Atopic Dermatitis: The Itch that Rashes

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Atopic Dermatitis

- Epidemiology[1]
  - 10-20% of children
  - 1-3% of adults
  - Often associated with allergic asthma and allergic rhinitis

Age of onset	Percent
<1	58
1-5	26
6-15	8
16-25	8
26-40	3

1. Beltrani VS. In: Atlas of Allergies and Clinical Immunology, 3rd Edition. Editor: Fireman P. 2006.

Atopic Dermatitis

- No objective test
- Diagnosis based on key features[1]
  - Pruritic dermatitis (essential feature)
  - Location
    - Infants/Children – facial and extensor surfaces
    - Adults – flexural surfaces
  - Chronic/Relapsing Dermatitis

1. Leung DYM et al. Annals Allergy Asthma Immunol. 2004;93(2).

Atopic Dermatitis

- Frequently Associated Features[1]
  - Personal/Family History of Atopy
    - 80% develop allergic rhinitis or asthma[1]
  - Xerosis
  - Cutaneous Infections
  - Non-specific dermatitis of hands and feet
  - Elevates serum IgE
  - Positive immediate-type allergy skin test
  - Early age of onset

1. Leung DYM et al. Annals Allergy Asthma Immunol. 2004;93:3(Supplememnt 2).

Atopic Dermatitis

- Risk Factors
  - Parental history (maternal>>paternal)
  - Female (1.3:1)
  - Higher SES
  - Fewer siblings
  - Freedom from early life infections (Hygiene Hypothesis)
  - Urban setting
  - Maternal smoking during pregnancy

Atopic Dermatitis

- Itching

  1) Xerosis (dryness)
     - Trigger for pruritis
     - Impaired epidermal barrier function
       - Decreased water permeability barrier
       - Increased transepidermal water loss

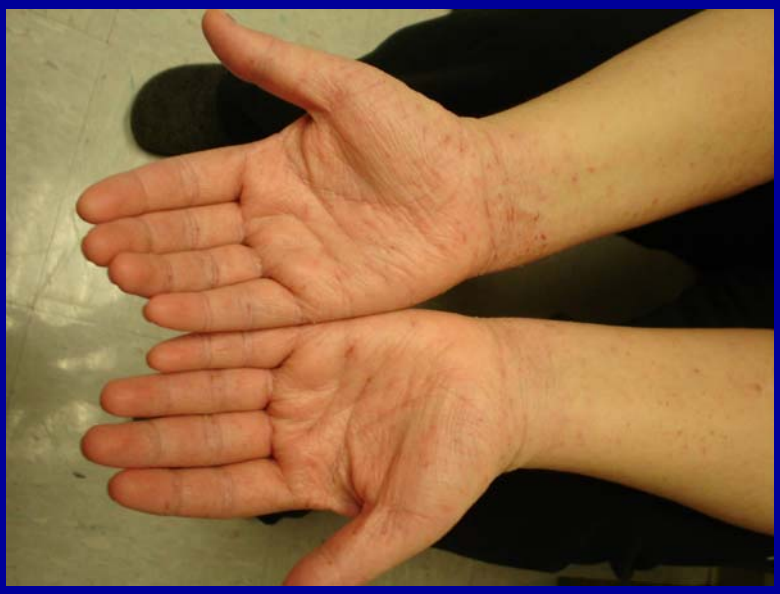
  2) Disturbed regulation of “itch” sensation in CNS

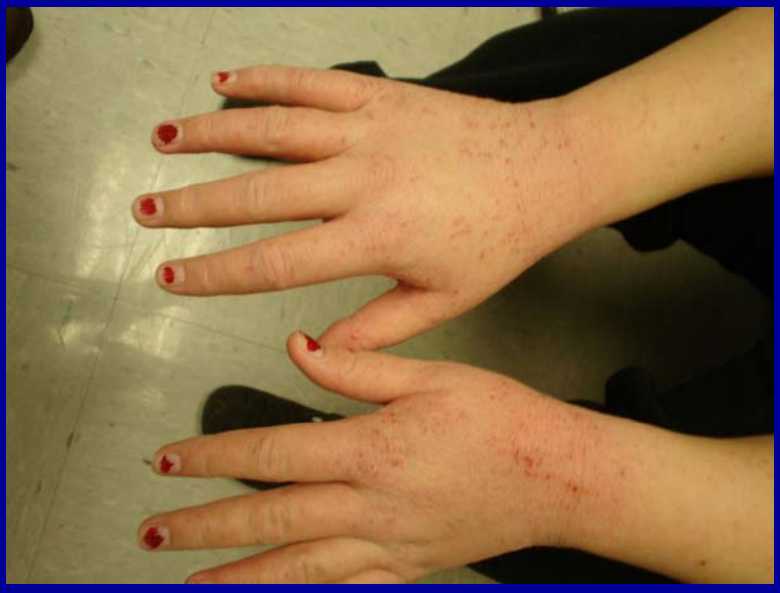
Atopic Dermatitis

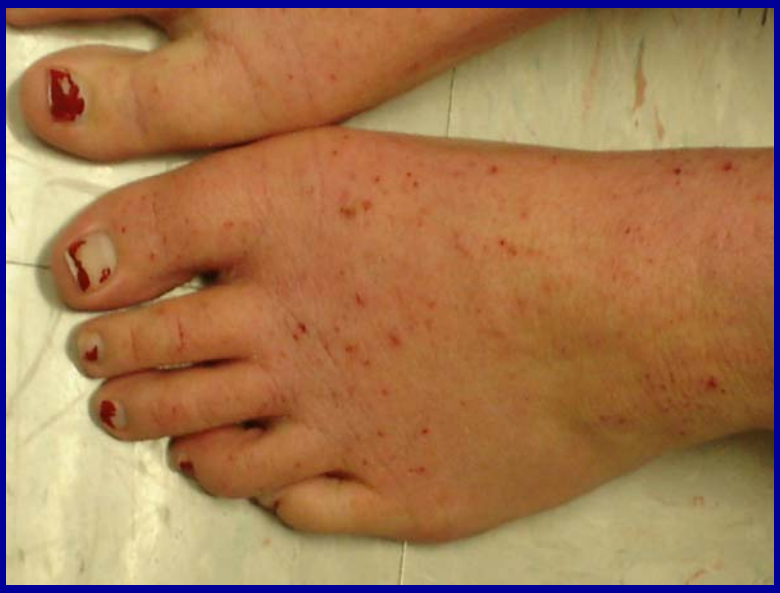
- Itching
  3) Inflammation
  - Increased Th2 cells resulting in
    - Increased IgE and specific IgE
    - Increased Eosinophils
    - Increased Eosinophilic mediators (ECP, MBP)
  - Decreased Th1 cells
  - Increased basophil and mast cell histamine release
  - Chronic macrophage activation
    - Increased GM-CSF, IL-10, PGE_2
  - Increased soluble IL-2 receptor levels
  - Increased number of high-affinity IgE-bearing Langerhan's cells
  - T-cell skin homing receptors (cutaneous lymphocyte associated antigen)

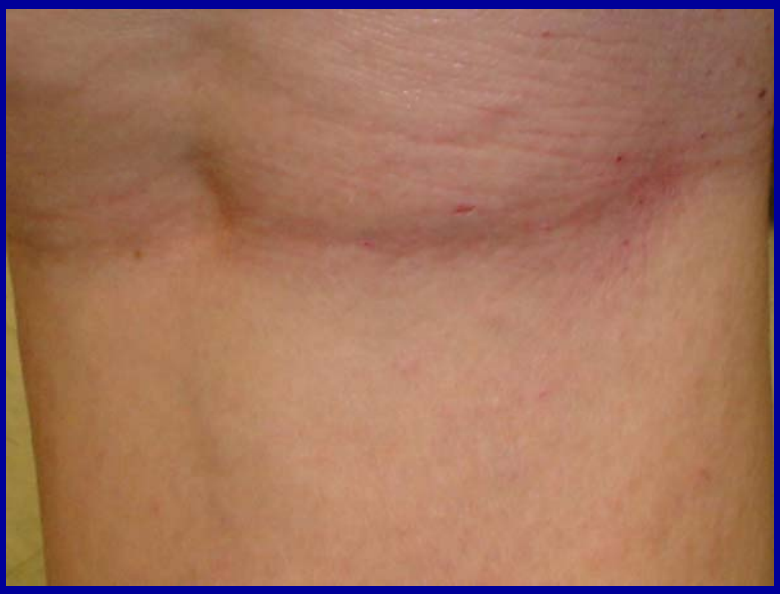
Atopic Dermatitis

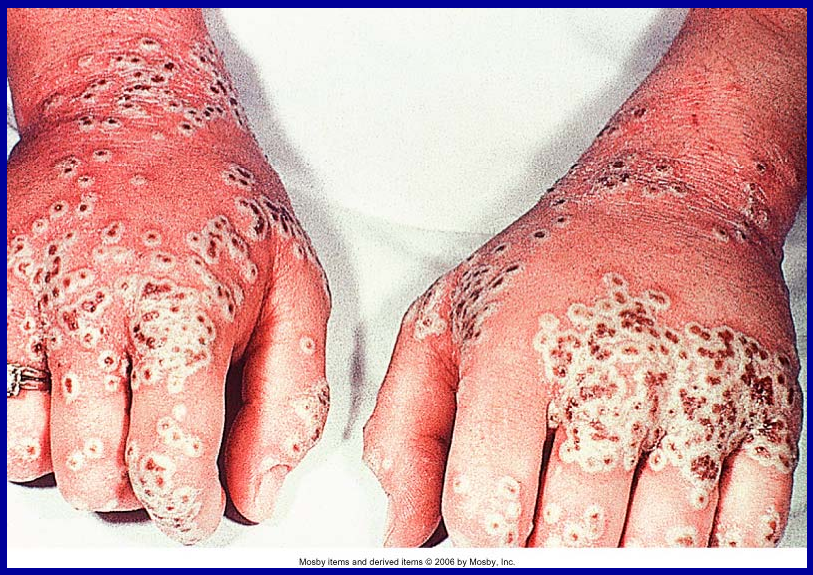
- Acute and subacute lesions
  - Intensely pruritic, erythematous papulovesicles associated with excoriation and serous exudate
- Chronic lesions
  - Lichenification
  - Papules
  - Excoriation
- All stages with xerosis







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Atopic Dermatitis

- Triggers[1]
  - Heat and exercise induced sweating
    - Abnormal pattern of thermoregulation
    - May reflect intrinsic disturbance of parasympathetic nervous system

1. Beltrani VS. J Allergy Clin Immunol. 1999;104:S87-S98.

Atopic Dermatitis

- Triggers
  - Epidermal antimicrobial peptide deficiency
    - *Staphylococcus aureus* is found in >90% of atopic dermatitis lesions
      - May exacerbate or maintain skin inflammation in AD by acting as a superantigen (stimulating marked activation of T cells and macrophages) or due to the presence of superantigen-specific IgE[1]
      - Inherent deficiency in cathelicidens, β-defensins (antimicrobial peptides)
    - Ceramide deficiency in skin (resulting from high expression of sphingomyelin deacylase)[2]
      - Leads to dry skin that is more susceptible to infection

1. Bunikowski R et al. J Allergy Clin Immunol. 1999;103:119-124.

2. Hara J et al. J Invest Dermatol. 2000;115:406-413.

Atopic Dermatitis

- Triggers[1]
  - Allergens
    - Typically high to very high serum IgE levels
    - Food sensitivity triggers lesions in 20-30% of children[2]
      - milk, egg, peanut, soy, wheat, fish and tree nuts account for nearly 90% of positive challenges
    - Contact sensitivity to house-dust mite plays a role in ~35%
    - Approximately 85% of patients demonstrate specific IgE
      - Causative role in atopic dermatitis for these implicated allergens is not firmly established

1. Beltrani VS. J Allergy Clin Immunol. 1999;104:S87-S98.

2. Sicherer SH, Sampson HA. J Allergy Clin Immunol. 1999;104:S114-22.

Atopic Dermatitis

- Triggers[1]
  - Irritants
    - (solvents, disinfectants, coarse bedding, household fluids (fresh fruit juices, wool, perfumes)
  - Contact allergens
    - (animal dander, HDM, molds)
  - Microbial agents
    - (viral, Staph, Pityrosporon; candida and dermatophytes, rarely)
  - Foods
    - (vasodilatory (alcohol, spicy) >> contactants > allergens)

1. Beltrani VS. J Allergy Clin Immunol. 1999;104:S87-S98.

Atopic Dermatitis

- Triggers[1]
  - Psyche
    - (stress, anxiety, sleep deprivation)
  - Climate
    - heat and sweating – increased itching
    - cold/dry weather – damage to stratum corneum barrier -> increased susceptibility to irritants and increased pruritis
  - Hormones
    - (puberty, menstrual cycle)

1. Beltrani VS. J Allergy Clin Immunol. 1999;104:S87-S98.

Atopic Dermatitis

- Course[1]
  - Earlier age at onset the more severe the course
  - Chronic and relapsing
  - Usually resolves by age 2 and the remainder improve by puberty

1. Leung DYM et al. Annals Allergy Asthma Immunol. 2004;93(2).

Atopic Dermatitis

- Adult DDx[1]
  - Allergic Contact Dermatitis
  - Cutaneous T-cell Lymphoma
  - Glucagonoma Syndrome
  - Irritant Contact Dermatitis
  - Pellagra
  - Pityriasis Rubra Pilaris
  - Psoriasiform Eruptions
  - Scabies
  - Seborrheic Dermatitis
- Pediatric DDx[1]
  - Acrodermatitis Enteropathica
  - Agammaglobulinemia
  - Ataxia-telangiectasia
  - Hyper-IgE Syndrome
  - Netherton's Syndrome
  - Phenylketonurea
  - Scabies
  - Seborrheic Dermatitis
  - Wiskott-Aldrich Syndrome

1. Leung DYM et al. Annals Allergy Asthma Immunol. 2004;93(2).

Atopic Dermatitis

- Treatment
  - Cannot be cured with medications but resolves in 60-70% of kids

Atopic Dermatitis

- Treatment
  - Avoidance of all potential triggers
    - Keep indoor humidity between 25-40%
      - Low humidity in winter increases xerosis (humidifier)
      - High humidity in summer increases sweating/body heat (A/C)
    - Temperature (68-72^0 F)
    - Clothing
      - Cotton and soft synthetics is preferable
      - Wash new clothes and sheets
    - Inhalant/Contact/Food allergen control
      - Especially HDM, molds
      - Food Triggers

Atopic Dermatitis

- Treatment
  - Emollients (moisturizers) – may be applied 4-6 x per day
    - Range from Hydrophilic (oil in water) to more occlusive hydrophobic (water-in-oil) preparations
    - Occlusion with ointments>>creams and lotions
      - Ointments provide better lubrication but trap body heat and sweat and may exacerbate AD in summer

Atopic Dermatitis

- Treatment
  - Emollients (moisturizers) – may be applied 4-6 x per day
    - Use after 20-30 min lukewarm bath ('patting' dry with a towel)
      - 1st apply steroid cream to erythematous, pruritic areas
      - Apply emollient to other areas
    - Vasoline® is the best; also Aquaphor®, Eucerin®, Nivea®, Nutraderm®
    - Avoid those with fragrances
    - 8% ceramide – containing cream (Triceram cream)
      - Helps to repair damaged barrier function and enhances water holding function[1]

1. Chamlin SL et al. Arch Dermatol. 2001;137:1110-1112.

Atopic Dermatitis

- Treatment
  - Soaps and Bath Oils
    - Neutrogena®, Basis®, Dove®, Olay Sensitive Skin Bars®, Cetaphil®
    - Lubath®, Alpha Keri Bath Oil®, Aveeno®
    - Sodium chloride to bath (isotonic bath to minimize symptoms) – 2 ½ teaspoons of table or rock salt per 1 gallon of water

Atopic Dermatitis

- Treatments
  - Oral antihistamines to decrease pruritis, but are often not effective[1]
  - Use of topical antihistamines is not recommended because of potential cutaneous sensitization[2]
  - Leukotriene modifiers may have additional anti-inflammatory properties[3]

1. Klein PA et al. Arch Dermatol. 1999;135:1522-1525.
2. Shelley WB et al. J Am Acad Dermatol. 1996;34:143-144.
3. Yanase DJ et al. J Am Acad Dermatol. 2001;44:89-93.

Atopic Dermatitis

- Treatments
  - Topical steroids
    - For inflamed, erythematous and pruritic areas 2-4 times per day
    - Increased occlusion and less drying
      - Ointments > Creams > Lotions > Gels
    - Occlusive dressings increase the potency of topical steroids but are also associated with more systemic effects
    - Group 1 (highest potency) – Group 7 (lowest potency)
      - ONLY Group 7 topical steroids on the face
  - Dressings (will increase absorption and potency of topical steroids)
    - Wet dressings during acute flares

Topical Steroids

Group I	
	Betamethasone dipropionate 0.05% (cream and ointment)
	Clobestasol propionate 0.05% (cream and ointment)
	Diflorasone diacetate 0.05% (ointment)
	Halobetasol propionate 0.05% (cream and ointment)
Group II	
	Amcinonide 0.1% (ointment)
	Betamethasone dipropionate 0.05% (cream and ointment)
	Desoximetasone 0.25% (cream)
	Desoximetasone 0.05% (gel)
	Diflorasone diacetate 0.05% (ointment)
	Fluocinonide 0.05% (cream, gel, ointment, and solution)
	Halcinonide 0.1% (cream)
	Mometasone furoate 0.1% (ointment)
Group III	
	Amcinonide 0.1% (cream and lotion)
	Betamethasone dipropionate 0.05% (cream)
	Betamethasone valerate 0.1% (ointment)
	Desoximetasone 0.05% (cream)
	Diflorasone diacetate 0.05% (cream)
	Fluocinonide 0.05% (cream)
	Fluticasone propionate 0.005% (ointment)
	Halcinonide 0.1% (ointment and solution)
	Triamcinolone acetonide 0.1% (ointment)
Group IV	
	Hydrocortisone valerate 0.2% (ointment)
	Flurandrenolide 0.05% (ointment)
	Fluocinolone acetonide 0.025% (ointment)
	Mometasone furoate 0.1% (cream)
	Triamcinolone acetonide 0.1% (cream)
Group V	
	Betamethasone dipropionate 0.05% (lotion)
	Betamethasone valerate 0.1% (cream)
	Fluticasone acetonide 0.025% (cream)
	Fluticasone propionate 0.05% (cream)
	Flurandrenolide 0.05% (cream)
	Hydrocortisone valerate 0.2% (cream)
	Prednicarbate 0.1% (cream)
Group VI	
	Alclometasone dipropionate 0.05% (cream and ointment)
	Betamethasone valerate 0.05% (lotion)
	Desonide 0.05% (cream)
	Flucinolone acetonide 0.01% (cream and solution)
	Triamcinolone acetonide 0.1% (cream)
Group VII	
	Hydrocortisone hydrochloride 1% (cream and ointment)
	Hydrocortisone hydrochloride 2.5% (cream, lotion, and ointment)
	Hydrocortisone acetate 1% (cream and ointment)
	Hydrocortisone acetate 2.5% (cream, lotion, and ointment)
	Pramoxine hydrochloride 1.0% (cream, lotion, and ointment)
	Pramoxine hydrochloride 2.5% (cream, lotion, and ointment)

1. Leung DYM et al. Annals Allergy Asthma Immunol. 2004;93(2).

Atopic Dermatitis

- Treatments
  - Calcineurin Inhibitors
    - Protopic® (tacrolimus) (0.03% <age 2-15> and 0.1%) and Elidel® (pimecrolimus) (1%)
      - Inhibit T-cell IL-2 synthesis
      - 2nd line agent - use if traditional therapy is not effective
      - Good agent (1st line) for the face, eyelids, lips, hands, feet
      - May burn during application for first 5-7 days
      - Apply BID
      - Decrease in pruritis in most patients within 3 days
      - Steroid sparing effect
      - Pimecrolimus 1% cream has been shown to be well tolerated and effective in infants age 3-23 months with AD[1]

1. Ho VC, et al. J Pediatr 2003;142:155-62.
2. Kapp A et al. J Allergy Clin Immunol 2002;110:277-84.

Atopic Dermatitis

- Treatments
  - Calcineurin Inhibitors
    - Black Box Warning
      - Not for use in children under the age of 2
      - Systemic use in animals and human transplant studies demonstrate increased risks for developing infections, lymphomas and skin malignancies
        - » Murine study demonstrated risk at 45 mg/kg/day but not at 15 mg/kg/day (pimecrolimus, Elidel®)
        - » Human transplant dosing is typically between 0.075-0.2 mg/kg/day for tacrolimus

Atopic Dermatitis

- Calcineurin Inhibitors
  - American Academy of Allergy, Asthma and Immunology/American College of Allergy Asthma and Immunology Position Statement[1]
    - "Current data do not support the use of the black box warning on topical pimecrolimus and tacrolimus"
      - Lymphoma formation is generally associated with high-dose and sustained systemic exposure to [these agents]
      - Reported cases of lymphoma [from these agents] are not consistent with lymphomas observed with systemic therapy
      - Actual rate of lymphoma formation reported to date [for these agents] is lower than that predicted in the general population

1. Fonacier L et al. J Allergy Clin Immunol. 2005;115:1249-1253.

Atopic Dermatitis

TABLE IV. Pimecrclimus analysis of malignancy rates[5]

	<5	5-9	10-14	15-19	Total children	Total adults	Total (US)
Person-years of exposure	278,842	118,196	65,224	33,431	495,694	237,030	732,724
Expected no. of cases (SEER)[11,11a]	1.8	1.0	0.7	0.5	4.0	42.1	46.1
Reported cases[5]	1	0	0	0	1	2	3

On the basis of the person-years of exposure, there is no evidence of increased incidence of non-Hodgkin's lymphoma in any age group in patients receiving pimecrolimus.
SEER, Surveillance Epidemiology and End Result.

1. Fonacier L et al. J Allergy Clin Immunol. 2005;115:1249-1253.

Atopic Dermatitis

- Treatments
  - Antibiotics (*S. aureus*)
    - Skin infections with weeping/crusting
    - Topical mupirocin (Bactroban®) if local infection
    - Oral cefuroxime bid X 10-14 days if multi-focal or impetigo
      - If no clinical improvement after 2 weeks, obtain a culture for sensitivities
  - Systemic Steroids
    - Only for short term management of severe AD
      - Generous taper to prevent rebound
      - Intensify skin treatments during taper
    - Do not use chronically

Atopic Dermatitis

- Treatments
  - Coal tar
    - For chronic, recalcitrant, lichenified plaques
    - Do not use on acutely inflamed skin as it may cause additional skin irritation
    - May decrease topical steroid use
    - Mild crude coal tar (liquor carbonis detergens, LCD) is less irritating to the skin than other OTC preparations
      - Compounded in 2-5% strengths
      - Petrolatum or Aquaphor vehicle

Atopic Dermatitis

- Treatments
  - Severe AD
    - Phototherapy (PUVA)
    - Cyclosporin A
    - Azathioprine
    - Mycophenolate mofetil (purine biosynthesis inhibitor)
    - IVIg
    - IFN-γ
    - Omalizumab (Xolair®)
    - Hospitalization (erythrodermic, widespread severe skin disease, resistant to outpatient therapy)
      - Removes patient from environmental triggers
      - Provide education, improve compliance