPONSIVE
• Psoriasis (intertriginous)	• Psoriasis	• Palmo-plantar psoriasis
• Atopic dermatitis (children)	• Atopic dermatitis (adults)	• Psoriasis of nails
• Seborrheic dermatitis	• Nummular eczema	• Dyshidrotic eczema
• Intertrigo	• Primary irritant dermatitis	• Lupus erythematosus
	• Papular urticaria	• Pemphigus
	• Parapsoriasis	• Lichen planus
	• Lichen simplex chronicus	• Granuloma annulare
		• Necrobiosis lipoidica diabeticorum
		• Sarcoidosis
		• Allergic contact dermatitis, acute phase
		• Insect bites

Potency

POTENCY RANKING OF SOME COMMONLY USED TOPICAL GLUCOCORTICOSTEROIDS

CLASS 1 (SUPERPOTENT)

- Clobetasol propionate gel, ointment, cream, lotion, foam, spray and shampoo 0.05%
- Betamethasone dipropionate gel* and ointment* 0.05%
- Diflorasone diacetate ointment* 0.05%
- Fluocinonide cream 0.1%
- Flurandrenolide tape 4 mcg/cm^2
- Halobetasol propionate ointment and cream 0.05%

CLASS 2 (HIGH POTENCY)

- Amcinonide ointment 0.1%
- Betamethasone dipropionate cream*, lotion*, gel and ointment 0.05%
- Clobetasol propionate solution ("scalp application") 0.05%
- Desoximetasone ointment and cream 0.25% and gel 0.05%
- Diflorasone diacetate ointment and cream* 0.05%
- Fluocinonide gel, ointment, cream and solution 0.05%
- Halcinonide ointment, cream and solution 0.1%
- Mometasone furoate ointment 0.1%
- Triamcinolone acetonide ointment 0.5%

CLASS 3 (HIGH POTENCY)

- Amcinonide cream and lotion 0.1%
- Betamethasone dipropionate cream and lotion 0.05%
- Betamethasone valerate ointment 0.1%
- Diflorasone diacetate cream 0.05%
- Fluticasone propionate ointment 0.005%
- Triamcinolone acetonide ointment 0.1% and cream 0.5%

CLASS 4 (MEDIUM POTENCY)

- Betamethasone valerate foam 0.12%
- Desoximetasone cream 0.05%
- Fluocinolone acetonide ointment 0.025%
- Flurandrenolide ointment 0.05%
- Hydrocortisone valerate ointment 0.2%
- Mometasone furoate cream and lotion 0.1%
- Triamcinolone acetonide ointment (Kenalog®) and cream 0.1% or spray 0.2%

CLASS 5 (MEDIUM POTENCY)

- Betamethasone dipropionate lotion 0.05%
- Betamethasone valerate cream and lotion 0.1%
- Clocortolone pivalate cream 0.1%
- Fluocinolone acetonide cream 0.025% or oil and shampoo 0.01%
- Fluticasone propionate cream and lotion 0.05%
- Flurandrenolide cream and lotion 0.05%
- Hydrocortisone butyrate ointment, cream and lotion 0.1%
- Hydrocortisone probutate cream 0.1%
- Hydrocortisone valerate cream 0.2%
- Prednicarbate ointment and cream 0.1%
- Triamcinolone acetonide ointment 0.025% and lotion 0.1%

CLASS 6 (LOW POTENCY)

- Alclometasone dipropionate ointment and cream 0.05%
- Triamcinolone acetonide cream 0.1% (Aristocort®)
- Betamethasone valerate lotion 0.1%
- Desonide gel, ointment, cream, lotion and foam 0.05%
- Fluocinolone acetonide cream and solution 0.01%
- Triamcinolone acetonide cream and lotion 0.025%

CLASS 7 (LOW POTENCY)

- Topicals with hydrocortisone, dexamethasone and prednisolone

In our hospital

* Class 1

* Class 2

* Class 3

* Class 4

* Class 5

* Class 6

* Class 7

Regional

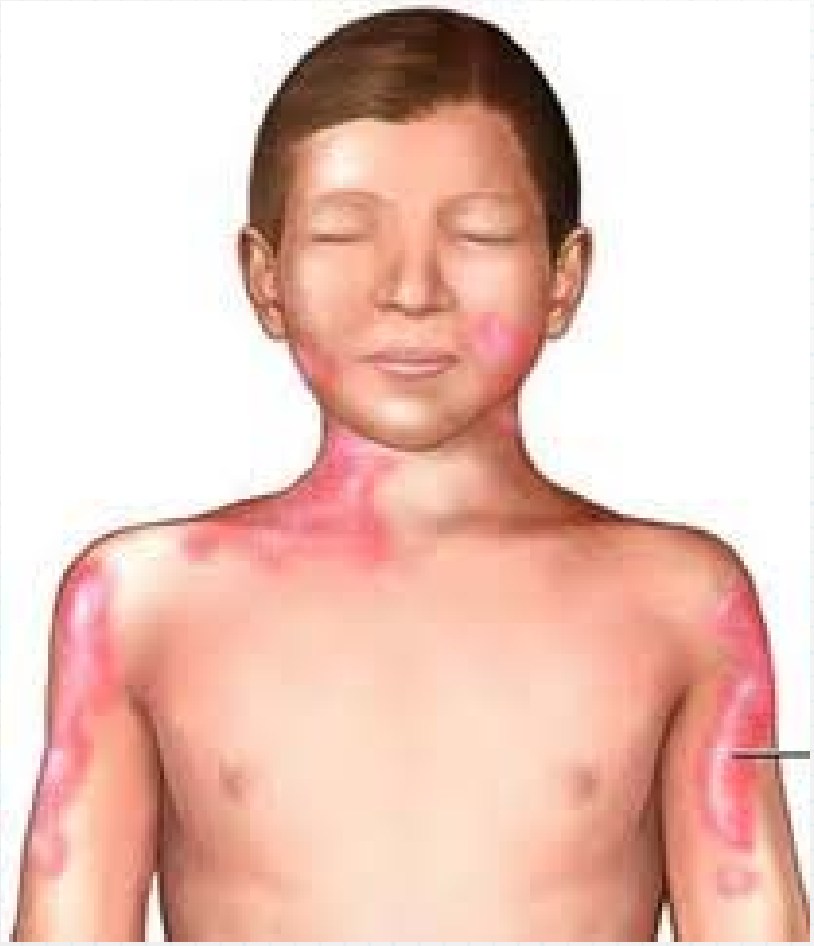
BOX 214-1 REGIONAL DIFFERENCES IN PENETRATION[a]

1. Mucous membrane
2. Scrotum
3. Eyelids
4. Face
5. Chest and back
6. Upper arms and legs
7. Lower arms and legs
8. Dorsa of hands and feet
9. Palmar and plantar skin
10. Nails

Prescribing steroids

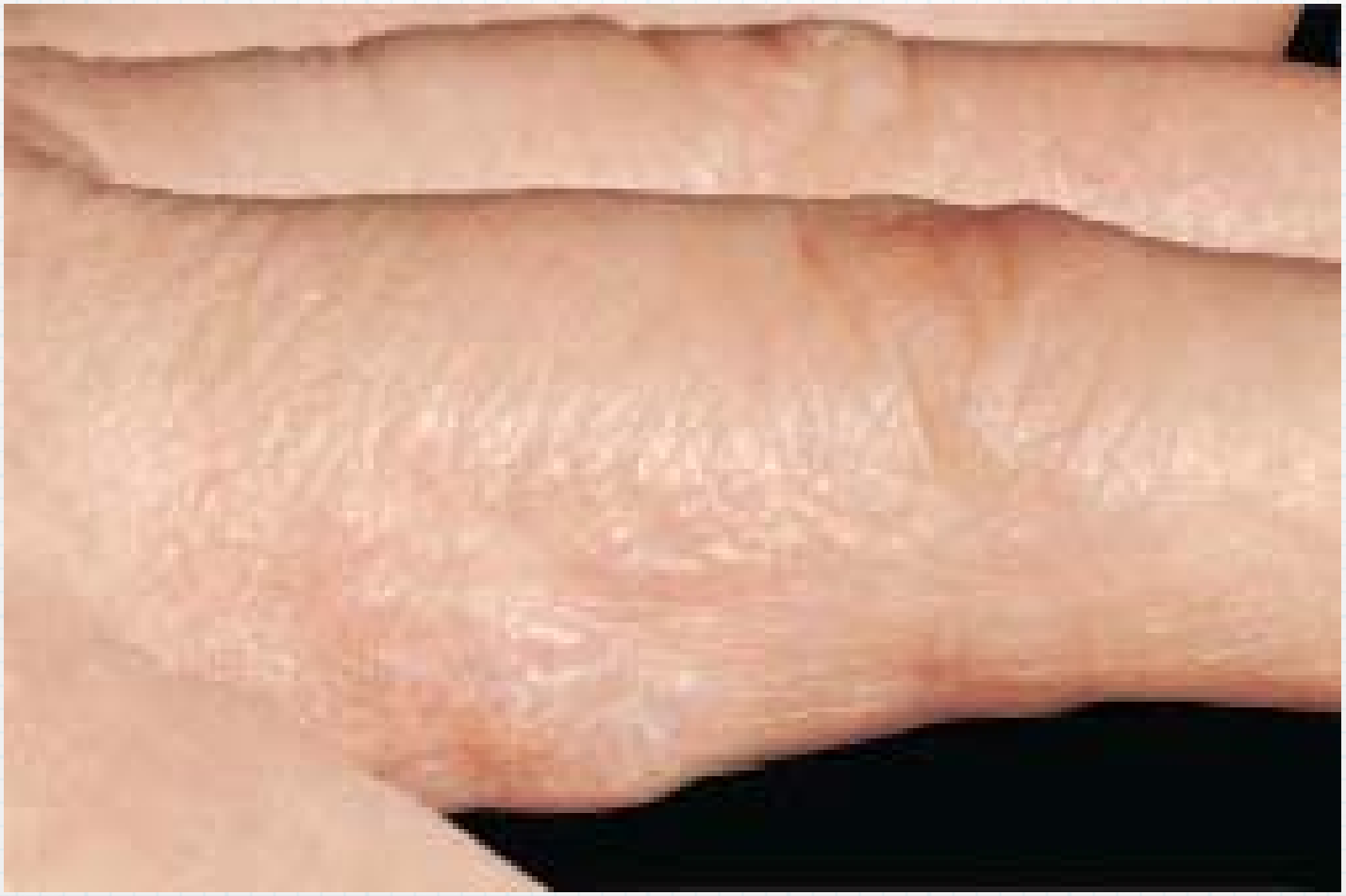
FACTORS THAT AFFECT PERCUTANEOUS ABSORPTION
CHARACTERISTICS OF THE PATIENT/SKIN
• Patient age – Suboptimal skin barrier function in neonates, especially if premature (see Table 129.7) • Diseases, physical injuries or chemical exposures that disrupt skin barrier function (e.g. Netherton syndrome) • A thicker stratum corneum decreases absorption • Skin hydration and/or occlusion increase absorption (e.g. in a skin fold) • Anatomic location (approximate ratio of absorption compared to the forearm) – *Higher absorption:* scrotum (40), face (10), axilla (4), scalp (3) – *Intermediate absorption*: trunk (1.5), arm (1) – *Lower absorption*: palm (0.8), ankle (0.4), sole (0.1)
PROPERTIES OF THE MEDICATION/ITS APPLICATION
• Drug/prodrug properties that increase absorption – Smaller molecular size and/or lower frictional coefficient – Increased lipophilicity – Increased concentration and/or solubility • Vehicle composition • Application under occlusion increases absorption (e.g. ointment, occlusive dressing)

Prescribing steroids



- Indication
- Disease responsiveness
- Location
- Potency

Example 1



Dyshidrotic hand eczema

* Disease responsiveness ??
* Location.....

* Choose.....

Dyshidrotic hand eczema

* Disease responsiveness ??
* Location..
* Choose..

BOX 214-1 REGIONAL DIFFERENCES IN PENETRATION[a]

1. Mucous membrane
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8. Dorsa of hands and feet
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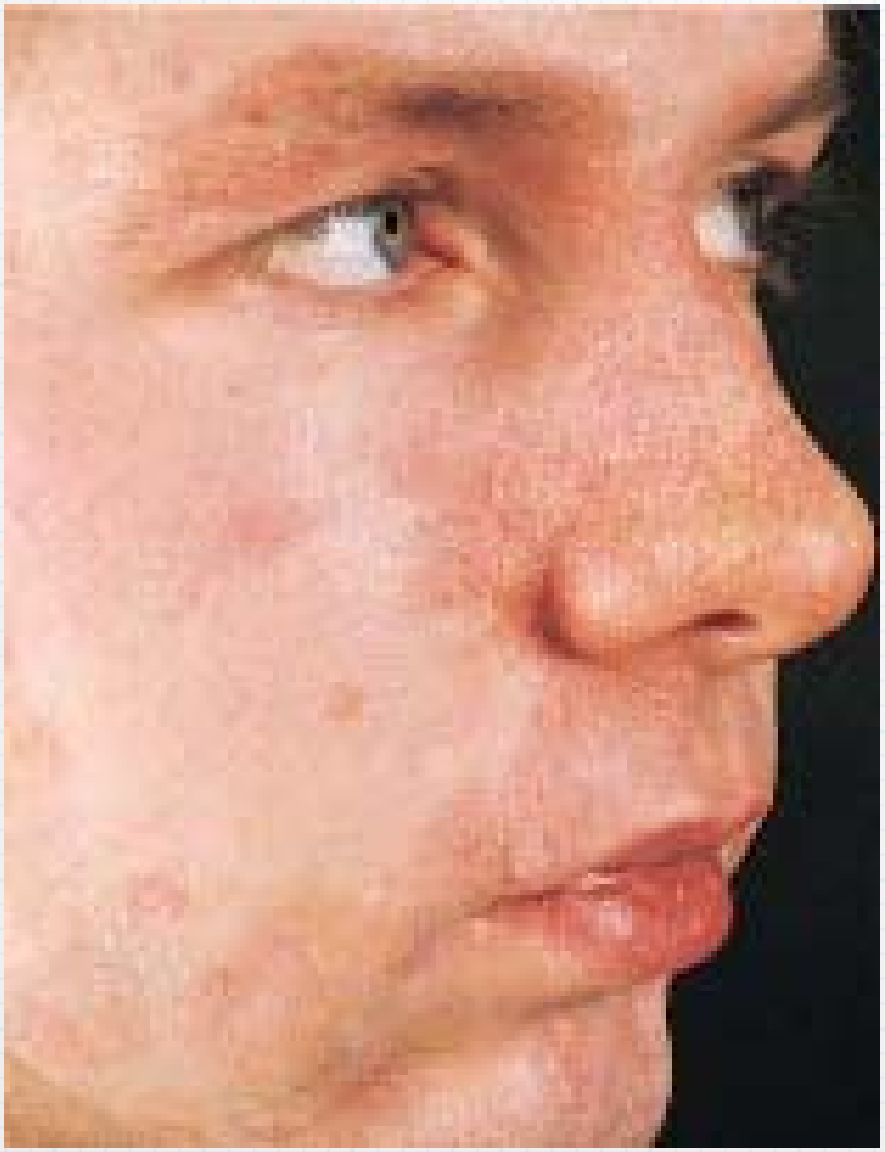
10. Nails

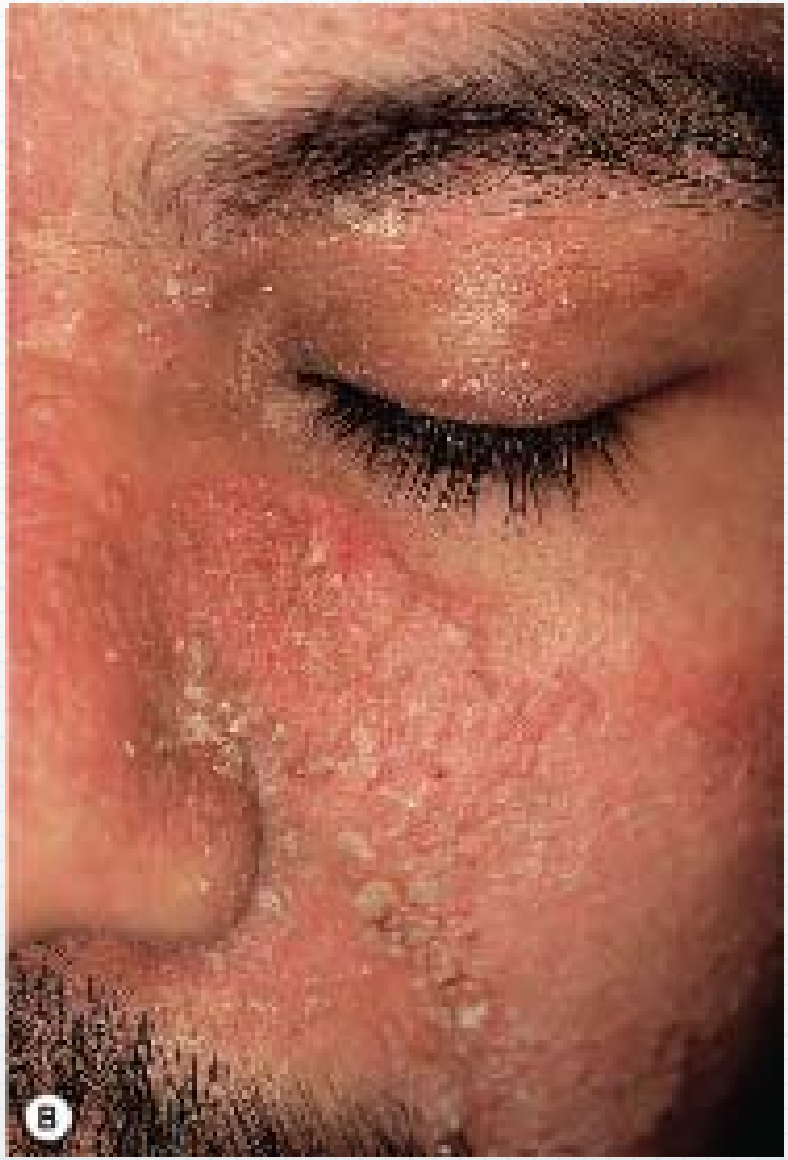
LEAST RESPONSIVE

- Palmo-plantar psoriasis
- Psoriasis of nails
- Dyshidrotic eczema
- Lupus erythematosus
- Pemphigus
- Lichen planus
- Granuloma annulare
- Necrobiosis lipoidica diabeticorum
- Sarcoidosis
- Allergic contact dermatitis, acute phase
- Insect bites

Class 1—Superpotent

Example 2





Seborrheic dermatitis

- Disease responsiveness
- Location

- Choose....

Seborrheic dermatitis

* Disease responsiveness
* Location
* Choose....

HIGHLY RESPONSIVE

- Psoriasis (intertriginous)
- Atopic dermatitis (children)
- Seborrheic dermatitis
- Intertrigo

BOX 214-1 REGIONAL DIFFERENCES IN PENETRATION[a]

1. Mucous membrane
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10. Nails

Class 6—Mild strength

Class 7—Least potent

Principle when initiating steroids

- Initiate lowest potency to sufficiently control disease
- Highly responsive dz = weak steroid
- Less responsive dz = medium/high steroid
- When large surface area involved, Rx with low to medium potency preparation is recommended

- Highly potent steroid should be used for short period (2-3 week) or intermittently
- Once disease control is partially achieved : switch to less potent, reduce frequency of application

AVOID !!!

- Infection
- Ulcer
- Atrophy

Topical anti-fungals

Topical anti-fungals

Imidazole group

TABLE 219-3
Indications for the Use of Topical Imidazoles

- Dermatophytoses
  - Tinea pedis/tinea manum
  - Tinea cruris
  - Tinea corporis
  - Tinea faciei (the unbearded face)
- Pityriasis versicolor
- Mucocutaneous candidiasis[a]
  - Cutaneous candidiasis
  - Vulvovaginal candidiasis[b]
  - Oral candidiasis (thrush)[c]
  - Perlèche
- Seborrheic dermatitis[d]

How to apply anti-fungals?

- Include normal skin for a radius of 2 cm
- Should be continued at least 1 week after lesion resolved

- Tinea corporis/cruris : 2 week
- Tinea pedis : 4 week

Allylamine group

TABLE 219-5
Indications for the Use of Topical Allylamines and Benzylamines

- Dermatophytoses
  - Tinea pedis/tinea manum
  - Tinea cruris
  - Tinea corporis
  - Tinea faciei (the unbearded face)
- Pityriasis versicolor[a]

[a]Although butenafine is approved by the U.S. Food and Drug Administration for use in pityriasis versicolor, the availability of numerous, more cost-effective remedies limits use in this clinical situation.

* Terbinafine is 2-30 times more potent than azole antifungal agents against common dermatophytes in vitro.
* Limited evidence suggests that topical allylamine may be preferred over topical imidazoles for cetain dermatophyte infection
* The mycologic cure rates are significantly higher a month after treatment has stopped

Application

Terbinafine	Tinea pedis (interdigital)—twice daily	At least 1 wk
	Tinea pedis (plantar)—twice daily	At least 2 wk
	Tinea elsewhere—once or twice daily	At least 1 wk, up to 4 wk

Nystatin

- Indication
- Mucocutaneous candidiasis
- Caused by C.albicans
- Other susceptible species: C.parapsilosis, C.krusei, C.tropicalis
- Not effective : Dermatophyte, Pityrosporum

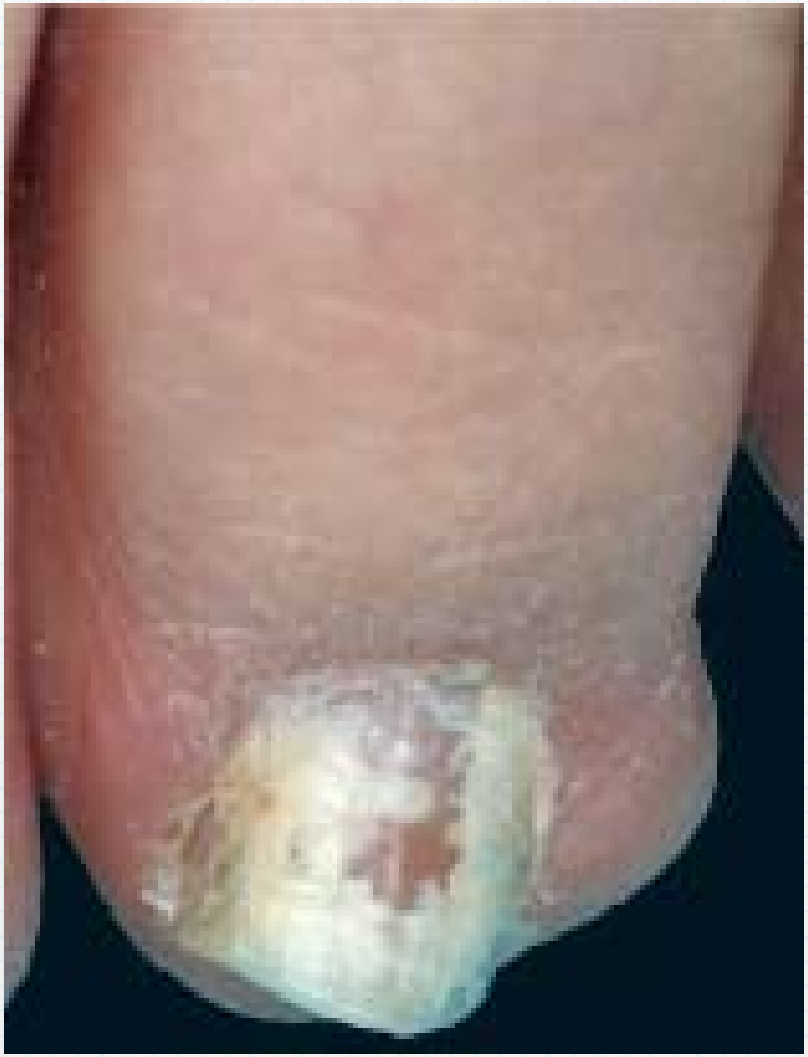
Dosing

- 400,000-600,000 unit PO qid
- Swish in mouth several min → swallow
- Duration : 2 week

Tolnaftate

- Dermatophyte: Less efficacy than topical imidazole, allyllamine
- Ineffective for candidiasis

Dx and Rx



- Dx: onychomycosis
- Rx: systemic anti-fungal

Indication : systemic anti-fungals

- Superficial fungal infections: widespread, severe or resistant to topical antifungals
- Onychomycosis
- Tinea capitis
- Deep fungal/Systemic fungal infections

Topical nail antifungals

- 5% w/v amorolfine in the form of hydrochloride
- Treatment can take 6-12 months

Once a week

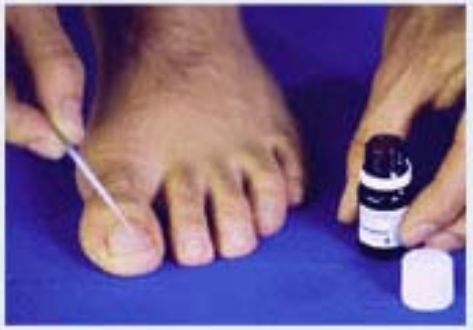
Dosage and administration

Step 1:

Use the nail file provided to file the nail

Step 2:

Wipe the nail with the cleansing pad provided to remove any contaimi-nants



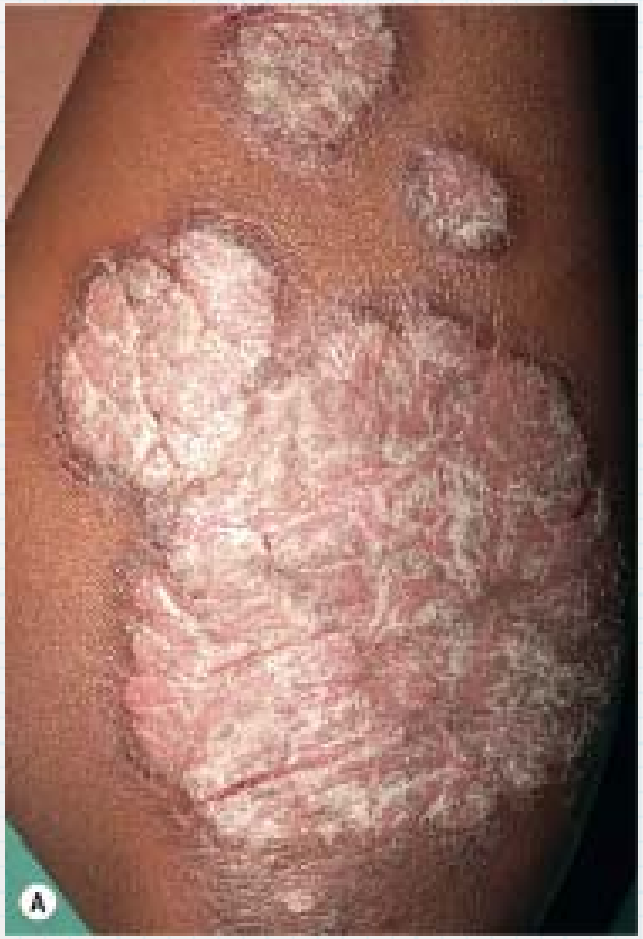
Step 3:

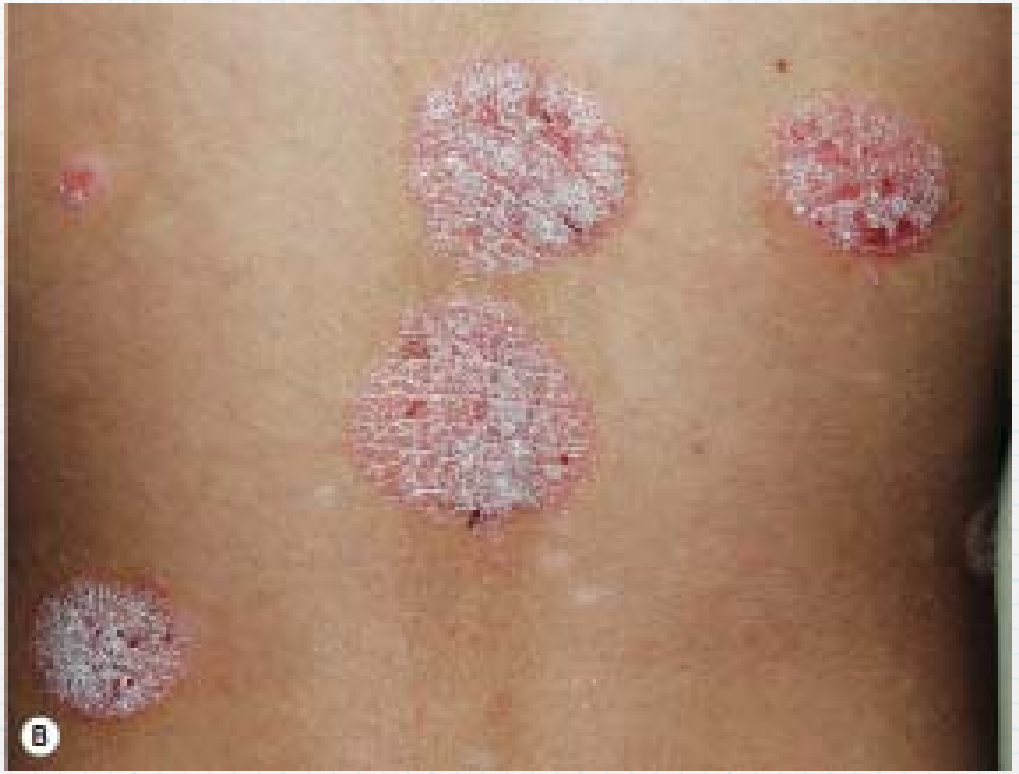
Apply the lacquer to the nail by using the spatula provided

Step 4:

Allow the nail lacquer to dry for 3-5 minutes

Topical therapy for psoriasis





1. Topical steroids

INDICATIONS AND CONTRAINDICATIONS FOR TOPICAL CORTICOSTEROIDS
INDICATIONS
• Mild to moderate psoriasis: first-line treatment as monotherapy or in combination • Severe psoriasis: often in combination with a vitamin D_3 analogue, a topical retinoid, anthralin or tar • Monotherapy for flexural and facial psoriasis (usually mild strength) • Recalcitrant plaques often require occlusion (plastic, hydrocolloid)
CONTRAINDICATIONS
• Bacterial, viral and mycotic infections • Atrophy of the skin • Allergic contact dermatitis due to corticosteroids or constituents of the formulation • Pregnancy or lactation*
*Can consider limited use of mild- to moderate-strength corticosteroids.

2. Vitamin D analogues

Calcipotriol

Calcipotriol + betamethasone dipropionate

Vitamin D analogues

- Inhibiting proliferation and promoting differentiation of keratinocytes
- Immunomodulatory actions such as decreasing production of inflammatory mediators

Vitamin D analogues

INDICATIONS AND CONTRAINDICATIONS FOR VITAMIN D_3 ANALOGUES
INDICATIONS
• Mild to moderate psoriasis: first-line treatment as monotherapy or in combination • Severe psoriasis: combination treatment
CONTRAINDICATIONS
• Involvement requiring more than the maximally recommended quantity, e.g. 100 g/week of calcipotriene/calcipotriol (see Table 8.4) • Abnormality in bone or calcium metabolism* • Renal insufficiency • Allergy to the vitamin D_3 analogue or constituents of the preparation • Pregnancy or lactation
*For example, sarcoidosis, bone metastases.

Side effects

- Most common side effect: irritation, burning and stinging at the application site
- Limits the use of vitamin D analogues on the face and in intertriginous areas

Vitamin D analogues

Calcipotriol

Calcipotriol + betamethasone dipropionate

3. Tar (LCD)

- Liquor carbonis detergens is a distillate of crude car tar
- Typically used in concentrations of 3%-10%.

Tar

- Coal tar is thought to suppress DNA synthesis, which may lead to normalization of epidermal differentiation in conditions such as psoriasis.
- It appears to have anti-inflammatory, antimicrobial and anti-pruritic effects

Disadvantages

- Unpleasant odor, messiness and staining potential
- Acneiform eruptions, folliculitis and irritant contact dermatitis

Disadvantages

- Tar has been implicated as a potential carcinogen
- However, the evidence that topical tar formulations used in the treatment of skin disease result in an increased risk of skin cancer is inconclusive

Other topical Rx for psoriasis

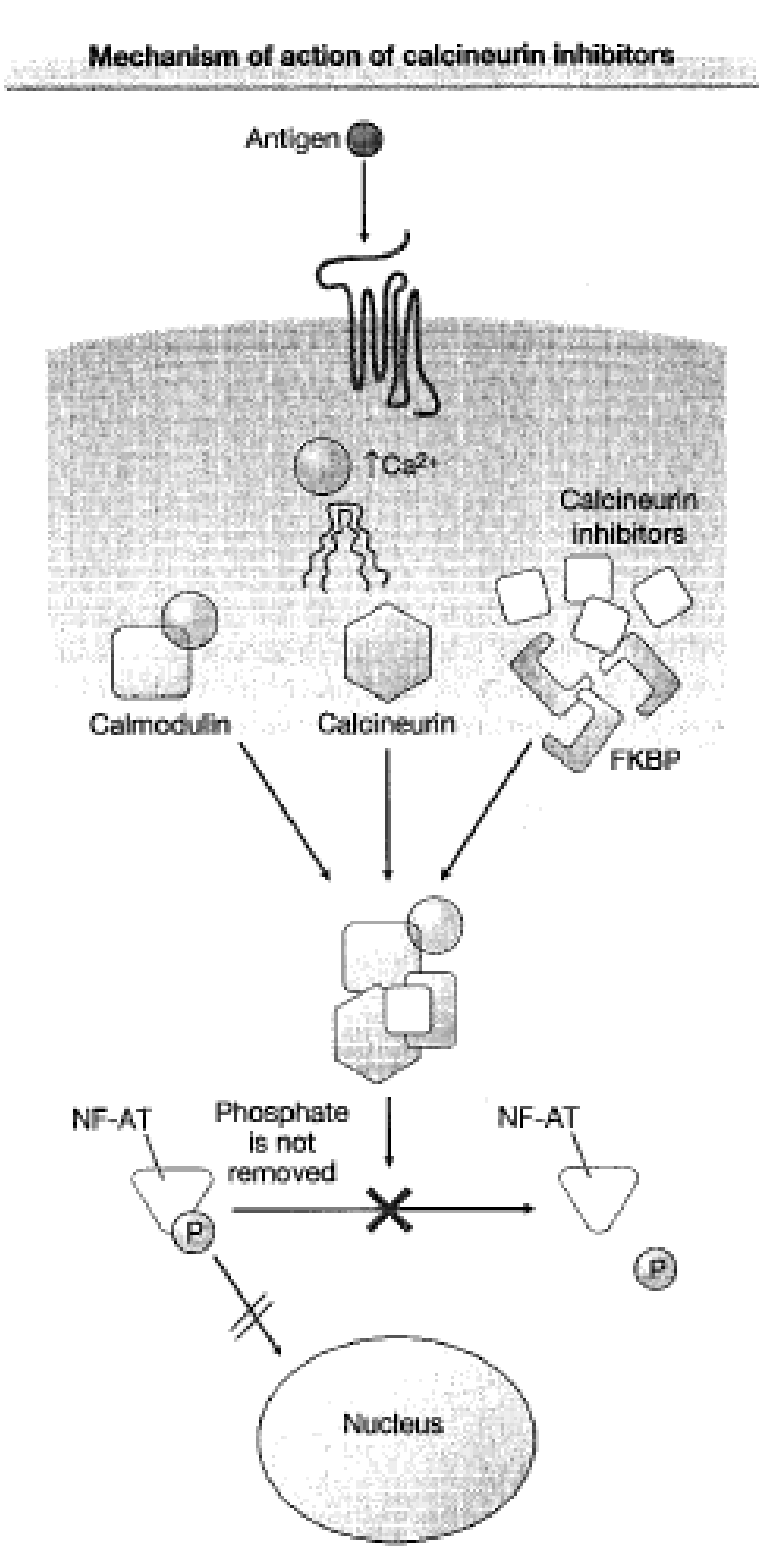
- Anthralin : 2nd line Rx
- Calcineurin inhibitors : facial, flexural psoriasis

- Tazarotene : Not available, 2nd line Rx

Topical calcineurin inhibitors (TCI)

Tacrolimus 0.1%, 0.03% (Protopic)

Pimecrolimus 1% (Elidel)



- Drug prevent calcineurin from dephosphorylating NFAT → inhibit nuclear translocation
- Decrease T cell proliferation
- Reduced inflammatory cytokine production

Indications

Tacrolimus (ointment)

- 0.1% ---> 15 yr
- 0.03% -→ 2-15 yr
- Moderate to severe atopic

Pimecrolimus (1% cream)

- 1% -→ > 2 yr
- Mild to moderate atopic

PIMECROLIMUS AND TACROLIMUS

- Second-line therapy for atopic dermatitis
- Children older than 2 years
- Adults
- Short-term, noncontinuous chronic therapy

Off-label use

Complications

PIMECROLIMUS AND TACROLIMUS

- Elevated blood levels and risk of systemic immuno-suppression
- Unclear long-term risk of lymphoproliferative disease
- Unclear long-term malignancy risk
- Eczema herpeticum

Risk & Precautions

PIMECROLIMUS AND TACROLIMUS

- Application site reactions, including itch, burning, stinging, redness, flushing with alcohol
- Avoid use on premalignant or malignant skin conditions, including cutaneous T-cell lymphoma
- Skin infections, including *S. aureus*, dermatophytosis, and herpes simplex
- Lymphadenopathy
- Light exposure, including phototherapy
- Immunocompromised
- Netherton syndrome
- Renal insufficiency
- Pregnancy category C
- Lactation
- Flu-like symptoms
- Worsening acne

FROM THE ACADEMY

Guidelines of care for the management of psoriasis and psoriatic arthritis

Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions

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Dallas, Texas; Cleveland, Ohio; Birmingham, Alabama; Winston-Salem, North Carolina; Philadelphia, Pennsylvania; Chicago and Schaumburg, Illinois; Boston, Massachusetts; San Francisco and Palo Alto, California; New York, New York; St Louis, Missouri; and Detroit, Michigan

JAAD July 2011

TREATMENT OF PATIENTS WITH LIMITED DISEASE

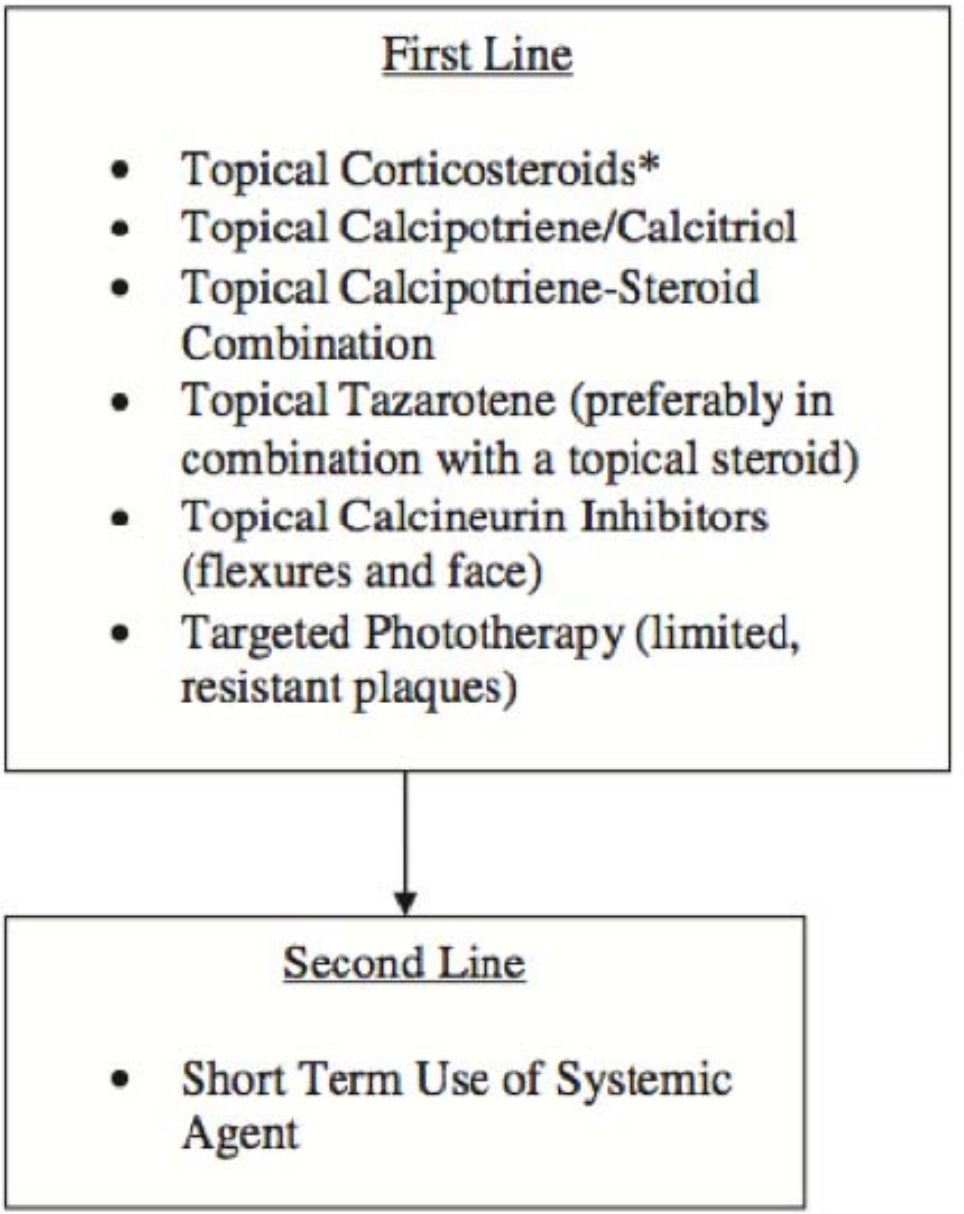
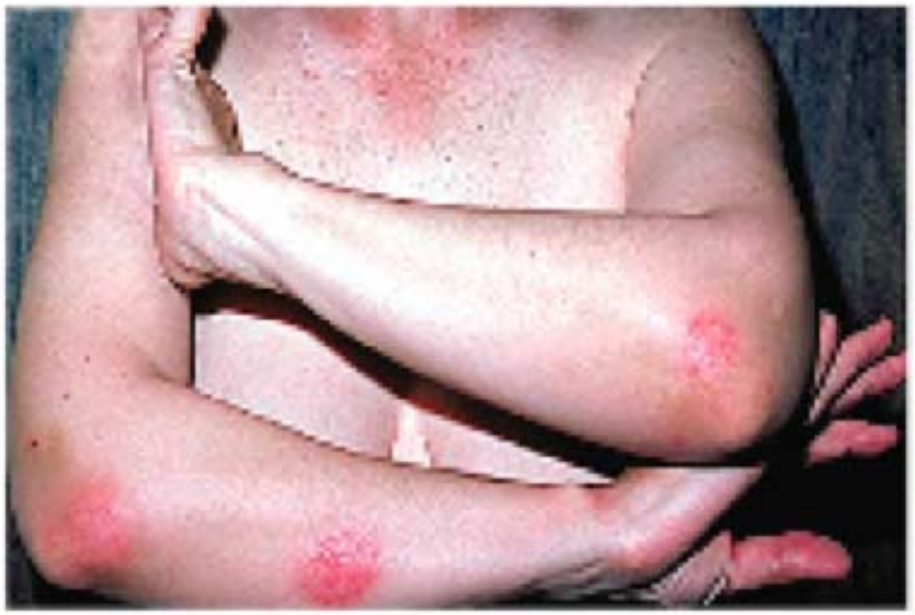
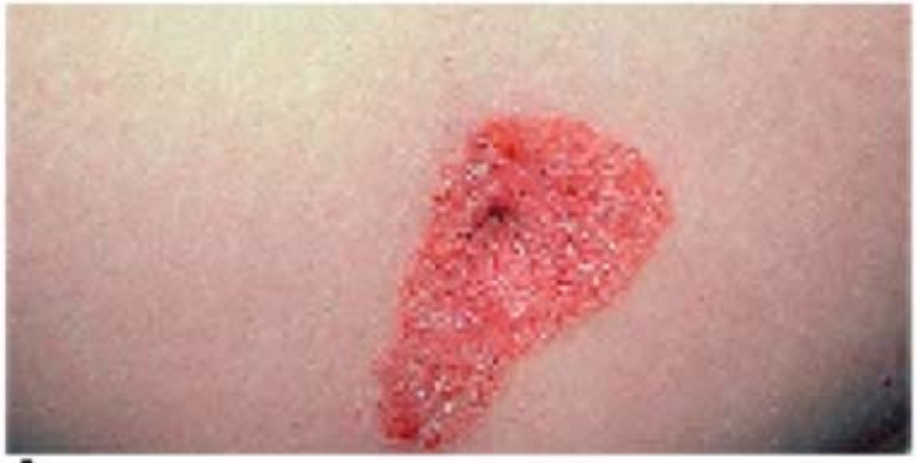


Fig 2. Algorithm for treatment of patients with limited disease. *Note the use of more potent topical corticosteroids must be limited to the short term, ie, <4 weeks, with gradual weaning to 1-2 times a week usage once adequate control is obtained, and the introduction of a secondary agent, eg, vitamin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

Sample case

- A 25-year-old woman with a several-year history of psoriasis
- Recently she has noted significant worsening with the onset of colder weather
- Previous treatments include coal tar and 2.5% hydrocortisone cream with limited response.
- Her psoriasis now involves multiple areas of her body including the trunk and all 4 limbs.





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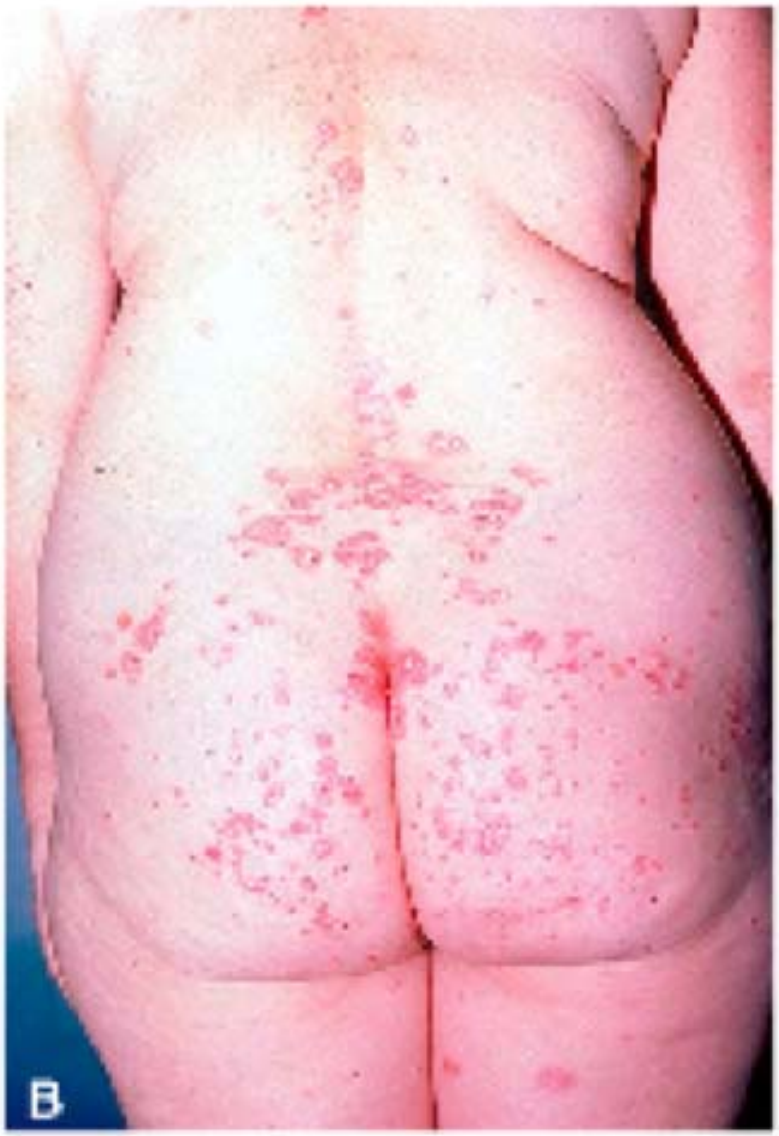
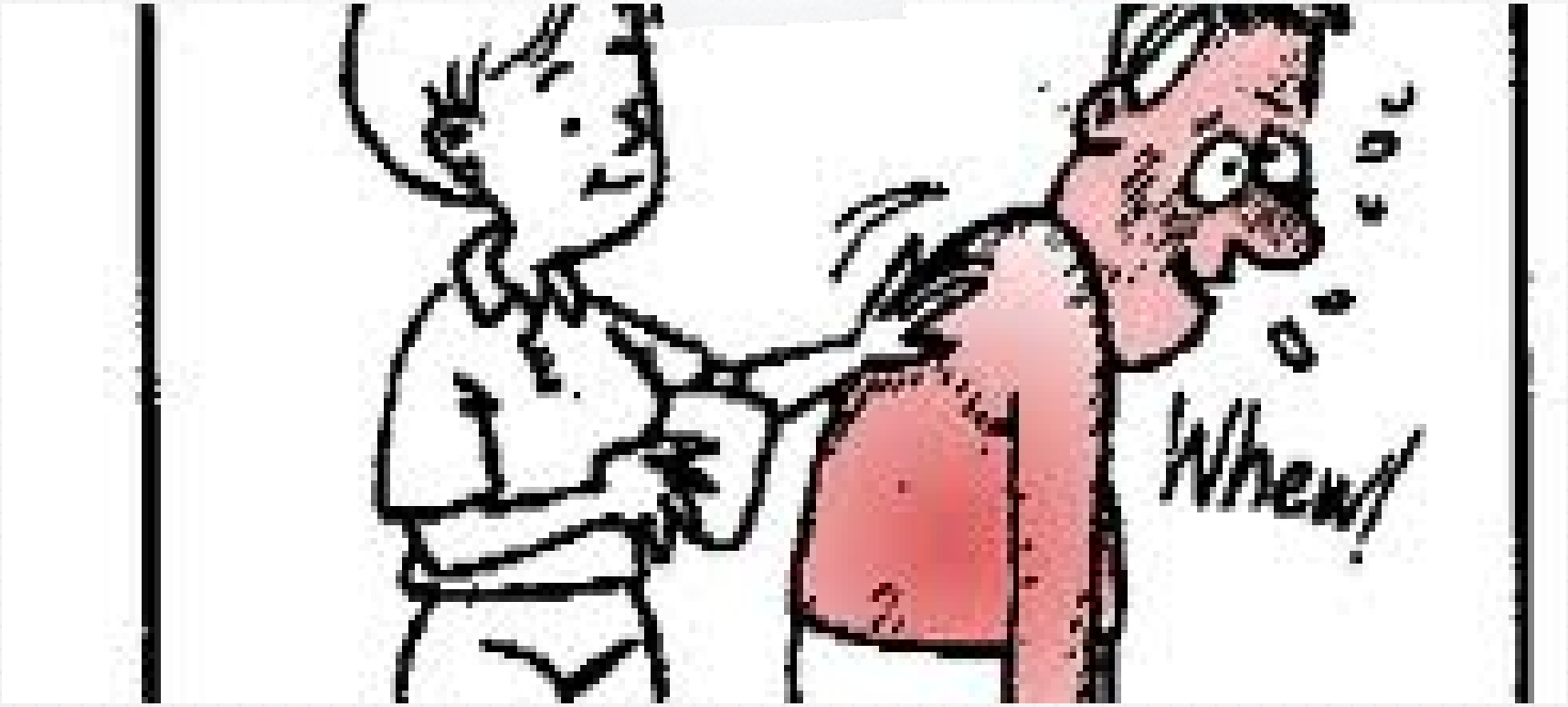


B

The scalp, nails, and mucosal surfaces are uninvolved.
There is no evident of joint inflammation.

In this patient

- A potent topical corticosteroid ointment was initially prescribed for use on her elbows, knees, and back plaques, with slow reduction in frequency of use during a 4-week period and the introduction of a vitamin D agent once adequate clearing was obtained.
- Medium-potency topical corticosteroid ointment was used for 2 weeks for her intertriginous psoriasis, followed by maintenance therapy with topical tacrolimus ointment



Thank you