# Atopic Dermatitis

- a chronic, pruritic, inflammatory skin disease which includes dryness, erythema, oozing and crusting, and lichenification.
- Pruritus is a hallmark symptom and is responsible for much of the disease burden for patients with dermatitis
    - Antihistamines are widely used as adjuncts for pruritus in atopic dermatitis.
        - Sedating antihistamines tend to be most effective, e.g., Diphenhydramine (Benadryl, Hydroxyzine (Atarax, Vistaril)
        - Non-Sedating antihistamines are occasionally effective: e.g., Loratidine(Claritin), Cetirizine (Zyrtec), Fexofenadine (Allegra)

# Atopic Dermatitis (cont.)

- Topical corticosteroids and emollients are mainstay for atopic dermatitis
- Emollients: Lac-Hydrin, Lubriderm, Aveeno, Nutraderm, Vaseline Intensive Care, etc…)
- The choice of corticosteroid potency should be based on: (1) patient's age, (2) affected body area, and (3) degree of inflammation

## Mild to Moderate Disease

- Low potency corticosteroid cream/ointment
  - Hydrocortisone 0.5-1% cream is applied 1-2 times daily for 2-4 weeks
- Emollients can be applied before or after corticosteroids

## Atopic Dermatitis (cont.)

### Moderate Disease

- Medium to high potency corticosteroid cream/ointment, e.g., Triamcinolone = TMC 0.1% (moderate potency); Betamethasone Dipropionate 0.05% (high potency).
- In acute flares, high potency steroid may be used for 2 weeks, followed by lower potency steroid.
- The face and skin folds are areas of high risk for atrophy with steroids; therefore a high potency steroid may be used up to 5 days to achieve a rapid response. Then the patient may be switched to a lower steroid product.

# Atopic Dermatitis (cont.)

## Moderate Disease

### Topical Calcineurin Inhibitors: Tacrolimus (Protropic)

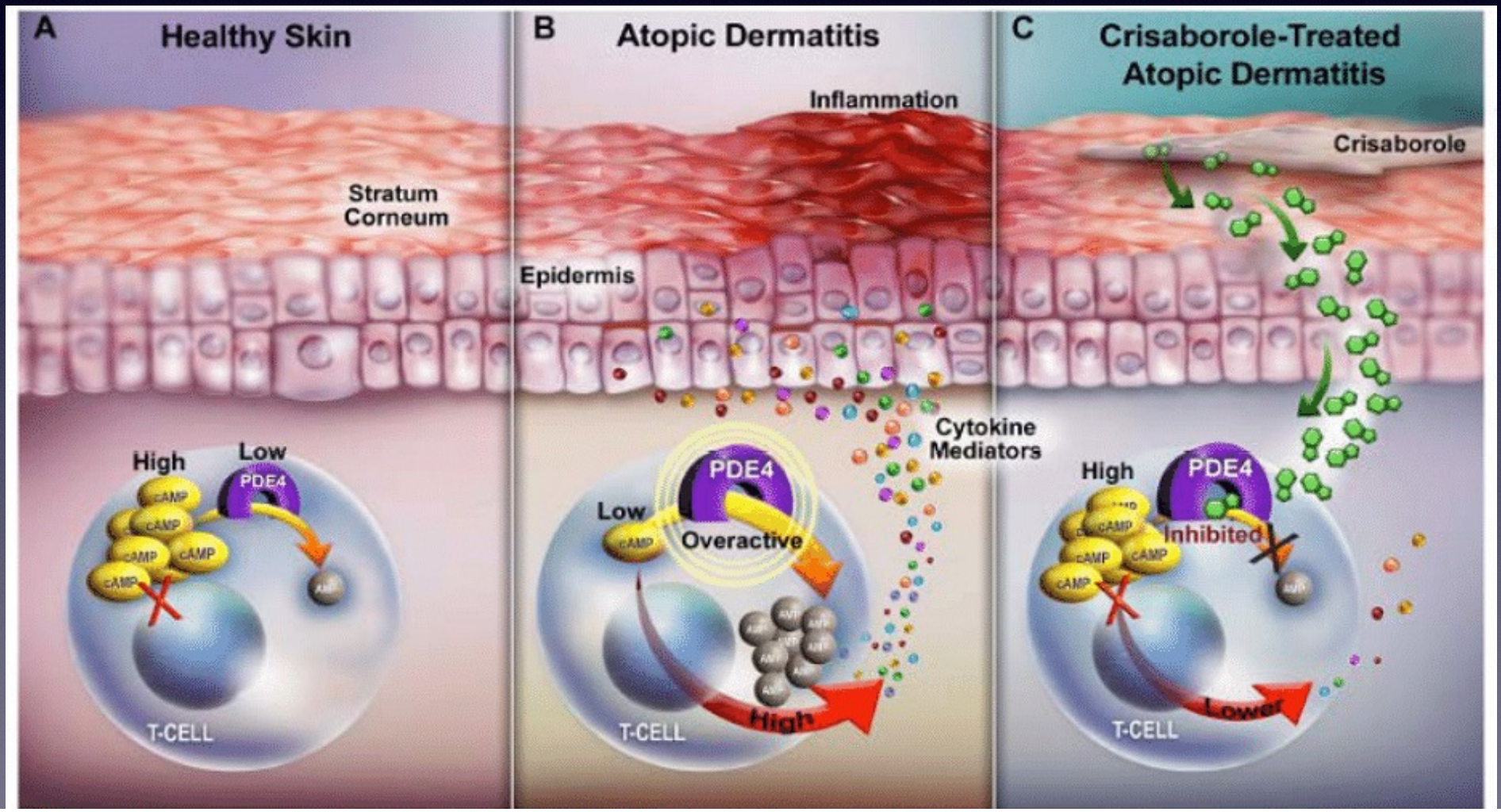
- Tacrolimus is a non-steroidal immuno-modulating agent → inhibits cytokine production.
  - Tacrolimus does not cause skin atrophy or other corticosteroid side effects.
  - Tacrolimus is comparable in efficacy to moderate potency steroid.
- FDA: use tacrolimus as a 2nd line agent in patients unresponsive to other treatments.
  - Avoid use in children under 2 years-old.
  - Avoid use in immunocompromised patients
  - Pregnancy category: C

# Atopic Dermatitis (cont.)

## Moderate Disease

## Crisaborole (Eucrisa) Topical Ointment

- MOA: Phosphodiesterase-4 (PDE-4) inhibitor in T cells → increase cAMP → decrease cytokine release



# Atopic Dermatitis (cont.)

## Moderate Disease

### Crisaborole (Eucrisa) Topical Ointment (cont.)

- Dosage: Apply thin layer to affected area(s) BID
- Side Effects: (1-10%): application site pain, burning, stinging; (<1%): contact urticaria
- Cost: $619 - $662 / 60 GM tube (Pfizer paid $5.2 B for patent from Anacor Pharmaceutics in 2016)

# Atopic Dermatitis (cont.)

## Moderate Disease

### Treatment of Acute Exacerbations in Chronic Disease

- A short course of systemic (i.e., oral) corticosteroid taper is useful in aborting acute exacerbation of chronic atopic dermatitis: Prednisone 40-60 mg/day x 3-4 days, then 20-30 mg/day for 3-4 days.

## Atopic Dermatitis (cont.)

## Moderate - Severe Disease

### Oral Cyclosporine (Sandimmune, Neoral)

- Cyclosporin is a calcineurin inhibitor → inhibits cytokine production.
- In adults, oral cyclosporine is a short-term treatment option: 3-5 mg/kg/day in BID dosing for 6 weeks. Then the dose is reduced until condition is stable, then cyclosporin is discontinued and treatment with topical corticosteroids is resumed.

# Atopic Dermatitis (cont.)

## Moderate - Severe Disease

Oral Cyclosporine (Sandimmune, Neoral)

- Side Effects: nephrotoxicity, hypertension, hypertrichosis, gum hyperplasia, and increased susceptibility to serious infections (due to immunosuppression).

# General Principles of Topical Corticosteroids

1. Topical corticosteroids should be applied BID since —> QID dosing is not necessarily better than BID or TID, and is more expensive

2. Preparations should be rubbed in thoroughly, preferably when skin is moist (e.g., after bathing) since hydration of skin increases percutaneous absorption —> improves therapeutic results

3. For maintenance treatment: use low to medium potency steroids (e.g., HC 1% or TMC 0.025%)

4. Thin-skinned areas of the body (e.g., face, flexures → knees, elbows, armpits, groin) and occluded areas are more prone to side effects of topical corticosteroids.

5. Children and geriatrics are at risk for systemic corticosteroid toxicities: high potency steroids used for > 2 weeks —> risk for systemic toxicity

6. With chronic condition, discontinue therapy gradually —> reduces potential for rebound flares

# Corticosteroids Indications and Contraindications

## Indications

Topical corticosteroids are drugs of choice for **inflammatory and pruritic conditions** (e.g., psoriasis, allergic contact dermatitis, atopic eczema, etc…

## Contraindications

Skin disorders with predominantly **infectious etiologies** are worsened by topical corticosteroids: acne vulgaris, ulcers, scabies, warts, fungal infections.

- Exception: during acute phase, topical corticosteroid products are sometimes combined with antibiotic and antifungal agents if marked inflammation is present (e.g., Corticosporin, Lotrisone).
    - Corticosporin Cream (neomycin + polymyxin B)
    - Lotrisone  Cream (betamethasone + clotrimazole)

# Side Effects of Topical Corticosteroids

Adverse effects are influenced by:

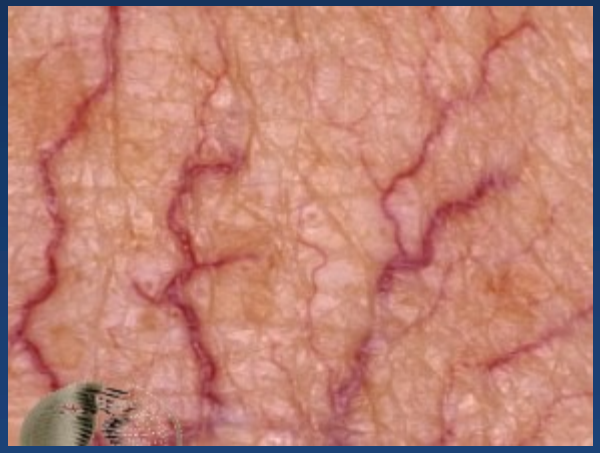
(1) potency of preparation,
(2) frequency of application,
(3) duration of use,
(4) anatomic site of application, and
(5) patient specific factors

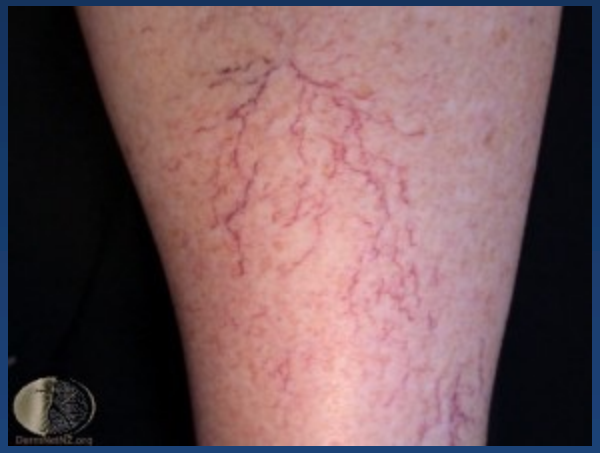
# Side Effects of Corticosteroids

1. Epidermal and Dermal Atrophy
   - generally takes several weeks to occur
   - usually reversible within 2 months after stopping the corticosteroid
   - inguinal, genital, perianal area are most vulnerable

# Side Effects of Topical Corticosteroids (cont.)

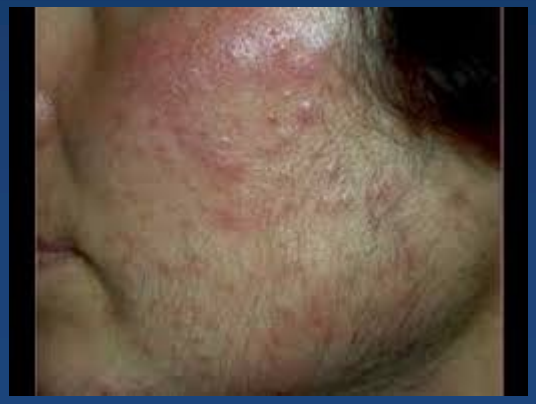
1. Telangiectasia (face, neck, groin, upper chest)
   - an abnormal dilation of red, blue, or purple superficial capillaries, or venules typically localized just below the skins surface
   - commonly referred to as "spider veins"
   - may not be reversible after discontinuing corticosteroid

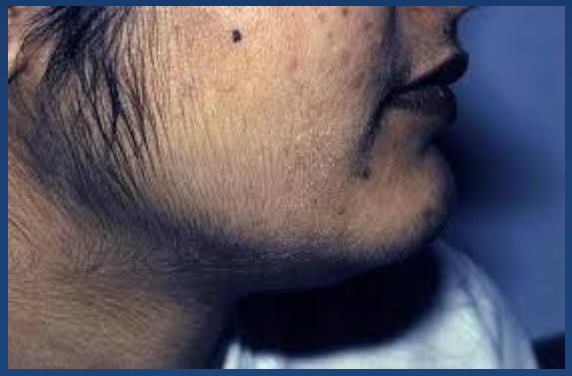




3. Striae (groin, axillary, inner thigh)
   - "stretch marks" —> usually permanent


4. Fine hair growth (face)
   - generally reversible





# Side Effects of Topical Corticosteroids (cont.)

3. Hypopigmentation
   - predominantly a problem of dark-skinned patients
   - generally reversible after corticosteroid treatment is discontinued

4. Acne
   - Although short-term use can suppress inflammation in acne, long-term use can trigger a flare of acne

5. Systemic absorption -> adrenal suppression (HPA- axis suppression)
   - Prolonged (several weeks to months) of application of high-potency steroids to large areas of body, especially if occlusion is used.

# Dermatophyte (Tinea) Infections

Dermatophytes (Trichophyton, Epidermophyton, Microsporum genera) are the prevailing causes of fungal infections of the skin, hair, and nails.

- Dermatophytes metabolize keratin and present with: tinea pedis (foot), tinea corporis (body surface), tinea cruris (jock itch), tinea capitis (scalp), and tinea unguium (nail = onychomycosis)

- Majocchi's granuloma is dermatophyte invasion into the dermal or subcutaneous tissue via penetration of hair follicles.

# Dermatophyte (Tinea) Infections

Most dermatophyte infections can be managed with topical antifungal agents:

- Clotrimazole (Lotrimin) cream (OTC) - BID dosing
- Miconazole (Micatin) cream (OTC) - BID dosing
- Econazole (Spectazole) cream- Once daily dosing
- Ketoconazole (Nizoral) Once per day (shampoo)

Note: Nystatin is an effective treatment for Candida infections; but is not an effective for dermatophytes.

# Dermatophyte (Tinea) Infections

## Oral Antifungal Agents

Oral antifungal agents are used for with extensive skin involvement (Majocchi's granuloma), nail involvement (onychomycosis), and patients who fail topical therapy

- Terbinafine (Lamisil): 250 mg daily for 2 weeks
- Itraconazole (Sporonox): 200 mg BID for 1 week
- Fluconazole (Diflucan): 150 mg weekly for 2-6 wks

Pediatric doses of these oral agents are weight based.

## Adverse Effects of Oral Antifungal Agents

- Terbinafine (Lamisil): headache (13%), diarrhea (6%), nausea (3%) dyspepsia (4%), rash (6%)
- Itraconazole (Sporonox): headache (4%), nausea (11%), vomiting (5%), diarrhea 3%), rash (9%)
- Fluconazole (Diflucan): headache (2-13%), nausea (2-7%), diarrhea (2-3%), vomiting (2-5%)

Pregnancy: Not recommended in pregnancy unless potentially life-threatening fungal infections occurs.

- Terbinafine: NA (information not available)
- Itraconazole: Category C*
- Fluconazole: 1st trimester use of high doses (>400 mg/day → cleft palate, abnormal facies, heart dz

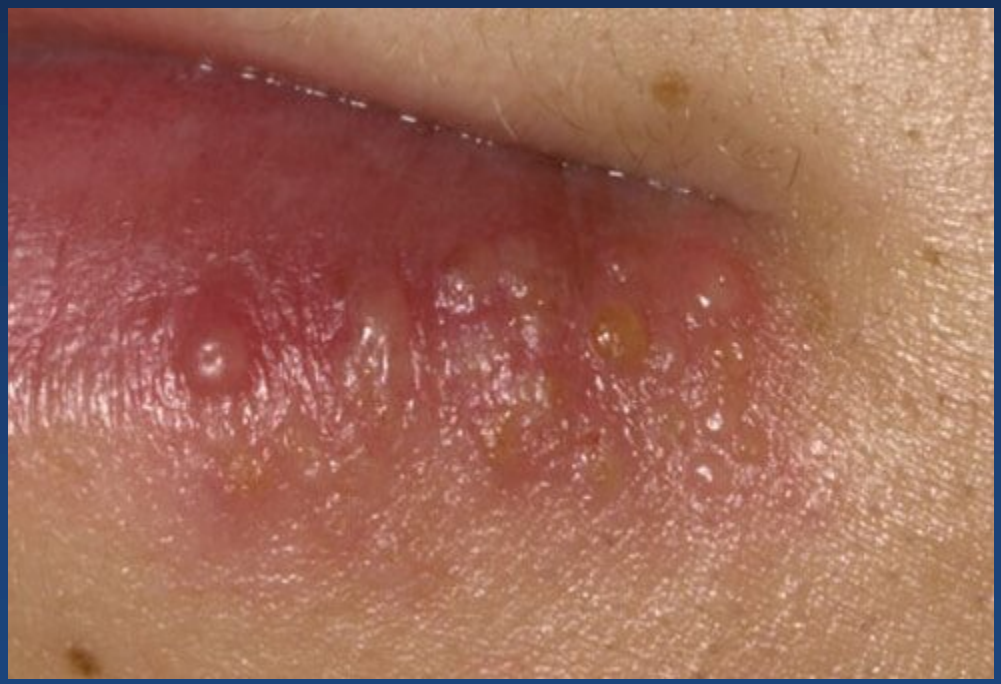
* Itraconazole (UpToDate - 2024): "pregnancy risks have not been associated with short-term use, but teratogenicity has not been adequately studied."

# Dermatophyte (Tinea) Infections (cont.)

Use of topical combination antifungal and corticosteroid products (e.g., Lotrisone = clotrimazole + betamethasone) may be beneficial for short-term relief of pruritus and inflammation.

# Treatment of HSV-1 Infections (Immunocompetent Host)

- HSV-1 may cause vesicular lesions of the lips and oral mucosa
- Reactivation of prior HSV-1 occurs in the trigeminal sensory ganglion



# Treatment of HSV-1 Infections

Available antiviral agents interfere with DNA polymerase —> inhibits DNA replication

1. Acyclovir (Zovirax)
   - PO, IV, and topical cream/ointment

2. Valacyclovir (Valtrex)
   - PO

3. Famcyclovir (Famvir)
   - PO

# General Considerations of Antivirals

- Famvir and Valtex have greater bioavailability and are dosed less frequently —> more expensive
    - Acyclovir: 400 mg PO TID or 200 mg PO 5x daily
    - Famcyclovir (Famvir): 500 mg PO TID
    - Valacyclovir (Valtrex): 1000 mg PO BID
- Duration of tx: 7-10 days
- Topical acyclovir needs to be dosed 5 times daily
    - High frequency/cost and limited efficacy of acyclovir cream favors oral acyclovir use
- Renal Insufficiency: dosage adjustments required based on creatinine clearance levels
- Pregnancy category: B

Episodic Treatment: Studies have demonstrated that rapid initiation of the following regimens at a well-defined prodrome hastens the healing of lesions by up to 2 days.

Acyclovir: 200 or 400 mg 5 x daily for 5 days

Famciclovir: 750 mg BID for 1 day or 1500 mg x 1 dose

Valacyclovir: 2 gm BID x 1 day

Conclusion: single-day dose of famciclovir (Famvir) or valacylovir offers convenience and lower cost than 5 days of acyclovir.

# Treatment of HSV-1 Infections (cont.)

## Adverse Effects of Antivirals

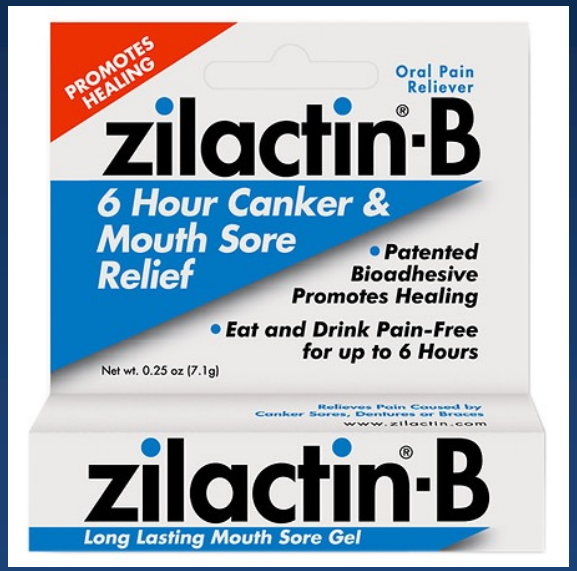
- Acyclovir (Zovirax): nausea (2-5%), vomiting (3%), diarrhea (2-3%), headache (2%)
- Famciclovir (Famvir): headache (23%), nausea (13%), diarrhea (2-9%), vomiting (1-5%)
- Valacyclovir (Valtrex): headache (14-35%), neutropenia (<18%), nausea (6-15%), vomiting (1-6%) dizziness (2-4%)

# Treatment of HSV-1 Infections (cont.)

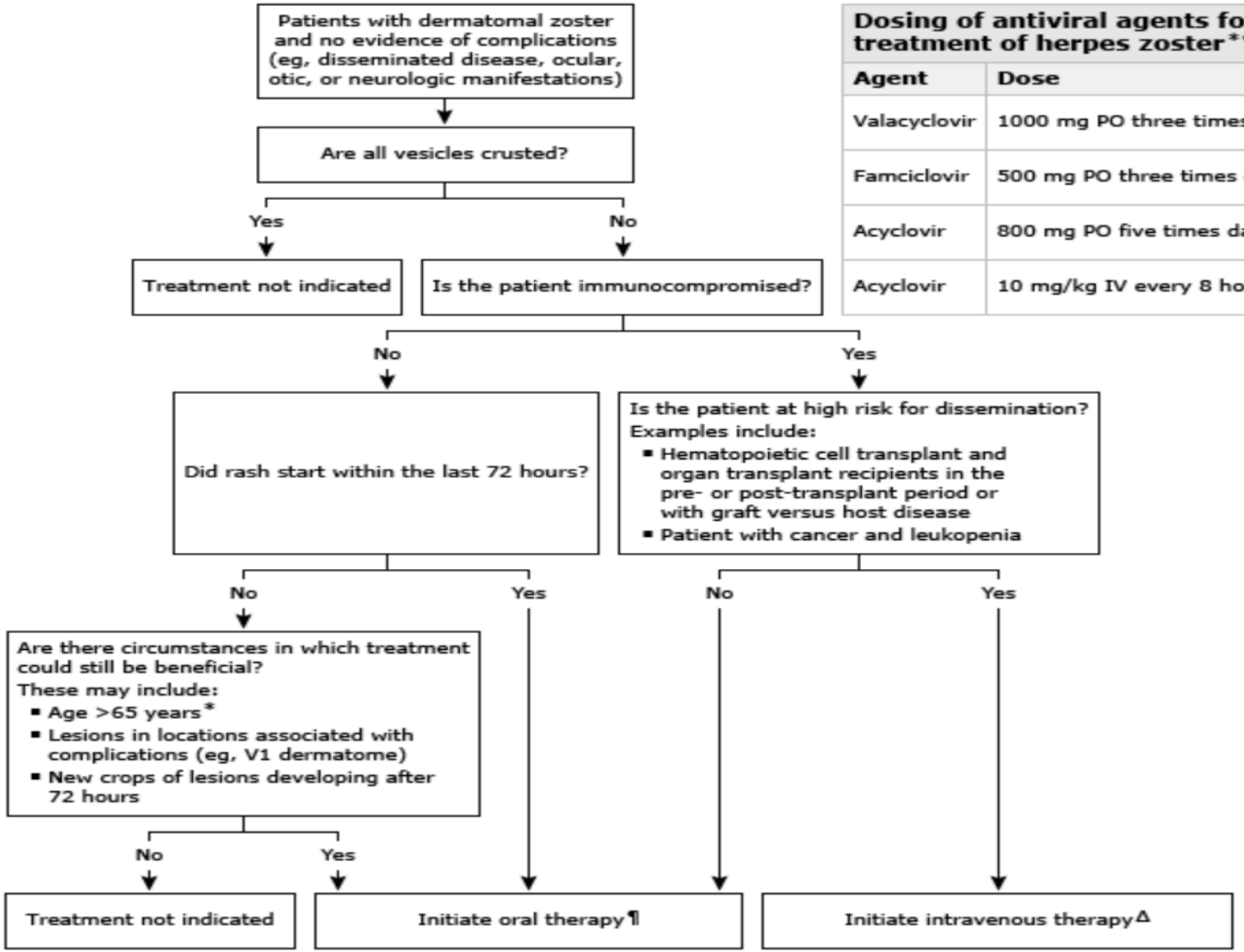
Adjunctive Therapy for painful oral and labial lesions:

- Viscous Lidocaine - short term pain relief (10-15 mins)

- Zilactin-B (hydroxy-propyl cellulose with benzocaine)
  → adheres to mucosa, protects lesions from irritants, and relieves pain benzocaine for up to 6 hours (Walgreens: $8.49)



# Herpes Zoster (Shingles) → Pharmacologic Management




**Dosing of antiviral agents for treatment of herpes zoster*¶◇**

| Agent | Dose |
|---|---|
| Valacyclovir | 1000 mg PO three times daily |
| Famciclovir | 500 mg PO three times daily |
| Acyclovir | 800 mg PO five times daily |
| Acyclovir | 10 mg/kg IV every 8 hours |

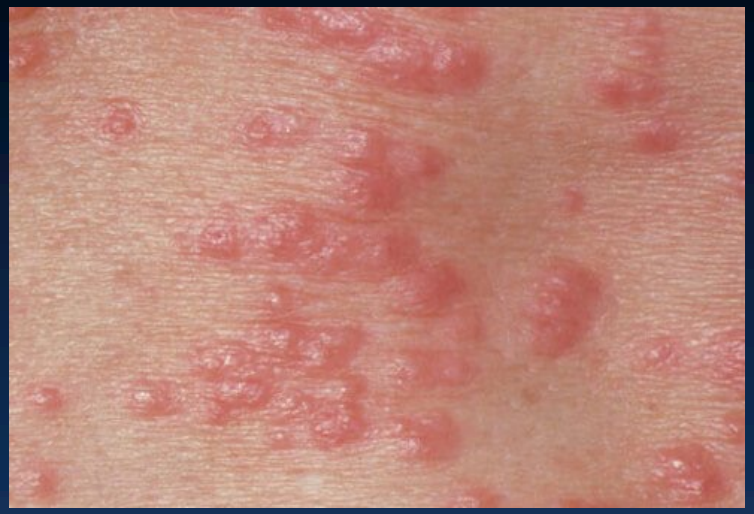
## Herpes Zoster (Shingles) → Adjunctive Therapy

In zoster-associated pain, use of opioids, tricyclic antidepressants (TCA), and gabapentin (Neurontin) are used as necessary to treat neuropathic pain.

NOTE: Systemic corticosteroids (in immunocompetent) are effective in reducing acute pain, improving quality of life, and returning patients to normal activities much more quickly.

- Prednisone 3-week regimen, starting at 60 mg/day) does not increase the risk of dissemination in immunocompetent patients.

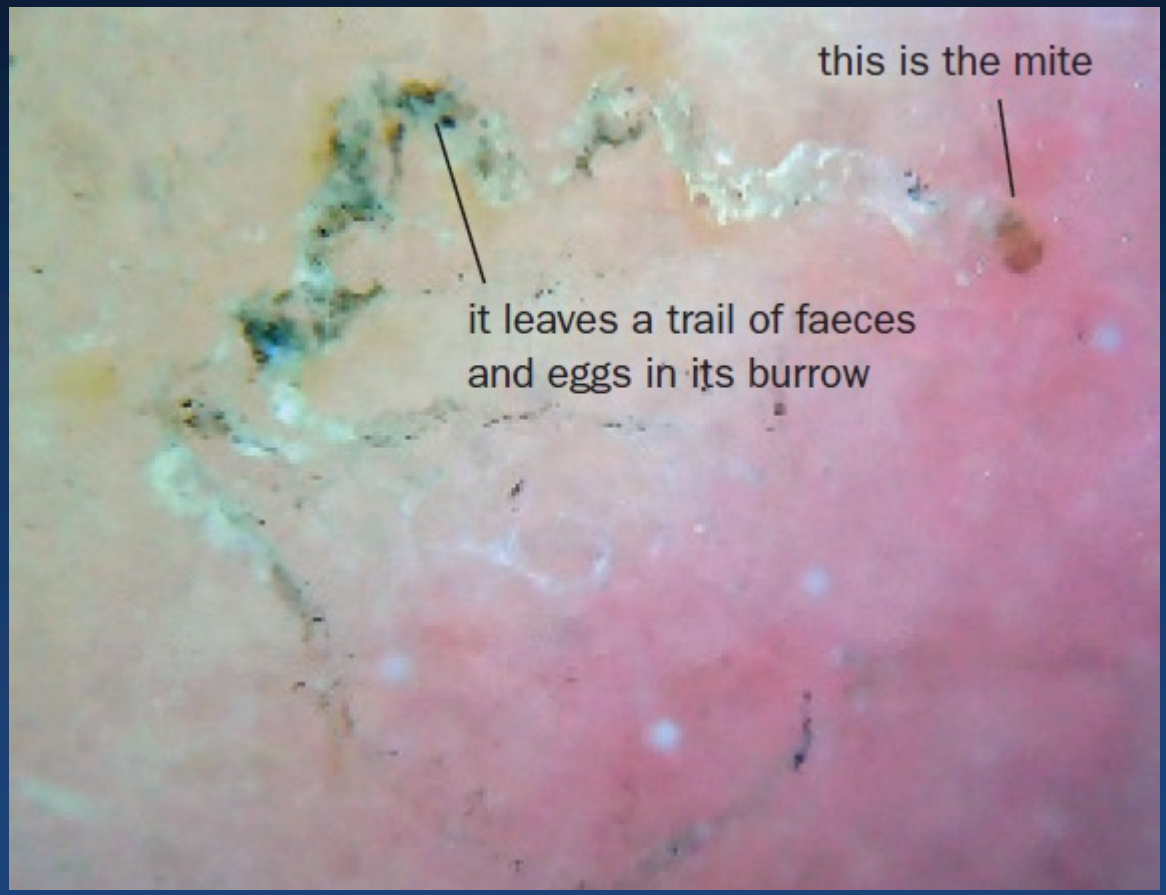
# Management of Scabies



Scabies: Infestation of the skin by the human itch mite, *Sarcoptes scabiei*. The initial symptom of scabies are red, raised bumps that are intensely itchy. A magnifying glass will reveal short, wavy lines of red skin, which are the burrows made by the mites.

Sarcoptes scabiei burrows into the skin and causes symptoms of itching and rash.

# Management of Scabies (cont.)



# Treatment of Scabies

- Topical Permethrin Cream (Elimite): Rx / OTC is 1st line treatment, with cure rates > 90%
- MOA: Permethrin is a neurotoxin which impairs function of voltage-gated Na channels in insects
  → disruption of neurotransmission
- Administration: message permethrin cream into skin from neck to soles of feet. (60 gm tube – 1 adult)
  - Permethrin should be removed by shower/bath after 8-14 hours (usually overnight).
  - Permethrin 2nd application is typically repeated in 1-2 weeks when necessary to eliminate mites.

## Permethrin Cream (Elimite)

- Efficacy: Permethrin is more effective than oral ivermectin (Stromectol) and Lindane (Kwell) cream.

  Note: Lindane has fallen out of favor due to systemic absorption and toxicity (i.e., seizures).

- Adverse Effects of Permethrin (Elimite)
  - Permethrin cream is well tolerated.
  - systemic absorption is low, and drug is metabolized quickly (unlike lindane)
  - Skin irritation is a potential side effect.

# Management of Scabies (cont.)

## Ivermectin (Stromectol)

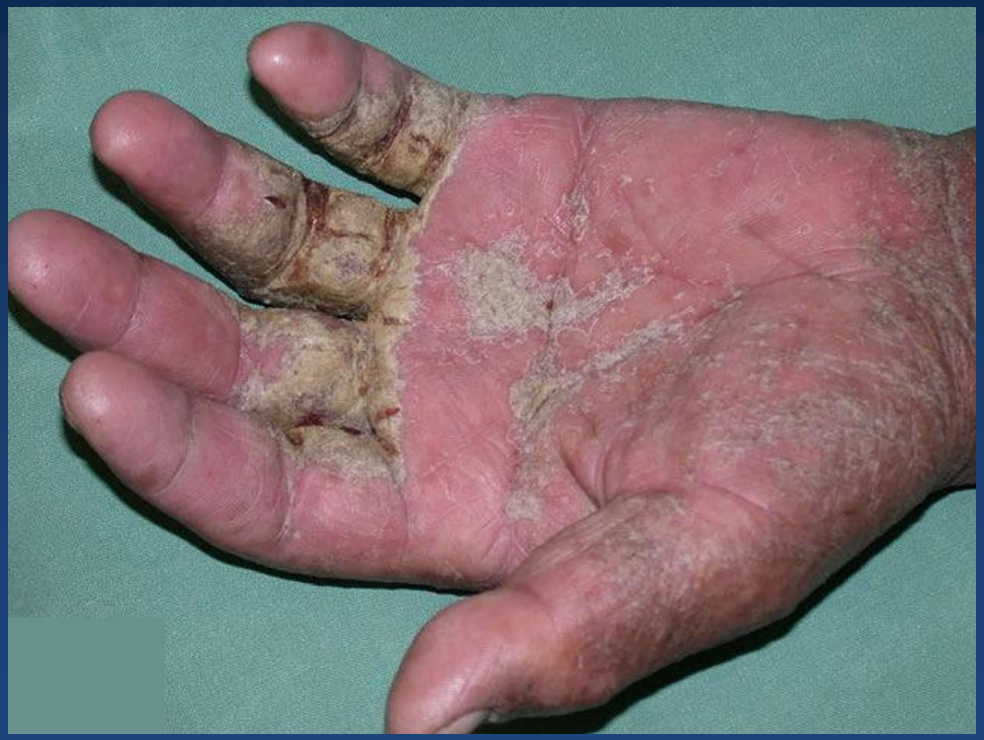
- Dose: 200 mcg/kg as a single dose followed by a repeated dose in 1-2 weeks.


- An anti-parasitic alternative to permethrin that has the advantage of ease of administration.
- Useful  for large scabies outbreaks in nursing homes where topical therapy can be impractical.
- Not recommended for pregnant women and children who weigh less than 15 kg → additional data is needed for safety in this population.

# Management of Scabies (cont.)

## Crusted Scabies

- CDC requires combination therapy:
  - permethrin applied daily for 7 days, then twice weekly until cure, AND
  - Ivermectin (200 mcg/kg/dose) on days 1, 2, 8, 9, & 15



# Management of Scabies (cont.)

Pruritus may persist up to 4 weeks after successful tx.

Treatment options for pruritus include:

- Antihistamines: Non-sedating antihistamines may be prescribed during the day and a sedating antihistamine (e.g., diphenhydramine) at night.
- Medium-high potency topical corticosteroids may also be prescribed to control itching.
- Oral glucocorticoid taper (e.g., Prednisone) for 1-2 weeks may be prescribed in severe cases of pruritus.