Atopic Dermatitis:
The Itch that Rashes

James Temprano, MD, MHA
Division of Allergy and Immunology
University of Kentucky

Atopic Dermatitis

• Epidemiology¹
  – 10-20% of children
  – 1-3% of adults
  – Often associated with allergic asthma and allergic rhinitis

<table>
<thead>
<tr>
<th>Age of onset</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>58</td>
</tr>
<tr>
<td>1-5</td>
<td>26</td>
</tr>
<tr>
<td>6-15</td>
<td>8</td>
</tr>
<tr>
<td>16-25</td>
<td>8</td>
</tr>
<tr>
<td>26-40</td>
<td>3</td>
</tr>
</tbody>
</table>

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


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

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)

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

• Triggers
  – Heat and exercise induced sweating
    • Abnormal pattern of thermoregulation
    • May reflect intrinsic disturbance of parasympathetic nervous system

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
    – Inherent deficiency in cathelicidens, β-defensins (antimicrobial peptides)
    • Ceramide deficiency in skin (resulting from high expression of sphingomyelin deacylase)
      – Leads to dry skin that is more susceptible to infection


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Atopic Dermatitis

• Triggers
  – Allergens
    • Typically high to very high serum IgE levels
    • Food sensitivity triggers lesions in 20-30% of children
      – 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

Atopic Dermatitis

• **Triggers**
  – **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)


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Atopic Dermatitis

• **Triggers**
  – **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)

Atopic Dermatitis

• Course
  – Earlier age at onset the more severe the course
  – Chronic and relapsing
  – Usually resolves by age 2 and the remainder improve by puberty


Atopic Dermatitis

• Adult DDx
  – Allergic Contact Dermatitis
  – Cutaneous T-cell Lymphoma
  – Glucagonoma Syndrome
  – Irritant Contact Dermatitis
  – Pellagra
  – Pityriasis Rubra Pilaris
  – Psoriasiform Eruptions
  – Scabies
  – Seborrheic Dermatitis

• Pediatric DDx
  – Acrodermatitis Enteropathica
  – Agammaglobulinemia
  – Ataxia-telangiectasia
  – Hyper-IgE Syndrome
  – Netherton’s Syndrome
  – Phenylketonuria
  – Scabies
  – Seborrheic Dermatitis
  – Wiskott-Aldrich Syndrome

Atopic Dermatitis

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

  • 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°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
  – 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 effective¹
  – Use of topical antihistamines is not recommended because of potential cutaneous sensitization²
  – Leukotriene modifiers may have additional anti-inflammatory properties³

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

<table>
<thead>
<tr>
<th>Group</th>
<th>Steroids</th>
</tr>
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<tbody>
<tr>
<td>Group I</td>
<td>Betamethasone dipropionate 0.05% (cream and ointment)</td>
</tr>
<tr>
<td></td>
<td>Clobetasol propionate 0.05% (cream and ointment)</td>
</tr>
<tr>
<td></td>
<td>Diflurane dipropionate 0.05% (ointment)</td>
</tr>
<tr>
<td>Group II</td>
<td>Aminocortic 0.1% (ointment)</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate 0.05% (cream and ointment)</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone 0.05% (gel)</td>
</tr>
<tr>
<td></td>
<td>Fluorimetic acid 0.05% (cream, gel, ointment, and solution)</td>
</tr>
<tr>
<td></td>
<td>Halobestrol 0.1% (cream)</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate 0.1% (ointment)</td>
</tr>
<tr>
<td>Group III</td>
<td>Aminonide 0.1% (cream and lotion)</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate 0.1% (ointment)</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Diflurane dipropionate 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Fluorimetic acid 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Halobestrol 0.1% (ointment and solution)</td>
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<tr>
<td></td>
<td>Triamcinolone acetonide 0.1% (ointment)</td>
</tr>
</tbody>
</table>

Group IV: Hydrocortisone valerate 0.2% (ointment)
Flurandrenolide 0.05% (cream)
Flucinolone 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% (lotion)
Fluticasone propionate 0.025% (cream)
Fluticasone propionate 0.05% (cream)
Flurandrenolide 0.05% (cream)
Hydrocortisone valerate 0.2% (cream)
Prednisolone 0.1% (cream)

Group VI: Alclometasone dipropionate 0.05% (cream and ointment)
Betamethasone valerate 0.05% (lotion)
Desocort 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)
Prednisolone hydrochloride 1.5% (cream, lotion, and ointment)
Prednisolone hydrochloride 2.5% (cream, lotion, and ointment)

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


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

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### TABLE IV. Pimecrolimus analysis of malignancy rates\(^5\)

<table>
<thead>
<tr>
<th>Person-years of exposure</th>
<th>(-5)</th>
<th>5-9</th>
<th>10-11</th>
<th>15-19</th>
<th>Total children</th>
<th>Total adults</th>
<th>Total (US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected no. of cases (SEER)(^6)</td>
<td>2784.42</td>
<td>138.296</td>
<td>65.224</td>
<td>33.431</td>
<td>499,494</td>
<td>237,030</td>
<td>732,724</td>
</tr>
<tr>
<td>Reported cases(^7)</td>
<td>1.5</td>
<td>1.0</td>
<td>0.7</td>
<td>0.5</td>
<td>4.0</td>
<td>25.1</td>
<td>26.1</td>
</tr>
</tbody>
</table>

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 Results.

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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)
    • IV Ig
    • IFN-γ
    • Omalizumab (Xolair®)
    • Hospitalization (erythrodermic, widespread severe skin disease, resistant to outpatient therapy)
      – Removes patient from environmental triggers
      – Provide education, improve compliance