

Update on Food Allergy Research

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Overview

- Children's Memorial Food Allergy Study
- Peanut Oral Immunotherapy (OIT)
- OIT for Cow's Milk and Egg Allergy
- Extensively Heated Milk and Egg
- Chinese Herbal Formula
- Consortium for Food Allergy Research (CoFAR)
- Immune Tolerance Network

CMH Food Allergy Study

- Objective: to understand the natural history and cause of food allergy
- Description: family based design (child with food allergy diagnosis, parents +/- siblings with baseline and follow-up assessments)
- Enrollment target: 1000 families

Food Allergy Study Enrollment To Date

Completed Baseline Visits

(Goal: 1000 families)

	Families	Adults	Children
Case	792	1188	1396
Control	151	185	287

Food Allergy Study 2009

- Food allergy knowledge, attitudes, and beliefs in the United States (Gupta et al)
 - 2,148 adults were surveyed
 - Participants answered 64% of knowledge based questions correctly
 - Strengths were areas related to symptoms/severity and triggers/environmental risks of food allergy
 - Poor knowledge of the distinction between food allergy and intolerance, the absence of a cure, and current means to treat food allergy
 - Higher scores in those with self-reported prior knowledge/familiarity with food allergy
 - Respondents tended to minimize the stigma associated with food allergy and to oppose specific food allergy policies in schools

Food Allergy Study 2009

- Familial aggregation of food allergy and sensitization to food allergens: a family based study (Tsai et al)
 - This study demonstrated strong familial aggregation of food allergy and sensitization to food allergens, especially among siblings- results indicated that food-specific IgE is influenced by both genetic and environmental factors

Food Allergy Study AAAAI 2009

- Protective effects of Early Fresh Fruit Ingestion on the Development of Food Allergy (Kim et al)
 - Introduction of fresh fruit before 6 months was protective against the development of food allergy
 - Introduction of jarred fruits or vegetables before 6 months was not protective
 - Further studies are needed to look at baby food processing and early food intake including micronutrients

Peanut Oral Immunotherapy

- Clinical efficacy and immune regulation with peanut oral immunotherapy (Jones SM, et al. JACI 124(2):292-300).
 - Desensitization- change in threshold of ingested food antigen needed to cause allergic symptoms
 - Tolerance-induction of long-term immunologic changes associated with the ability to ingest food without symptoms and without ongoing therapy

Peanut Oral Immunotherapy

- Subjects: age 1-16 with peanut allergy (symptoms within 60 minutes of ingestion, positive skin prick test and positive ImmunoCAP ≥ 15) or a reaction within 6 months and ImmunoCAP ≥ 7
- Exclusion: severe, life-threatening anaphylaxis to peanut, severe or poorly controlled asthma

Peanut Oral Immunotherapy

- OIT protocol
 - Initial day escalation: dose began at 0.1mg peanut protein that was doubled every 30 minutes up to 50mg (or highest tolerated dose)
 - Buildup Phase: patients ingested the daily dose of peanut protein in 2-3 bites at home every day
 - Doses were increased 25mg every 2 weeks until 300 mg were reached- dose escalations occurred in the clinic
 - Maintenance phase: subjects continued 300mg of peanut protein daily until the food challenge- after the challenge they increased to a daily OIT dose of 1800mg if peanut IgE remained >2 after 12 months on the maintenance dose

Peanut Oral Immunotherapy

- Oral food challenge
 - 4 doses (300mg, 600mg, 1200mg, 1800mg) of peanut protein (7.8g of peanut flour). It was stopped at 3,900mg or objective symptoms.

Peanut Oral Immunotherapy

- Results:
 - 39 subjects were enrolled
 - Median first reaction 15 months of age
 - 54% had an additional food allergy (tree nut, egg, cow's milk, fish, and soy)
 - All 39 completed the initial day escalation
 - 10 (25%) withdrew
 - 6 discontinued for personal reasons-all had reactions on initial day escalation similar to subjects who continued
 - 4 discontinued for allergic reactions to OIT that did not resolve with continued treatment or dose reduction (3/4 had gastrointestinal complaints)

Peanut Oral Immunotherapy

- Results
 - Clinical response during initial day escalation
 - 36 patients (92%) experienced some symptoms during the initial day
 - 69% upper respiratory (itch, sneeze, mild laryngeal)
 - 44% mild to moderate nausea/abdominal pain
 - 21% diarrhea or emesis
 - 62% mild or moderate skin symptoms
 - 15% wheezing

Peanut Oral Immunotherapy

- Results
 - Clinical response to build up/maintenance
 - 46% had symptoms after build up dose
 - there were rare, typically minor symptoms during home dosing
 - 1.2% upper respiratory
 - 1.1% skin
 - 2 subjects received Epi after home dosing
 - Oral food challenge
 - 29 subjects had an open challenge to peanut
 - 27/29 (93%) reached total peanut dose of 3.9g (13 peanuts) with no more than mild symptoms
 - 2 stopped after 2.1g (1 parental anxiety, 1 mild urticaria and vomiting)

Peanut Oral Immunotherapy

- Conclusion
 - OIT induced clinical desensitization in the 29 subjects with peanut allergy who completed the study
 - Subjects will complete 3 years of maintenance and in those with significant drops in peanut specific IgE additional oral food challenges will be performed to see if tolerance has developed

OIT for Cow's Milk and Egg Allergy

- There are a growing number of studies of OIT for egg and milk allergy in children
- Success rates vary, but are generally between 70-80%
- However, OIT in these studies may only achieve desensitization rather than tolerance
- Staden et al (2007) in a study of egg or milk OIT found that 64% achieved desensitization, when treatment was stopped and food challenged performed 2 months later only 36% had tolerance, this matched tolerance in untreated controls

Extensively Heated Milk and Egg

- Up to 70% of egg-allergic children tolerate baked egg
 - Introduction of baked egg into diet is associated with decrease skin prick tests wheal size and increasing ovalbumin and ovomucoid IgG4 antibody
- Up to 70% of milk-allergic children tolerate baked milk
 - Introduction of baked milk into diet is associated with decrease skin prick tests wheal size and increasing casein IgG4 antibody
 - Those who reactions baked milk tend to have more severe reactions (35% required Epi vs 0% in egg)

Chinese Herbal Medicine

Food Allergy Herbal Formula (FAHF-2)

- Started: 12/2007- 12/09
- Sponsor: National Center for Complementary and Alternative Medicine
- Location: Mt Sinai School of Medicine
- In mice, treatment with FAHF-2 daily for 6 wks eliminated peanut induced anaphylaxis for 5 weeks after therapy
- Description: safety and effects of various doses of FAHF-2 given by mouth 3 times a day for 7 days, then 6 months in persons with food allergy (peanut, tree nut, fish, shellfish) aged 12-45 yrs
- Enrollment target: 18
- 1^o Outcome: safety



COFAR

- Established in July 2005
- NIH funded
- Participating Centers:
 - Duke University
 - Johns Hopkins University
 - Mt Sinai School of Medicine
 - National Jewish Health
 - University of Arkansas
- www.cofargroup.org

Study #1

Observational Study of Food Allergy

- Started 6/2006
- Objective: development of peanut allergy in infants aged 3-15 months with known milk or egg allergy
- Duration: 5 year follow-up
- 1^o Outcome: development of peanut allergy
- Enrollment target: 400 (completed)

Study #2

Oral desensitization to egg with subsequent induction of tolerance for egg-allergic children

- Started 7/2007
- Description
 - 2 yr treatment study of powdered egg or placebo given by mouth to egg allergic subjects aged 6-18 yr
 - Randomized, double blind, placebo controlled
- 1^o Outcome: % of persons who can tolerate 10gm of egg white* 4-6 wks after stopping egg study treatment
- Enrollment target: 55 (completed)

*roughly equivalent to whites from 3 large eggs

Study #3

Peanut Sublingual Immunotherapy

- Started 4/2008
- Description
 - 4 yr study of liquid peanut or placebo administered under tongue for 2 years to peanut allergic persons aged 12-40 yrs
 - Randomized, double blind, placebo controlled
- 1^o Outcome: % of subjects who tolerate a specified amount or a 10x higher amount of peanut compared to baseline peanut challenge
- Enrollment target: 40 (enrollment ongoing)

Study #4

Peanut vaccination EMP-123

- Start: March 2009
- Human Phase 1 safety trial
- Description: investigate safety and side effects of peanut vaccine in healthy volunteers first and then peanut allergic patients
- Studies in mice are promising
- Ages 18-40 years



Immune Tolerance Network

Does eating peanuts during infancy make the immune system tolerant or sensitive to peanuts consumed later on? Does one approach work better than the other in preventing peanut allergy in children?

www.leapstudy.co.uk

Early vs Late Exposure To Peanut?

- Study compared prevalence of peanut allergy among Israeli and UK Jewish children and found a prevalence 10X higher in the UK (0.17% vs 1.85%)
 - The median monthly consumption of peanut protein in Israel infants aged 8-14 months is 7.1g of peanut protein per month
 - In the UK infants eat 0 g per month
- Studies show that household peanut consumption may be a risk factor for peanut allergy



LEAP Study

- Location: UK
- Description
 - this study tests 2 approaches: avoidance of peanut vs repeated consumption of peanut-containing foods in high risk* infants aged 4-10 mos
 - Intervention group: age-appropriate peanut snack 3x/week
 - Avoidance group: avoidance til age 3 yrs
 - Randomized, parallel group trial

*diagnosed with eczema and/or egg allergy

LEAP Study

- 1^o Outcome: the proportion of kids that develop peanut allergy by age 5 years
- Enrollment target: 480 (increased to 640)
- This study will also prospectively assess immune parameters related to development of allergy and tolerance
- Anticipated duration: 7 years

Summary

- Large, well designed studies of food allergy are in progress in the USA and internationally.
- Etiology, natural history
- Desensitization vs. Tolerance
- Treatment
- Prevention

The future looks brighter for those with food allergy... *new approaches are on the horizon*



Thank you!