Advanced Therapeutics: Managing the Severe and Refractory Eczema Patient

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Diagnostic Considerations
QUESTION: Foods and AD

• How do you assess the contribution of food allergy (FA) in severe eczema?

FA and AD

• FA and AD are highly associated.
  – Up to 37% of children <5 years with moderate to severe AD will have IgE-mediated FA
• Whether FA can exacerbate AD is controversial (lack of well-designed avoidance trials in patients with AD)
  – Several studies found improvement in pruritus when patients with egg allergy and AD were placed on egg-free diet
    Lever R et al, Pediatr Allergy Immunol 1998
FA and AD misconceptions

• Eczematous flares can be erroneously attributed to foods by patient/parent
  – May be precipitated by irritants, humidity, change in temperature, infections

• Thus, AD may continue to flare in patients with FA despite strict elimination diet

Practical considerations: when to consider testing to foods in AD

• When proper skin care is not working in child
• When eczema flares are consistently associated with a specific food as a trigger
• If the child is not growing well

*Milk, egg, and peanut are the most common allergens in young children (test judiciously)

*The younger the child and the more severe the AD, the greater likelihood that child has FA

Guillet G & MH, Arch Dermatol 1992
QUESTION: Foods and AD

• If you eliminate a food (e.g. eggs or milk) for a period of time to see if it is contributory, are you increasing the risk of anaphylaxis when you reinstitute that same food?

QUESTION: Foods and AD

Actually 2 questions:
• If you eliminate a food (e.g. eggs or milk) for a period of time to see if it is contributory, what is the risk of a reaction when you reinstitute that same food?

• What are the risks for a severe reaction or anaphylaxis?
Factors to consider before reintroducing foods

• Has food elimination helped AD?
• How long has food been eliminated?
• How long/frequently was food in diet prior to elimination? (Is this an infant or teenager?)
• Has testing been performed? If so, results?

*When tolerance develops to food, reintroduction of food will NOT cause AD to recur or worsen.

Sampson & Scanlon, J Peds 1989

• 75 children (3-18 mos) with AD diagnosed with FA using DBPCFC
• Milk, peanut, egg most common
• Allergen-restricted diet for 1-2 years \( \rightarrow \) repeat DBPCFC: 31% FA resolved
• Patients with both skin + resp sx at initial OFC were less likely to have resolved FA
  – compared to those with skin only or skin + GI sx
Risk factors for severe food reactions

- Asthma!
- Amount of allergen ingested
- Form of food (raw, cooked, processed)
- Age of patient (teen, young adult)
- Degree of sensitization (threshold dose) at time of ingestion
- Rate of absorption (empty stomach, exercise, alcohol intake, etc)

QUESTION: Foods and AD

- What is the status of food patch testing in severe AD? Is there any role for it in refractory cases, wherein food-specific IgE-guided diet manipulation has already been attempted but with limited success?
Atopy Patch Test (APT)

- 2010 Food Allergy Guideline 8: NIAID-sponsored EP suggests that APT should not be used in routine evaluation of non-contact FA
  - No standard reagents available
  - No studies that specifically address APT methodology met inclusion criteria for report
  - Two large studies conclude there is no significant clinical value in using APTs for FA diagnosis

Mehl et al, JACI 2006 & Keskin et al, Ann Allergy Asthma Immunol 2005

QUESTION: Foods and AD

- Effect of super high IgEs on specific positive predictive value for milk, eggs, etc.?
- How to interpret without challenge?
“Super high” IgE levels

- Elevated total IgE levels frequently found in atopic individuals
- No studies to date provide support of use of total IgE in interpreting specific IgE levels
- Predictive value of ratio of sIgE to total IgE compared with DBPCFC for diagnosis of FA.

Conclusion: Ratio offers no advantage over sIgE alone.

Mehl A et al, Allergy 2005

Predictive value of food allergen-specific IgE levels

95% Predictive Level

<table>
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<tr>
<th>Allergen</th>
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<th>PPV</th>
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</table>

PPTV = Positive predictive value

Increasing probability of clinical reactivity with increasing level of food-antigen specific IgE value; note: values < 0.35 do not exclude allergic reactivity.

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Journal of Allergy and Clinical Immunology 2004; 113:805-819
QUESTION: Infections

- Is there any role for skin culture, as opposed to empiric use if anti-staphylococcal systemic antibiotics in severe AD flares?

- Occasional furuncle or recurrent clinical staph infections w/o infections, IgE > 10,000. No family history of Hyper IgE syndrome?

Infections

- Staph is incredibly common (> 90% in severe cases)
- Usually I do not culture anymore
- For some reason, MSSA > MRSA in this group so far...
- But in refractory cases, or if pustules or ulcers, culture could be important, esp immunosuppressed patients... so common, however
Therapeutics

QUESTION: TCIs

- How often is combination therapy with both a moderate potency corticosteroid and a topical immuno-modulator more helpful than either one alone?

- What is the most appropriate role for the use of calcineurin inhibitors?
- Maintenance tacrolimus twice weekly when eczema clear
- Was effective in reducing the number and frequency of disease exacerbations and improving health-related QoL


Synergy

- I have used a topical steroid in the AM and then a TCI in the PM; for some cases of severe, refractory disease, I think there may be synergy
- Also a nice way to transition for patients who feel stinging and burning with TCIs
- “The results of our small retrospective study suggest that TCPO may be more effective than either 0.1% tacrolimus or clobetasol propionate 0.05% ointment monotherapy in the treatment of recalcitrant CLE.”


QUESTION: Phototherapy

- Some area dermatologists are still using UV radiation in the treatment of eczema, even in young children. What is the role of UV treatment?
Phototherapy

- 1903 Nobel Prize in Medicine: Niels Ryberg Finsen, Danish pioneer of phototherapy
- *Om Lysets Indvirkninger paa Huden* (On the effects of light on the skin)
- Probably multiple mechanisms including increasing vitamin D which in turn enhances cathelicidin

Phototherapy

- Works in about 60% of refractory cases
- NB-UVB (311nm) seems very safe

Problems:
- Time
- Money (co-pays, parking, etc)

Home units...
QUESTION: Topical Steroids

• What is the highest class of steroids for how long with what frequency is your top dose for kids?

Topical Steroids

• No easy answer here… to some extent, I will use whatever it takes, even class 1 steroids on the face for brief bursts

• Pearl: for patients saying “as soon as I stop, it come RIGHT BACK” or “I have to use EVERY DAY”, steroid potency is probably too low*

*Provided all other areas of the tetrad are being maximized, of course
QUESTION: Systemic Medications

• How long is your trial of cyclosporine?

Cyclosporine: From PeDRA

• Rapid
• 5mg/kg/d, 300mg/d max
• Monitoring: BP q wk x 4 then q mo CBC, LFTs, BUN, Cr, CMP, uric acid, lipids monthly x 3 then every 8 wks
• Maintain x 3 mo then taper
• Limit to 1 yr
• (Pediatric Dermatology Research Alliance)
**Imuran: From PeDRA**

- Onset is 4-6 weeks
- Can use concurrent pred x 1 mo
- Baseline TPMT if normal: 2.5-3.5 mg/kg/d
- If intermediate TPMT: 1mg/kg
- Monitoring: CBC, LFTs, BUN, Cr at 2,4,8,12 wks then every 8 wks
- Maintain x 3 mo then taper
- Limit to 2 yrs

**QUESTON: Antibiotics**

- When and how long to treat with antibiotics for chronic management?

- In recalcitrant patient, if staph superantigen can play a role, and skin has staph w/o clinical infection, any role to try and decrease staph load?
Antibiotics

• Since the Paller bleach bath study, I have used less topical and systemic antibiotics than ever
• Bleach baths: qd when flaring, biweekly as maintenance
• Staph is ubiquitous and, for some reason, MRSA seems to be a less common colonizer here; I usually do not culture anymore
• Cephalexin still seems to be most helpful
• Usually 14 days, though I have used TMP-SMX longer term in some severe cases

QUESTION: Yeast

• Recalcitrant patient and malassezia/pityrosporum - if no clinical infection, leave it alone? KOH prep? What if positive?
**Yeast**

- A few interesting papers on head and neck dermatitis in young adults showing that Malassezia allergy may play a role

- Consider: Itraconazole daily x 2 mo then long-term weekly treatment 100mg po qd

- This has not worked well for me... but I do try and I have had 2 patients respond well... and about 10 fail the treatment


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**QUESTION: Pruritus**

- What role if any for anti-anxiety meds, sleep aids in children with intractable scratching and sleeplessness?
Pruritus

• Data is poor that anti-pruritics help our more severe cases (I wish they did help!)

• Even in my severe cases, I usually am able to taper these off once skin is better

• Hydroxyzine in kids; doxepin or mirtazapine in older patients can really help get through the night due to sedative effects

QUESTION: Immunotherapy

• Immunotherapy to house dust mites (HDM)?

• How effective IT might be in bad AD?
Allergen Immunotherapy: 3rd update of practice parameter (2011)

- Summary Statement 8: There are some data indicating that immunotherapy can be effective for atopic dermatitis when associated with aeroallergen sensitivity
- Bussman et al, JACI 2007: In review of 4 placebo-controlled studies, statistical analysis showed significant improvement in symptoms in AD patients who received SCIT.

Subcutaneous immunotherapy (SCIT)

- Werfel T et al, Allergy 2006
  - Multi-center, randomized, double-blind study of 51 adults with AD
  - Maintenance doses of 20, 2000, and 20,000 SQ-U weekly for 1 year
  - HDM SCIT effectively reduced AD in dose-dependent manner, as measured by SCORAD and topical corticosteroid use
Subcutaneous immunotherapy (SCIT)

- Bussman et al, Clin Exp Allergy 2007
  - Open pilot study to evaluate the benefit of HDM SCIT x 6 mos in 25 AD patients with HDM sIgE
  - Subjective and objective SCORAD improved significantly within 4 weeks of treatment
  - IL-10 levels increased; CCL17 and IL-16 decreased
  - HDM IgE decreased while IgG4 increased

Sublingual immunotherapy (SLIT)

- Pajno et al, JACI 2007 (Italy)
  - Randomized, double-blind, placebo-controlled study of 48 children (5-16 years) with HDM sensitization and AD (SCORAD >7), stratified by disease severity
  - SLIT or placebo for 18 months + standard therapy
  - Significant difference in SCORAD and use of rescue meds found only in patients with mild-moderate AD
  - Severe patients had only marginal benefit
  - SLIT discontinued in 2 patients because of exacerbation of dermatitis
QUESTION: Compliance

• Logistics of lubricating school-aged child interfering with therapy?

• How to sort out all of these medications/treatments?
Action Plan

AM:
1. Apply triamcinolone ointment to eczema areas
2. Apply moisturizer everywhere

During day:
1. Apply moisturizer everywhere 1-2 times

PM:
1. Dilute bleach bath for 10 minutes
2. Pat dry
3. Apply triamcinolone ointment to eczema areas
4. Apply moisturizer everywhere

Do this for several days (up to 1 week) until better. Once better...

QUESTION: Miscellaneous

• How to use wet wraps, and how safe are they?

• What is the “best” moisturizer?
Miscellaneous

• Wet wraps, bleach baths, unna boot instructions

www.eczemacarecenter.com

• The best moisturizer is one they will use...
• But... my favorites include the ones with ceramides since I think you can get similar effect to greasier products in less-greasy formulations

What to do when everything seems to fail...

Discussion...
THANK YOU!