Atopic Dermatitis

Penny Miller, B.Sc.(Pharm.), M.A.(Ed.)
Faculty of Pharmaceutical Sciences and Department of Family Practice, Faculty of Medicine, UBC

Learning Objectives

- Outline the predisposing risk factors and triggers for exacerbations
- Recommend appropriate preventative measures
- Describe effective approaches to treatment
- Relate treatment efficacy and toxicity of medications used to treat atopic dermatitis
- Outline supportive evidence for topical agents

Definition of Atopic Dermatitis

- A chronic inflammatory pruritic skin disease which occurs most frequently in children but can occur in adults and follows a relapsing course.
- It is often associated with elevated serum IgE levels and a personal or family history of Type I allergies (allergic rhinitis & asthma).

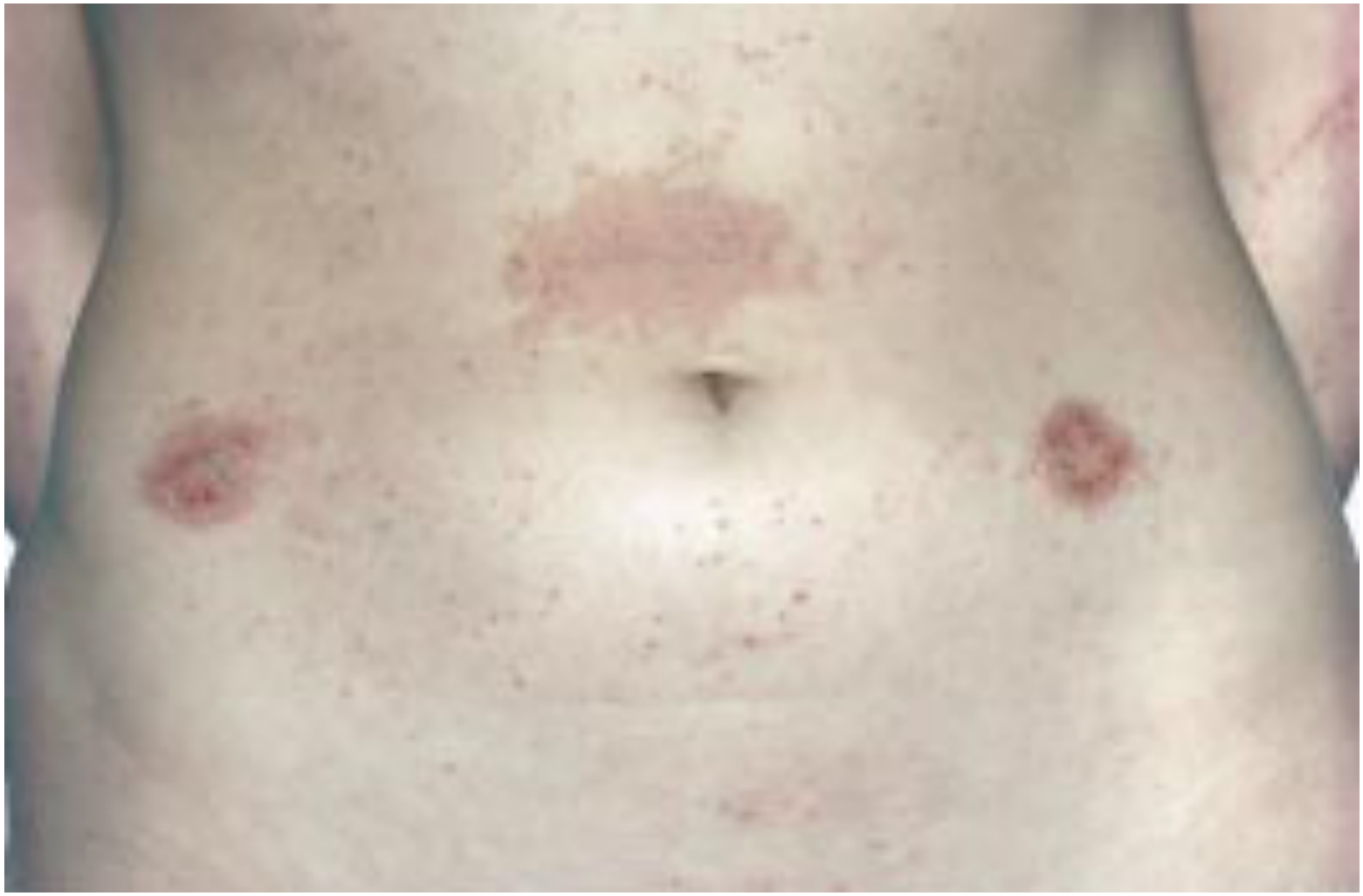
- J Am Acad Dermatol 2004;50:391-404 Guidelines of care for atopic dermatitis

“Eczema”

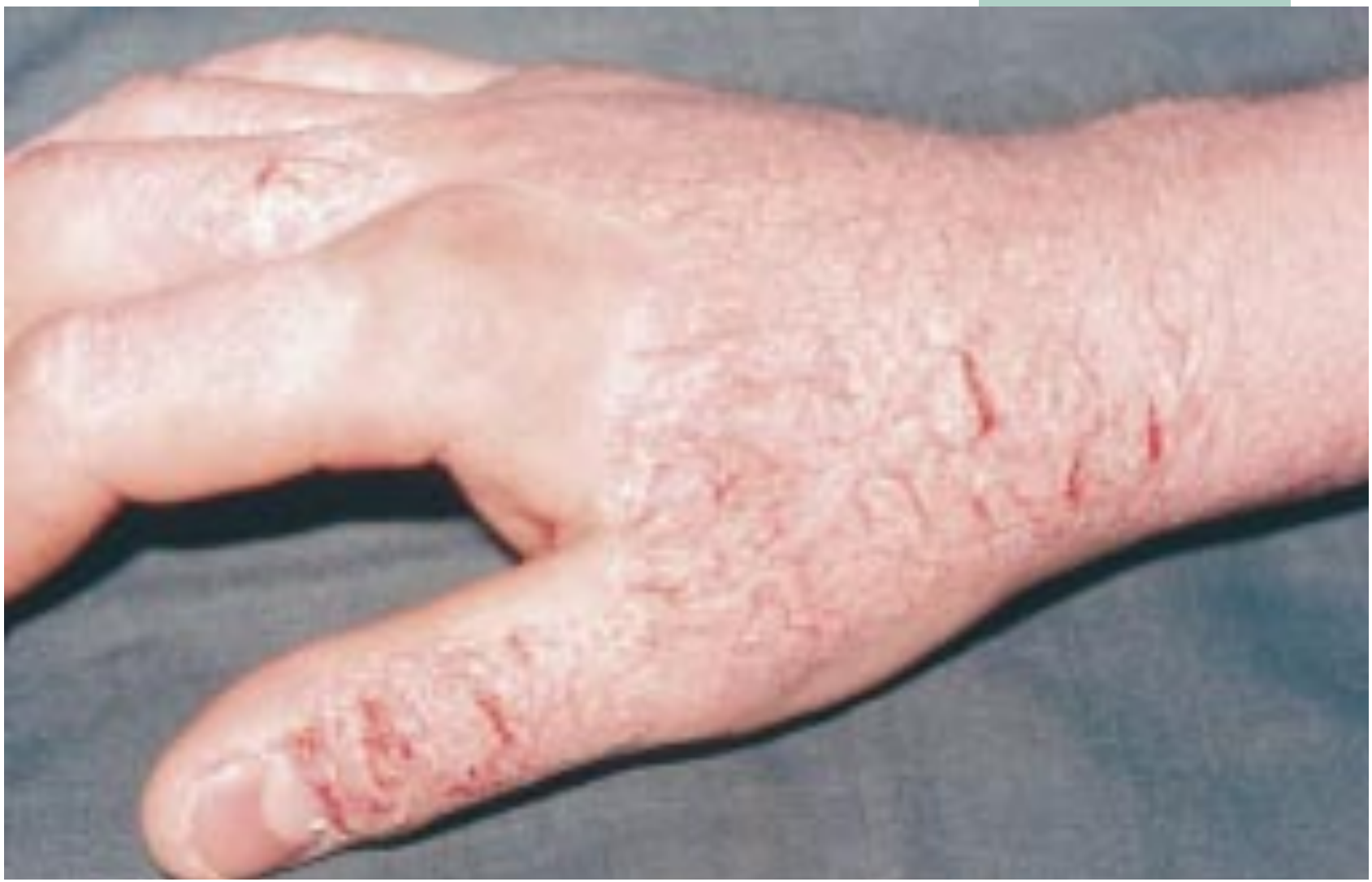
A generic term involving many conditions:

- Allergic contact dermatitis – an allergic reaction to a substance touching the skin (e.g. poison ivy, nickel, latex, lanolin, benzocaine, neomycin)
- Irritant contact dermatitis – usually a reaction of hand skin to detergents or chemicals
- Nummular eczema – small coin-shaped areas of red skin and weeping areas on trunk or lower legs of adults.

Allergic contact dermatitis to nickel studs in jeans



Irritant contact dermatitis of the hand



Epidemiology of Atopic Dermatitis

- Incidence is 14- 22% of children in Canada
- 80% of cases develop before age one
- 90% of cases are < 5 years of age
- 84% are mild cases, 14% are moderate and 2% are severe Br J Dermatol 1998;139:73-6
- Rare after age 40 Emerg Med Clin North Am 1985;3:677-92

Pathophysiology

- An inheritable condition with a 70% risk if both parents are affected
- Dry skin (disruption of water and skin lipids in stratum corneum) → pruritis
- Defective “off switch” for Th2 helper lymphocytes → cytokine release (inflammation)
- Increased IgE (antibody) levels

Signs and Symptoms

Acute:

- Pruritis
- Erythema
- Vesicles
- Exudate (crusts)

Chronic:

- lichenification (skin markings)
- Skin thickening
- Fissures
- Scaling

- Characterized by exacerbations and remissions
- Clinical presentation changes with age

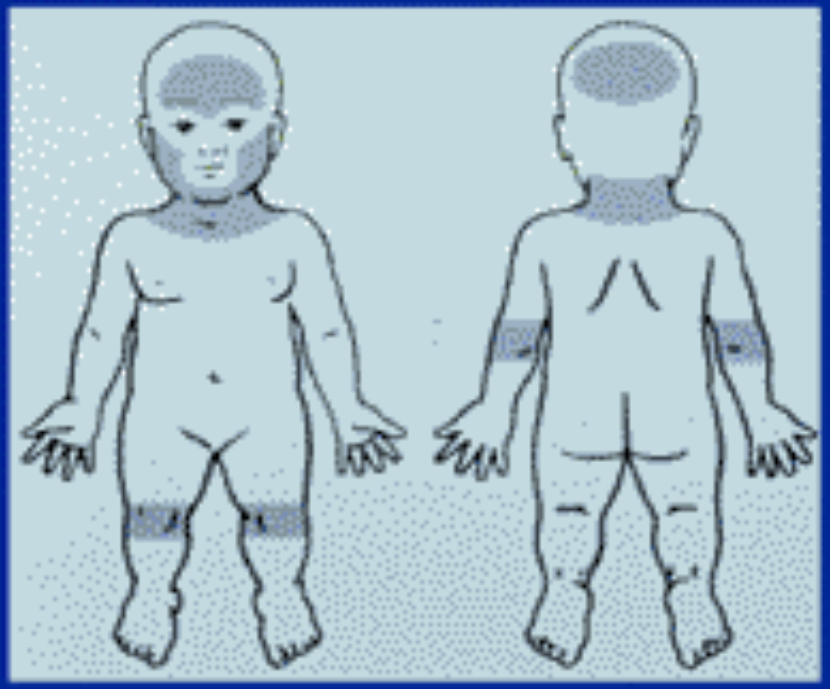
Infancy and childhood

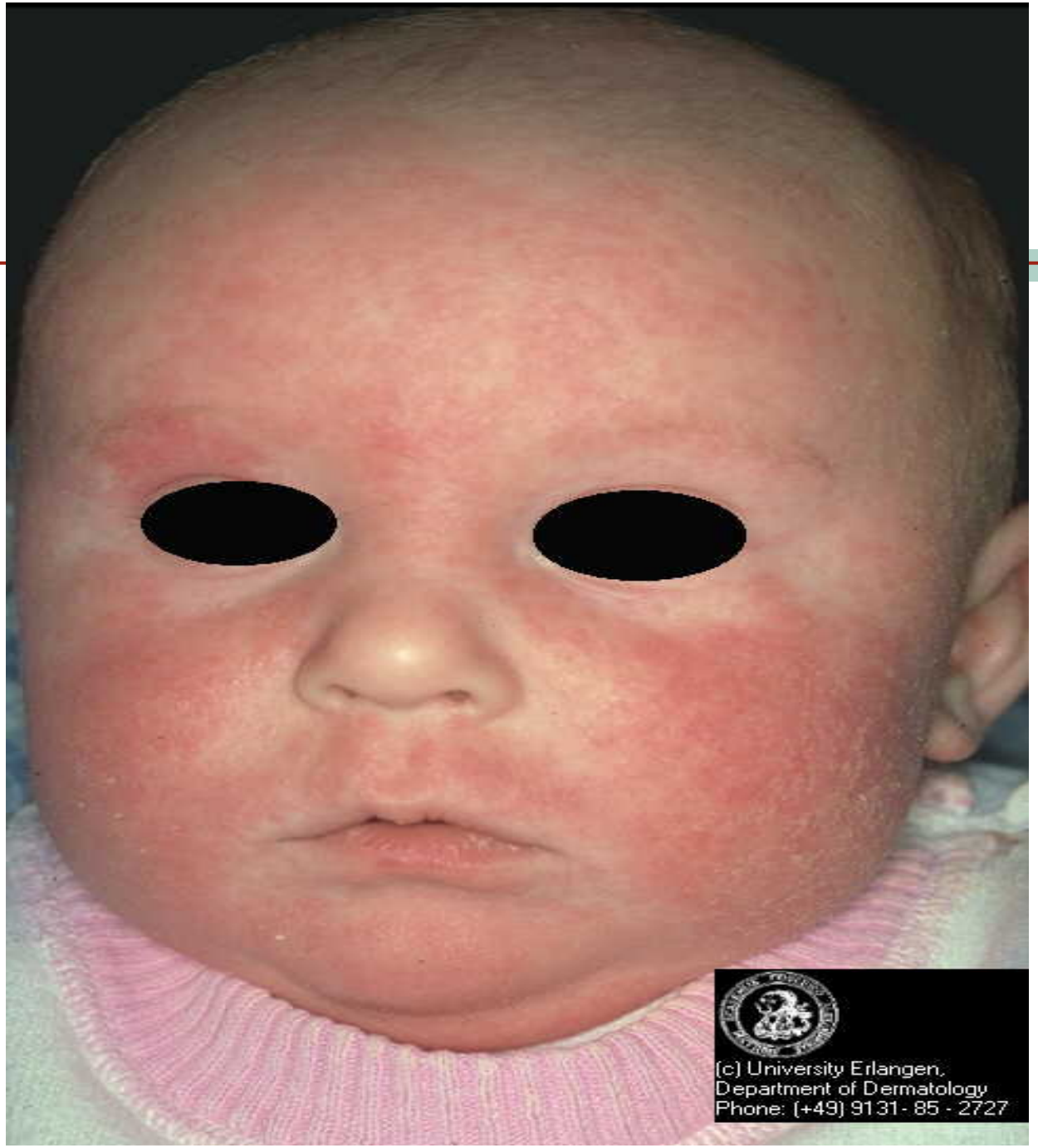
Commonly affected areas are:

- face (especially cheeks)
- Scalp
- Trunk
- Extensor surfaces of arms and legs

Infancy and Childhood

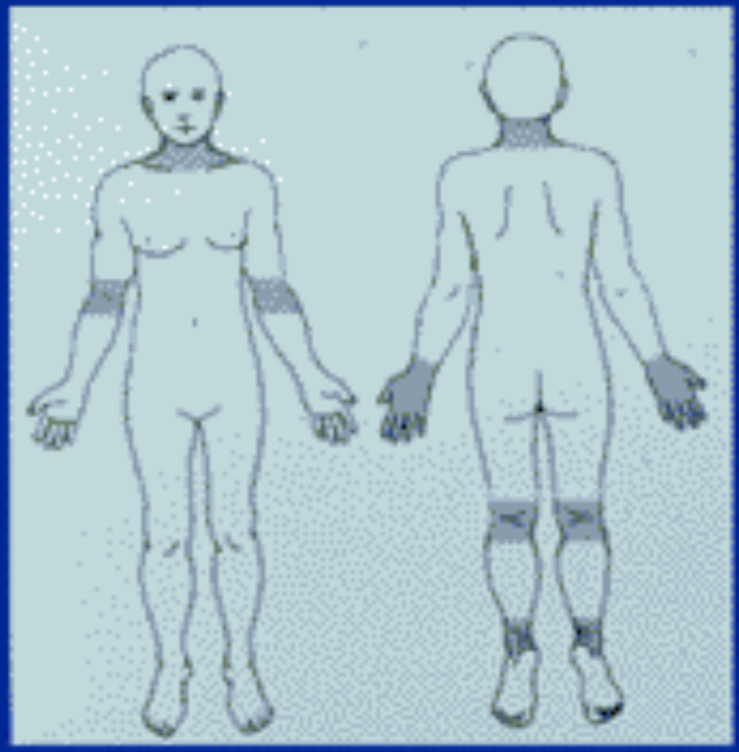
- Face is commonly affected
- Extensor surfaces of arms/legs
- Often associated with asthma and allergic rhinitis
- Condition generally improves with age




(c) University Erlangen,
Department of Dermatology
Phone: (+49) 9131 - 85 - 2727

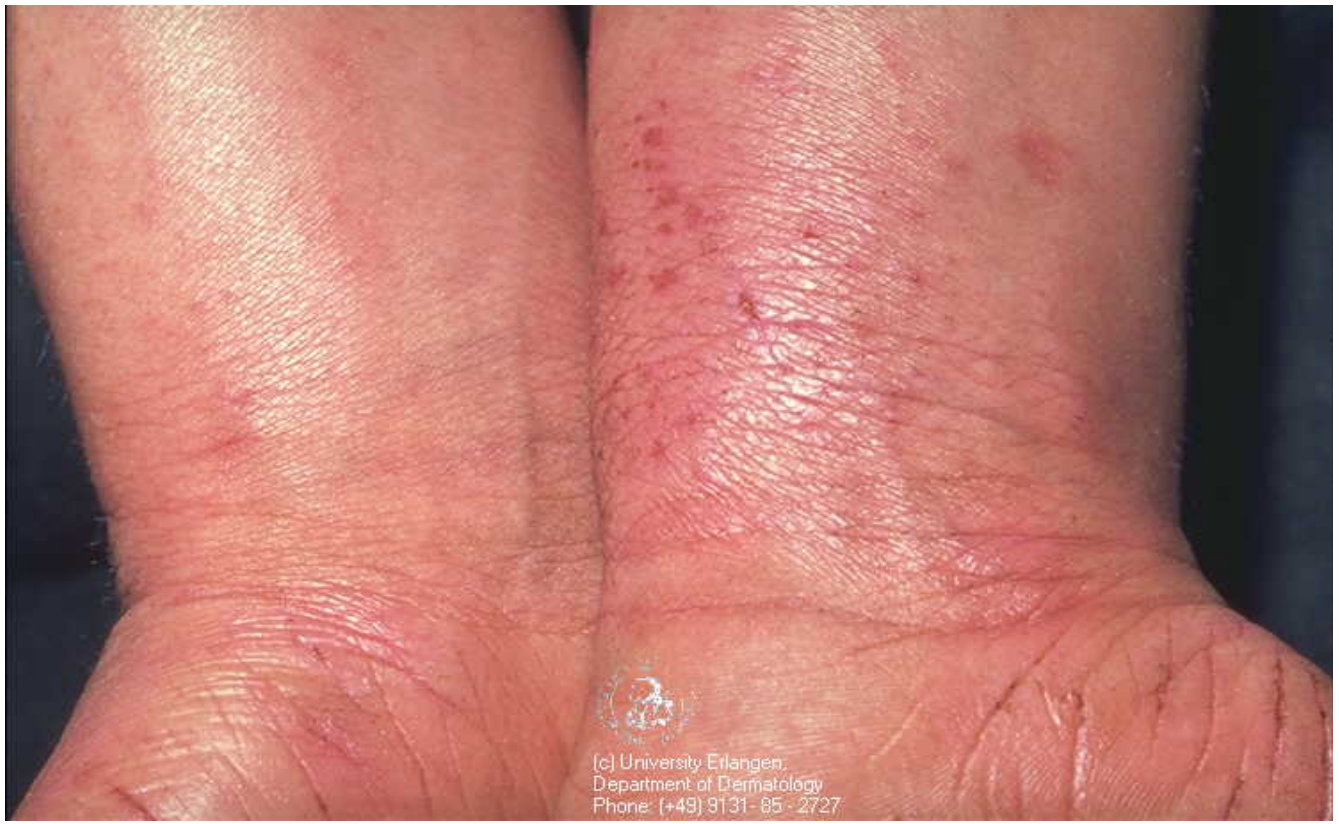
Adolescence and Adulthood

- Flexural surfaces are commonly affected
- Chronic involvement can lead to lichenification
- Condition generally improves with age



Adolescence and Adulthood

- Flexural surfaces are commonly affected
- Hands



Exacerbating Factors

- Climate – extremes of temperature and humidity levels (worsened with heavy perspiration, dry winter air)
- Irritants – Detergents, solvents

  -wool, nylon, polyester
- Foods -eggs
- Air borne allergens- dust mites, molds, dander, pollen
- Anxiety
- Infections – Staphylococcus aureus, Herpes simplex

Treatment Goals

- Decrease itching and resultant scratching (→excoriation, lichenification and sleep loss)
- Minimize recurrences
- Reduce treatment related local and systemic side effects

Management - Lubricants

- Lukewarm baths for 20 minutes, gently pat dry then follow by application of a moisturizer within 3 minutes
- Avoid bath oils with sensitizing lanolin or fragrances. Avoid irritating bath salts.
- Non-irritating soaps: Neutrogena, Pears, Lowila, Petrophyllic,plain white Dove, Caress, Tone, Dial, Cetaphil
- Therapeutic bath oils:
  - Aveeno bath oil, Keri bath oil

Management- Lubricants

- Emollients (moisturizers) sooth the itchiness and soreness
- Use up to 500 gm every one to two weeks
- Ointments- most occlusive but greasy and occlude sweat glands (for dry or lichenified lesions)
- Creams – useful for wet,weeping lesions
- Lotions – high water content and/or alcohol may cause further drying of skin through evaporation (useful for hairy areas)
- Gels – useful for hairy areas (contain alcohol)

Management -Lubricants

- Ointment based (occlusive and greasy)
  - Vaseline (petroleum jelly)
  - Hydrophilic petrolatum
  - Aquaphor
  - Mineral Oil (Baby oil)
  - Silicone preparations (occlusive but not greasy) – Barrier cream, Prevex
- Creams (less occlusive and greasy)
  - Moisturel (Neutrogena)
  - Glaxal Base
  - Aveeno
- Lotions (therapeutic)
  - Aveeno Lotion
  - Keri Lotion
  - Promani Lotion

Management - Lubricants

- Urea, Alpha-hydroxy acid (AHA), Lactic acid preparations (soften and rehydrate skin but may sting)
  - Uremol -10
  - Lac-hydrin
  - Dermalac
  - Lacticare (has fragrance)

Topical Corticosteroids

- Have anti-inflammatory, antipruritic, and vasoconstrictive effects
- DOSAGE FORMS:
  - Creams – wet lesions
  - Lotions – wet lesions in hairy areas
  - Gels –hairy areas
  - Ointments-dry, scaly or hyperkeratinized areas (less stinging)
- Occlusion-
  - Applying polyethylene film (plastic wrap) increases absorption 10 – 100 fold
  - Increases risk of atrophic striae and bacterial or fungal infections

Topical corticosteroids

- POTENCY:
  - *Lowest* (e.g. Hydrocortisone ½ or 1%)– use for thinned skin areas (face, eyelids, skin flexures, scrotum), in elderly, children, infants and for long-term treatment.
  - *Mid-Potency* (e.g. betamethasone 0.05%)- thick skin areas, intermittent use
  - *Highest* (e.g.Clobetasol 0.05% *Dermovate*) short-term exacerbations unresponsive to mid-potent agents. Do not use on large areas, or thinned skin areas.
- Menthol and/or camphor (0.25%) *Sarna* (or Phenol) may be added for additional itch control. Also, a local anesthetic (Pramoxine 1% *Sarna-P*)

Topical Corticosteroids Side Effects

- Skin atrophy
- Telangiectasia (prominent blood vessels)
- Striae (stretch marks)
- Acneiform eruption
- Hypertrichosis (localized hair growth)
- Delayed wound healing
- Infection(staph aureus or Herpes simplex)
- Tachyphylaxis (tolerance)(Occurs after several weeks or months usage) (Management is stopping treatment for 4 to 7 days; intermittent use or switch corticosteroid)

Topical Corticosteroid Systemic Side Effects

- Hypothalamic-pituitary-adrenal axis (HPA) suppression (kids < 2 years old with severe disease)
- Suppression of growth rate in children (monitor height and weight)
- Osteoporosis in adults

  (avoid long term use of potent steroids)
- Glaucoma

- * important to assess background risk factors for these side effects

Topical Corticosteroids Quantities Required (Adults)

Once or twice daily application

Area	Single application	Twice daily for 7 days
One hand	1 gram (pea size)	15 grams
Two hands; head; face; genitals	2 grams	30 grams
One arm; front or back of trunk	3 grams	45 grams
One leg	4 grams	60 grams
Whole body	30 grams	500 grams

Topical Corticosteroid

- Mild exacerbation
  - Use for 3-4 days only
  - Low potency (e.g.Hydrocortisone 1%)
- Moderate exacerbation
  - Taper over 2 weeks
    - Use twice daily for 7 days, then
    - Use once daily for 7 days

Topical corticosteroids

- Severe exacerbation
  - High Potency for one to two weeks
  - Try to avoid systemic steroids
  - Then, consider maintenance topical steroid with
    - Low potency daily or
    - High potency steroid twice weekly

      BMJ 2003; 326:1367-70

- Once daily application as effective as twice daily application. Health Technol Assess 2000;4(37):1- 191

Calcineurin Inhibitors (Topical Immunomodulators)

Tacrolimus 0.03% and 0.1% ointment (*Protopic*)

- macrolide immunomodulator

  Calcineurin is an enzyme involved in release of cytokines. Inhibition of this enzyme decreases T lymphocyte activation.

- Clinical response with bid application seen within one week (> 2 years of age)
- As effective as low to mid-potency steroids
- Side effects – burning, redness, pruritis, tolerance, varicella zoster infections, photosensitivity
- Advantage – no skin atrophy, minimal systemic absorption *but cases of high serum concentrations**
- Expensive $85 for 30 grams

Calcineurin Inhibitors- topical

- **Pimecrolimus** 1% cream (*Elidel*)
- Bid (> 2 years of age)
- Less effective than betamethasone valerate 0.1%
- Photosensitizing but less burning than tacrolimus
- Fewer studies (and only lasting one year)
- Cost $72 for 30 grams

Calcineurin Inhibitors- topical

- **CONCERNS :** immunosuppression and malignancy (*10 cancer cases in 3 years reported*)
- Systemic effects – increased susceptibility to infection, **lymphoma, skin cancer**, hypertension, renal toxicity, hyperglycemia, electrolyte imbalance
- **LESSONS LEARNED** Arch Dermatol 2006:142; 633-7
- Not to be used in Kids <2 years of age
- Not First line (in spite of aggressive marketing)
- Not for long-term treatment
- Not for immunocompromised patients

Efficacy EVIDENCE – Systematic review of Calcineurin Inhibitors (CI) vs placebo or vs corticosteroids(CCS)

- Design: (1997-2006 10 years) RCT's CIs reporting efficacy outcomes, in comparison to CCS or vehicle (placebo) or both. Data synthesis: of 210 articles, 19 studies were included, 10 for tacrolimus and 9 for pimecrolimus, involving 7378 patients of whom 2771 applied tacrolimus, 1783 applied pimecrolimus, and 2824 were controls.
- Both drugs were significantly more effective than a vehicle. However, two long-term trials comparing demonstrated the value of **pimecrolimus in reduction of flares and steroid-sparing effect after 6 months.** Compared to CCs, both 0.1% and 0.03% tacrolimus ointments were **as effective as moderate potency CCs,** and more effective than a combined steroid regimen. Tacrolimus was more effective than mild CCs.

- El-Batawy MM, Bosselia MA, Mashaly HM, Hafez VS.Topical calcineurin inhibitors in atopic dermatitis: a systematic review and meta-analysis. *J Dermatol Sci*. 2009 May;54(2):76-87

Cancer risk controversy and topical Calcineurin Inhibitors

- “There is no scientific evidence of an increased risk for malignancy due to a topical treatment with calcineurin inhibitors.”

- Thaci D, Salgo R. Malignancy concerns of topical calcineurin inhibitors for atopic dermatitis: facts and controversies. Clin Dermatol. 2010 Jan-Feb;28(1):52-6
- Patel TS, Greer SC, Skinner RB Jr. Cancer concerns with topical immunomodulators in atopic dermatitis: overview of data and recommendations to clinicians. Am J Clin Dermatol. 2007;8(4):189-94.

Pimecrolimus Cream and Infection?

- 1133 patients 3 - 23 months of age with mild to severe atopic dermatitis were treated for up to 2 years
- Treatment with 1% pimecrolimus cream was not associated with an increase in the overall incidence of non skin infections
- The incidence rates for total bacterial, fungal, parasitic, and viral skin infections were comparable for patients treated with 1% pimecrolimus cream and patients who received the vehicle

Pediatrics. 2006 Jan;117(1):e118-28

Coal Tar Preparations

- Antipruritic and antiinflammatory properties
- May reduce need for high potency corticosteroids (Few valid trials of efficacy)
- Side effects – offensive odour, stain clothing, folliculitis, photosensitivity

Antihistamines

- Pruritis in Atopic dermatitis is not histamine-related so efficacy is poor Arch Dermatol 1999;135:1522-25
- Potent sedating antihistamines e.g. hydroxyzine, doxepin taken 30- 60 minutes prior to bedtime may reduce sleep disturbance
- Non-sedating antihistamines e.g. loratidine, desloratidine, fexofenadine, etc are of no value
- Topical antihistamines are not recommended (may be sensitizing)

Systemic therapy

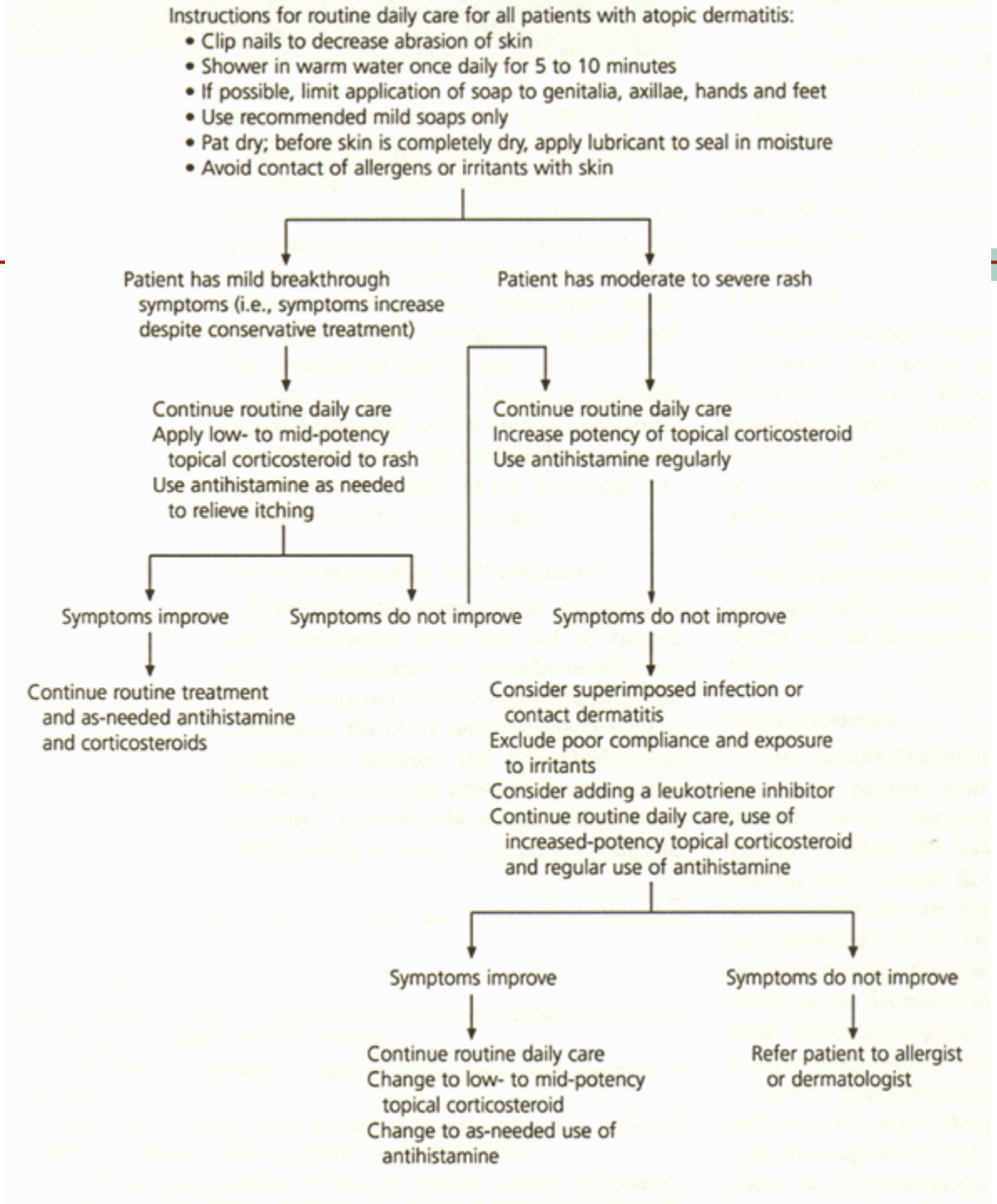
- Oral prednisone 0.5 – 1 mg/kd/day for one to two weeks if severe twice yearly
- Cyclosporine- immunosuppression
- Azathioprine- immunosuppression

Herbals:

- Evening Primrose Oil – shown to not be helpful
- Borage Oil – not effective

Phototherapy:

UVA and UVB is helpful 2 – 3 times weekly


Instructions for routine daily care for all patients with atopic dermatitis:
• Clip nails to decrease abrasion of skin
• Shower in warm water once daily for 5 to 10 minutes
• If possible, limit application of soap to genitalia, axillae, hands and feet
• Use recommended mild soaps only
• Pat dry; before skin is completely dry, apply lubricant to seal in moisture
• Avoid contact of allergens or irritants with skin
Patient has mild breakthrough symptoms (i.e., symptoms increase despite conservative treatment)
Patient has moderate to severe rash
Continue routine daily care
Apply low- to mid-potency topical corticosteroid to rash
Use antihistamine as needed to relieve itching
Continue routine daily care
Increase potency of topical corticosteroid
Use antihistamine regularly
Symptoms improve
Symptoms do not improve
Symptoms do not improve
Continue routine treatment and as-needed antihistamine and corticosteroids
Consider superimposed infection or contact dermatitis
Exclude poor compliance and exposure to irritants
Consider adding a leukotriene inhibitor
Continue routine daily care, use of increased-potency topical corticosteroid and regular use of antihistamine
Symptoms improve
Symptoms do not improve
Continue routine daily care
Change to low- to mid-potency topical corticosteroid
Change to as-needed use of antihistamine
Refer patient to allergist or dermatologist

References

- Hanifin et al (Task Force) Guidelines of care for atopic dermatitis. J Am Acad Dermatol 2004;30 (3): 391 -404
- Ellis C, Luger T. International Consensus conference on Atopic DermatitisII (ICCADII): clinical update and current treatment strategies. Br J Dermatol 2003;140 (suppl 6): 3 -10
- Lipozencic J, Wolf R. Atopic Dermatitis: An update and review of the literature 2007;25:605-612.
- Krakowski AC, Eichenfield MD, Dohil MA. Management of atopic dermatitis in the pediatric population. Pediatrics 2008;122:812-24.
- Hoare C, Li Wan Po A, Williams H. Systematic review of treatments of atopic eczema. Health Technol Assess 2000;4:1- 108
- El-Batawy MM, Bosselia MA, Mashaly HM, Hafez VS.Topical calcineurin inhibitors in atopic dermatitis: a systematic review and meta-analysis. J Dermatol Sci. 2009 May;54(2):76-87
- Ference JD, Last AR. Choosing topical Corticosteroids. Am Fam Physician 2009;9(2):135-40.