Objectives

- Review current recommendations for treatment of food allergy
- Discuss latest developments in the following:
  - Oral immunotherapy
  - Sublingual immunotherapy
  - Anti-IgE
  - Chinese herbal therapy
  - Epicutaneous immunotherapy
  - *Trichuris suis ova* therapy

Oral Immunotherapy Dosing Schematic

Summary of OIT Literature

- **Peanut**
  - Peanut oral immunotherapy modifies IgE and IgG4 responses to major peanut allergens
  - OIT induces individualized changes in IgE and IgG4 binding patterns.
  - Evidence of pathway-specific basophil anergy induced by peanut oral immunotherapy in peanut-allergic children
  - *Clin Exp Allergy* 2012 (42) 1197-1205.
  - OIT induces hyporesponsive state in basophils that is pathway specific.

Summary of OIT Literature

- **Peanut, cont.**
  - The safety of peanut oral immunotherapy in peanut-allergic subjects in a single-center trial
  - — 24 patients: 22 children, 2 adults
  - — Symptoms were mostly mild with 3 severe rxs

Text:
- Tree nut- and sesame-specific IgE do not decrease from baseline with peanut oral immunotherapy (OIT).
  - — Peanut OIT does not appear to affect sensitivities to tree nuts or seeds.
Allergen-specific oral immunotherapy for peanut allergy (Review)

Neumayer E, Wellerholt J, Devouge G, Simon FER, Shiloh S.

• 1 RCT – Varshney, et al. JACI 2011
  – 28 children enrolled
  – 19 received therapy (3 withdrew)
  – 16 able to tolerate 5 g of peanut after 4 g maint.
  – Placebo group able to tolerate 280 mg
  – Sig decrease in SPT wheal diameter, IL-5, IL-13 and increase in peanut-specific IgG4

• Conclusion: Effective, though with side-effects. Larger RCTs are needed.

Summary of OIT Literature

• Milk
  Changes in antigen-specific T-cell number and function during oral desensitization in cows milk allergy enabled with omalizumab
  \[\text{Mucosal Immunology} 2012; 25(1):367-78.\]
  • High dose OIT → deletion of allergen-specific T-cells rather than increase in Foxp3+ Tregs.
  • The safety and efficacy of sublingual and oral immunotherapy for milk allergy
    \[\text{J Allergy Clin Immunol} 2012 Jul; 130(1):449-55.\]
    • Both SLIT and OIT effectively treated CMA, with increased efficacy and increased systemic reactions with OIT.

• Oral immunotherapy for milk allergy (Review)
  Young SS, Koda LA, McDermit J, Ben-Shoshan N, Aladjem MR.

  • 5 RCTs published in 16 records b/t 2008-2012.
  • 196 patients involved – all children (2 to 17 years)
    – All protocols differed, and all but 1 had a build-up phase in an institution followed by periodic up-dosing.
  • Conclusions:
    – Milk OIT is effective at desensitizing. Tolerance development is unknown.
    – Adverse effects were common – almost all were mild.
    – For every 11 patients treated, 1 required epinephrine.
    – Overall quality of evidence is low.
    – Guidelines would be required prior to incorporation into practice.

Baked Egg

Dietary baked egg accelerates resolution of egg allergy in children
  \[\text{J Allergy Clin Immunol} 2011; 128(4):125-31.\]
  • Subjects in the baked egg group tolerated regular egg at a median time of 50 mos vs 78.7 mos in the comparison group.
  • Abstracts: 321, 322

Baked Milk

Dietary baked milk accelerates the resolution of cow’s milk allergy in children
  • Subjects who incorporated baked milk into their diet were 16 times more likely to become unheated milk tolerant than comparison group.
  • Abstracts: 301, 313
• 40 subjects, 12 to 37 years-old (median 15 y/o)
• Received peanut SLIT for 44 weeks
• 2 gram entry challenge, 5 gram desensitization challenge
• Responder: tolerated 5 gram challenge or 10-fold increase in threshold dose

**Anti-IgE Alone**

**Effect of Anti-IgE Therapy in Patients with Peanut Allergy**

*J Allergy Clin Immunol* 2011; 127(5):1309

- 84 patients, 12–60 y/o
- Sensitivity threshold in highest treated group changed significantly only in highest treated group (1/2 PN Æ 9 PN)

A phase II, randomized, double-blind, placebo-controlled oral food challenge trial of Xolair (omalizumab) in peanut allergy

- 14 subjects, 6 y/o and over, but trial discontinued by sponsor
- 44.4% of treatment vs 20% of placebo tolerated >1000 mg PN

**Kinetics of mast cell, basophil, and oral food challenge responses in omalizumab-treated adults with peanut allergy**

*J Allergy Clin Immunol* 2012; 130:1123-9

- 14 adults with h/o PNA
- Must fail an entry DBPCFC at a cumulative dose of 1000 mg or less
- 6 month, open-label study using omalizumab
- Measured threshold reactivity dose, SPTT, and BHR
Take home message:
- Omalizumab may lead to an increased threshold dose for food-allergic adults.
- Clinical response occurs early when the basophil, but not the mast cell, is suppressed, supporting a role for the basophil in acute food reactions.
**Epicutaneous Immunotherapy**

- Adhesive crown
- Dry layer of allergenic proteins
- Polarized polymer
- Water accumulation and condensation
- Natural Water loss – Evaporation of skin
- Interaction with Epidermal immune cells
- Solubilization and epicutaneous delivery of the proteins
- Interaction with Epidermal immune cells

**TSO**

- **Pig whipworm**
  - Helminth, does not cause systemic disease
  - Mainly asymptomatic in adult pigs but may cause diarrhea and prevent growth in piglets.
  - Not considered infectious in humans or if infectious, the human host is asymptomatic.

- **Efficacy**
  - Preliminary efficacy in Crohn’s Disease
  - No efficacy for treatment of MS in 1 small trial
  - AR – no efficacy but concerns re: study design

Jouvin MH, Kinet JP. *J Allergy Clin Immunol* 2012; 130:3-10.

**Conclusions**

- Several promising therapies
- Questions remaining:
  - Product delivery
  - Patient selection
  - Treatment of children with multiple food allergies
  - Use of modified food allergens?
  - Standardized dosing
  - Long-term efficacy (e. g. tolerance development)
  - Minimization of side-effects
  - Risks compared to avoidance
  - Reimbursement/ allocation of resources
  - QOL issues

**TSO**

- **Efficacy**
  - Autism – 15 y/o subject with improvement in behavioral symptoms and loss of pecan allergy.

- **Next steps**
  - Optimal doses and duration of treatment?
  - Which allergic diseases are best?
  - Should active substance be used rather than eggs?

Jouvin MH, Kinet JP. *J Allergy Clin Immunol* 2012; 130:3-10.

**EPIT for Milk Allergy**