Atopic Dermatitis: 
The Itch that Rashes

40th Annual Family Medicine Review 
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Atopic Dermatitis

- **Epidemiology**
  - 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)
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
Atopic Dermatitis

• Triggers\(^1\)
  – 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\(^1\)
      – Inherent deficiency in cathelicidens, \(\beta\)-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

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)

Atopic Dermatitis

• Triggers¹
  – 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\(^1\)
  – 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 DDx¹
  - Allergic Contact Dermatitis
  - Cutaneous T-cell Lymphoma
  - Glucagonoma Syndrome
  - Irritant Contact Dermatitis
  - Pellagra
  - Pityriasis Rubra Pilaris
  - Psoriasiform Eruptions
  - Scabies
  - Seborrheic Dermatitis

- Pediatric DDx¹
  - 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
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°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\(^1\)

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\(^3\)

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 I</th>
<th>Betamethasone dipropionate 0.05% (cream and ointment)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clobetasol propionate 0.05% (cream and ointment)</td>
</tr>
<tr>
<td></td>
<td>Diflorasone diacetate 0.05% (ointment)</td>
</tr>
<tr>
<td></td>
<td>Halobetasol propionate 0.05% (cream and ointment)</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Group II</th>
<th>Aminophylline 0.1% (cream)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Betamethasone dipropionate 0.05% (cream and ointment)</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone 0.25% (cream)</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone 0.05% (gel)</td>
</tr>
<tr>
<td></td>
<td>Diflorasone diacetate 0.05% (ointment)</td>
</tr>
<tr>
<td></td>
<td>Flucinonide 0.05% (cream, gel, ointment, and solution)</td>
</tr>
<tr>
<td></td>
<td>Halcinonide 0.1% (cream)</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate 0.1% (ointment)</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Group III</th>
<th>Aminophylline 0.1% (cream and lotion)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Betamethasone dipropionate 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate 0.1% (cream)</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Diflorasone diacetate 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Flucinonide 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Flucinonide propionate 0.005% (ointment)</td>
</tr>
<tr>
<td></td>
<td>Halcinonide 0.1% (ointment and solution)</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone acetonide 0.1% (ointment)</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Group IV</th>
<th>Hydrocortisone valerate 0.2% (ointment)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Flurandrenolide 0.05% (ointment)</td>
</tr>
<tr>
<td></td>
<td>Flucinolone acetonide 0.025% (ointment)</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate 0.1% (cream)</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone acetonide 0.1% (cream)</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Group V</th>
<th>Betamethasone dipropionate 0.05% (lotion)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Betamethasone valerate 0.1% (cream)</td>
</tr>
<tr>
<td></td>
<td>Fluticasone acetonide 0.025% (cream)</td>
</tr>
<tr>
<td></td>
<td>Fluticasone propionate 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone valerate 0.2% (cream)</td>
</tr>
<tr>
<td></td>
<td>Prednicarbate 0.1% (cream)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group VI</th>
<th>Alclometasone dipropionate 0.05% (cream and ointment)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Betamethasone valerate 0.05% (lotion)</td>
</tr>
<tr>
<td></td>
<td>Desonide 0.05% (cream)</td>
</tr>
<tr>
<td></td>
<td>Flucinolone acetonide 0.01% (cream and solution)</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone acetonide 0.1% (cream)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group VII</th>
<th>Hydrocortisone hydrochloride 1% (cream and ointment)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hydrocortisone hydrochloride 2.5% (cream, lotion, and ointment)</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone acetate 1% (cream and ointment)</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone acetate 2.5% (cream, lotion, and ointment)</td>
</tr>
<tr>
<td></td>
<td>Prazoxine hydrochloride 1.0% (cream, lotion, and ointment)</td>
</tr>
<tr>
<td></td>
<td>Prazoxine hydrochloride 2.5% (cream, lotion, and ointment)</td>
</tr>
</tbody>
</table>

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 1st 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 to 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

Atopic Dermatitis


**TABLE IV. Pimecrolimus analysis of malignancy rates**

<table>
<thead>
<tr>
<th></th>
<th>&lt;5</th>
<th>5-9</th>
<th>10-14</th>
<th>15-19</th>
<th>Total children</th>
<th>Total adults</th>
<th>Total (US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-years of exposure</td>
<td>278,842</td>
<td>118,196</td>
<td>65,224</td>
<td>33,431</td>
<td>495,694</td>
<td>237,030</td>
<td>732,724</td>
</tr>
<tr>
<td>Expected no. of cases (SEER)</td>
<td>1.8</td>
<td>1.0</td>
<td>0.7</td>
<td>0.5</td>
<td>4.0</td>
<td>42.1</td>
<td>46.1</td>
</tr>
<tr>
<td>Reported cases</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</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 Result.
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