Atopic Dermatitis: Updates on Evaluation and Management from the Practice Parameter

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Learning Objectives:

• Describe recent updates to the practice parameter on atopic dermatitis focusing on evaluation and management of atopic dermatitis

Question 1

• The ADPP were updated in 2012. When was the prior update?
  A. 1997
  B. 2001
  C. 2004
  D. 2007

Key updates in the ADPP

• Immunopathology/Genetics
• First-line Management and Treatment
  – Vitamin D
  – Proactive
  – Dilute bleach baths
• MRSA
• Quality of life & Emotional Stress

Atopic Dermatitis: A Practice Parameter Update 2012

Immunopathology and genetics

• Summary statement 4. The clinician show know that AD has become widely accepted as a disorder that is at least in part initiated by skin barrier defects.

Normal epidermis: a protective barrier

- The stratum corneum: a protein-lipid matrix
- Barrier against water loss and allergen/microbe entry

Defect in Epidermal Barrier Function in AD

- **Filaggrin** loss-of-function mutations: associated with ↑risk of AD, asthma associated with AD, ADEH, persistent AD

Question 2

A defect in epidermal tight junction function is due to a reduction in which of the following?

A. Filaggrin
B. Claudin-1
C. Loricrin
D. IL-4

Claudin-1 expression is reduced in AD

Stratum Corneum + Tight Junctions
2 barrier structures

Role of Tmem79/Matt in Atopic Dermatitis

- Matted mouse gene in the flaky (fig/ma) tail mouse
- Encodes protein matrin
  - Highly expressed in upper granular layer of epidermis
  - Controls lamellar granular transport function
  - Granules responsible for transferring lipids and proteases
- SNP in human TMEM99/MATT gene increases risk of AD in humans

Palmer CH et al. Nature Genetics, 2006; Weidinger S et al. JACI, 2008
Margolis DJ, Apter AI, JACI 2012:131; 912-917
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Immunopathology and genetics

- Summary statement 5. The clinician should know that an inadequate innate immune response to epidermal microbes is in part responsible for susceptibility to infections with *Staphylococcus aureus*, as well as viruses.

Vaccinia Induces Significantly Higher Levels of Cathelicidin in Normal & Psoriasis Skin

Clinical Implications

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- Summary statement 12. The clinician should be aware that atopic dermatitis is characterized by reduced skin barrier function, which leads to enhanced water loss and dry skin; therefore the clinician should recommend hydration with warm soaking baths for at least 10 minutes followed by the application of a moisturizer.

Question 3

- Which vitamin has been associated with localized innate immunity?
  A. Vitamin E
  B. Vitamin B12
  C. Vitamin C
  D. Vitamin D
The Vitamin D hypothesis

Vitamin D induction of Antimicrobial Peptides (AMP)

- Normals and AD
- 3 weeks oral vitamin D 4000 IU
- Skin biopsies pre and post
- Lesional and nonlesional skin in AD subjects


Vitamin D Induction of Antimicrobial Peptides
Normalized to Median of Pre-treatment Normals

Correlation between serum 25-hydroxyvitamin D levels and severity of AD in children

- Evaluate if low levels of vitamin D correlate with the severity of AD
- 37 children ages 8 mos to 12 years with AD enrolled at University of Verona in Verona, Italy
- Severity determined by SCORAD (Severity Scoring of AD)

Ref. Peroni DG et al British Journal of Dermatology
Volume 164, Issue 5, pages 1078-1082, 11 APR 2011

Correlation between serum 25-hydroxy vitamin D levels and severity of atopic dermatitis in children

Pilot study of 1000 IU Vitamin D for AD in eleven Boston children in winter

Change in

<table>
<thead>
<tr>
<th>IGA score</th>
<th>Vitamin D</th>
<th>Placebo</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>+ 1 (worse)</td>
<td>-</td>
<td>1 (17%)</td>
<td>1</td>
</tr>
<tr>
<td>0 (same)</td>
<td>1 (20%)</td>
<td>4 (67%)</td>
<td>5</td>
</tr>
<tr>
<td>- 1 (better)</td>
<td>4 (80%)*</td>
<td>1 (17%)</td>
<td>5</td>
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</tbody>
</table>

Total 5 6 11

*p<0.05

Follow-up study: Carmago, et al manuscript under second review
http://clinicaltrials.gov/show/NCT00879424
Clinical Implications
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Vitamin D
• Summary statement 29. Patients with atopic dermatitis may benefit from supplementation with vitamin D, particularly if they have a documented low level or low vitamin D intake. (or if their atopic dermatitis worsens in the winter.)


How to treat atopic dermatitis

Anti-inflammatory Treatment
Topical Steroid Application
AD Flare
Days 7-14:
Low potency – face
Mid-high potency
Recovery
Daily use
QOD use
Emollients

Aim for RARE FLARES


For patients with frequent flares

Proactive (OFF LABEL in USA) usage 2 times weekly to areas typically affected by AD


Aim for RARE FLARES

Topical Calcineurin Inhibitors
• Summary statement 22. Once a flare is controlled, the clinician might consider prescribing tacrolimus ointment twice daily, twice weekly to eczema-prone areas to prevent future flares.

Antihistamines

- Summary statement 27. Some patients may benefit from the use of antihistamines for the relief of pruritus associated with atopic dermatitis.
- Evidence-based review of 16 controlled studies revealed little objective evidence demonstrating the relief of pruritus when sedating or non-sedating antihistamines were used in the treatment of AD.
- Reduction of skin inflammation with topical glucocorticoids and calcineurin inhibitors will often reduce pruritus.

Immune response at the epithelial surface


The Epithelial Cell-Derived Atopic Dermatitis Cytokine TSLP Activates Neurons to Induce Itch


Source: Journal of Allergy and Clinical Immunology 2014; 133:348-349 (DOI:10.1016/j.jaci.2013.12.1047)

A sensory neuron-expressed IL-31 receptor mediates TH 2 cell-dependent itch through ion channels TRPV1 and TRPA1

Journal of Allergy and Clinical Immunology 2014; 133:348-349

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MICROBES

- Summary statement 38. The clinician should prescribe a short course of an appropriate antibiotic in patients who are clinically infected. In areas with high levels of MRSA, the clinician might want to obtain a skin culture and initiate treatment with clindamycin, doxycycline, or TMP-SMX while awaiting culture results.


Dilute Bleach Baths

- Summary statement 30. Clinicians should consider the addition of dilute bleach baths twice weekly to reduce the severity of atopic dermatitis especially in patients with recurrent skin infections.

Dilute Bleach Baths

- Patients with clinically infected AD
- All treated with Cephalexin
- Add 1/2 cup of 6% household bleach to a bath tub full of water two times per week
- Intranasal mupirocin ointment for 5 days monthly for patients and household
- Decrease secondary infections and disease severity


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Summary statement 42. The clinician should recognize that AD has a significant impact on quality of life and patients have an increased risk for psychological distress.

The clinician should ask about stress and emotional factors, which may cause exacerbations and induce immune activation as well as trigger pruritus and scratching.

Mental Health Comorbidity in AD

- Cross sectional study comparing No eczema to children with eczema
- 2007 National Survey of Children’s Health
- Questionnaire to parents
  - told by health care provider your child has
    - Ecema
    - ADD or ADHD
    - Depression
    - Anxiety
    - Behavior or conduct disorder problem
    - Autism
  - Parental description of severity of eczema


Mental Health Comorbidity in AD

- Mental health care usage
  - No eczema 7.89%
  - Eczema 12.12%
  - P < .0001
- Mean number of days of adequate sleep decreases as eczema severity increases
  - No eczema 6.09
  - Eczema 5.22
  - P < .0001


Changes in mean EASI scores over time

P = .02
P = .004

Question 4

Treatment for sleep problems in patients with atopic dermatitis should always include which of the following?

A. Use of sedating antihistamines.
B. Optimization of sleep hygiene.
C. Referral to a psychologist.
D. Use of wet dressings.

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Summary statement 43. The clinician should assess for sleep disturbances.

- Optimize sleep hygiene
- Treat AD inflammation aggressively to improve sleep
- Refer to psychologist or sleep specialist if needed

Clinical Implications

- Patient Education
  Summary statement 44. To achieve effective control of atopic dermatitis, the clinician should educate patients and family members about the chronic nature of the disease, exacerbating factors, and the safety/side effects of the medications. The clinician should also provide demonstrations of skincare techniques, written treatment plans, and information about patient support organizations.

Boston Children’s Hospital Atopic Dermatitis Center

- Multidisciplinary outpatient program for children with refractory AD
- Half day session per week
- Treatment team:
  - Nurse Practitioner
  - Psychologist
  - Nutritionist

www.childrenshospital.org/atopic

Review of BCH AD Center

- Overall 71% of patients had improvement in EASI score
- EASI score improvement correlated with:
  - Decreased parental concern with treatment side effects
  - Decreased itching
  - Better patient sleep
- Predictor of success - Improved parental ability to follow treatment regimen


Summary

- Skin barrier defects play a role in AD
- Vitamin D may be helpful in AD although more studies are needed
- For patients with frequent flares consider proactive therapy (OFF LABEL)
- Patients with AD (especially severe AD) have an increase in mental health & sleeping disorders
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