Pediatric Food Allergies

Elaine Medoff MD Assistant Prof Peds McGill University May 6, 2022

Disclosure

- Participated in Advisory Board Medexus (Rupall) 2022
- Participated in Advisory Board Bausch + Lomb (Emerade) 2021

Objectives

- Know the prevalence of most common pediatric food allergies
- Be aware of current recommendations for food allergy prevention
- Comprehend the use of Milk and Egg Ladders
- Understand what food oral immunotherapy is, and how it is done
- Appreciate the expected benefits from food OIT as well as the risks and drawbacks (using PN OIT as example)



Top 11 Food Allergies (90% of all food allergies)

Remit

- Milk
- Egg
- Wheat
- Soy

Persist

- PN
- TN
- Fish
- Shellfish
- Sesame
- Kiwi
- mustard

Allergy, Genes and Environment Network

SPAACE2SPAACE PROBABLE FOOD ALLERGY PREVALENCE (Apr 2020)

TABLE 1: Estimated Food Allergy Prevalence among Canadian children and adults (Probable food allergy self-reported through a nationwide AllerGen research survey)											
Food allergen		% Canadians with food allergy ¹		Canadian population ²	# Canadians with food allergy ³						
ANY FOOD		Children (0-17 years)	6.7%	7,029,310	470,963						
		Adults (18+ years)	5.9%	28,122,405	1,659,222						
1.	Peanut	Children (0-17 years)	3.2%	Data sources: 1. 2016 nationwide AllerGen survey Clarke et. al, JACI: In Practice (Apr 2020) 2. 2016 Statistics Canada Census 3. Prevalence calculation The number of Canadian children or adults with a food allergy is calculated using prevalence percent (%) ¹ for ANY FOOD allergen multiplied by the population data ² . The number of Canadian children or adults with a food allergy cannot be estimated by summing figures for specific allergens, as these figures would count Canadians with multiple food allergies more than once.	224,938						
		Adults (18+ years)	0.8%		224,979						
2.	Tree nut	Children (0-17 years)	2.1%		147,615						
		Adults (18+ years)	1.3%		365,591						
з.	Shellfish	Children (0-17 years)	0.9%		63,264						
		Adults (18+ years)	1.1%		309,346						
4.	Fish	Children (0-17 years)	1.1%		77,322						
		Adults (18+ years)	0.5%		140,612						
5.	Egg	Children (0-17 years)	1.8%		126,527						
		Adults (18+ years)	0.6%		168,734						
6.	Milk	Children (0-17 years)	1.2%		84,352						
		Adults (18+ years)	1.1%		309,346						
7.	Wheat	Children (0-17 years)	0.2%		14,059						
		Adults (18+ years)	0.5%		140,612						
8.	Sesame	Children (0-17 years)	0.3%		21,088						
		Adults (18+ years)	0.2%		56,245						
9.	Soy	Children (0-17 years)	0.3%		21,088						
		Adults (18+ years)	0.3%		84,367						
10.	Other	Children (0-17 years)	Not reported								
		Adults (18+ years)	Not reported								

JACI In Pr, 2020;8:1428-30

Food Allergy Prevention

Canadian Pediatric Society

• Posted December 17, 2021

Recommendations for clinicians:

- Consider infants at high risk for food allergy when they have a personal history of atopy or a first-degree relative (at least one parent or sibling) with an atopic condition (such as asthma, allergic rhinitis, food allergy, or eczema).
- Promote and support breastfeeding for up to 2 years and beyond, regardless of issues pertaining to food allergy prevention.
- There is still insufficient evidence to recommend modifying the maternal diet to prevent food allergy (i.e., by avoiding or ingesting particular allergenic foods during pregnancy and while breastfeeding).
- For mothers who cannot or choose not to breastfeed, hydrolyzed formulas should not be recommended to prevent atopic conditions (e.g., eczema, asthma, allergic rhinitis) in either high- or low-risk infants.
- When cow's milk protein formula has been introduced in an infant's diet, make sure that regular ingestion (as little as 10 mL daily) is maintained to prevent loss of tolerance.

- For high-risk infants, encourage the introduction of allergenic foods (e.g., cooked (not raw) egg, peanut) early, at about 6 months and not before 4 months of age, in a safe and developmentally appropriate way, at home. In infants at low risk for food allergy, allergenic foods can also be introduced at around 6 months of age.
- New foods, including commonly allergenic foods, can be introduced on successive days, with no evidence of harm to this approach.
- When allergenic foods have been introduced, make sure that ongoing ingestion of ageappropriate serving sizes is regular (i.e., a few times a week), to maintain tolerance.
- Pre-emptive screening for infant food allergies is not recommended. Families should be counseled that the risk of a severe reaction on the first exposure to an allergen is extremely low. 0.08% = 1/1,250 babies
- There is currently insufficient evidence to recommend vitamin D, omega 3, or pre- or probiotic supplements to prevent food allergies in infants.



HOW TO FEED YOUR BABY EARLY



ATCH FOR SIGNS OF AN ALLERGIC REACTION 0 Allergy symptoms usually develop within minutes of eating a food but can occur up to 2 hours after ingestion. Symptoms can be mild such as hives. Note that redness around the mouth may be due to skin irritation rather than allergy. More severe symptoms can include: Ø Swelling of the lips, eyes, or face Vomiting Widespread hives on the body Breathing symptoms such as repetitive cough, wheeze, or any difficulty breathing 0 A change in skin colour (pale, blue) Sudden tiredness/lethargy/seeming limp 0 There can also be behavioural changes such as irritability, inconsolable crying or clinging to a caregiver. Remember, if there are severe allergy symptoms, seek immediate medical attention/call 911. If the junior dose of an epinephrine auto-injector is on hand, it should be administered to an infant who is having an anaphylactic reaction.



Desensitization

- Process by which you introduce small amounts of a given allergen, progress slowly to try to increase tolerance
- Done with aeroallergen immunotherapy (SCIT&SLIT), done with medications (ASA, etc)
- Now done with foods (OIT)

Milk and Egg

- Known: 75% of children allergic to milk or to egg will tolerate baked forms (heating changes conformational epitopes of the proteins)
- Unknown: long term effects of baked milk inclusion in diet



and Hugh A. Sampson, MD New York, NY

- 88 pts avg age 6.6yo (2.1-17.3y)
 - 70 passed baked milk challenge
 - 18 others continued to strictly avoid all milk
 - Those who passed ate baked milk 1-3 servings per day
 - After 6 months, were challenged to baked cheese (cheese pizza serving)
 - After 6 months were challenged to unheated milk
- Natural hx control group 60 pts



TABLE I. Follow-up status of milk allergy

Final follow-up status	Initially baked milk tolerant (n = 65)	Initially baked milk reactive (n = 23)	Active intent-to-treat (n = 88)	Active per-protocol (n = 70)	Comparison (n = 60)
Unheated milk tolerant	39 (60%)	2 (9%)	41 (47%)	41 (59%)	13 (22%)
Baked milk/cheese tolerant	18 (28%)	3 (13%)	21 (24%)	21 (30%)	13 (22%)
Avoiding strictly	8 (12%)	18 (78%)	26 (29%)	8 (11%)	34 (56%)

- Tolerance of baked milk is a favorable px indicator for tolerance of unheated milk
- Introduction of baked milk appears to accelerate the tolerance to unheated milk when compared to avoidance
- Baked milk introduction is safe, convenient, well accepted
- Prescribing baked milk products represents an important shift in the tx paradigm for milk allergy

Same for baked egg



 Baked milk and baked egg introduction are considered modified forms of desensitization which can be started or continued at home, done at family's own rhythm



Chomyn et al. Allergy Asthma Clin Immunol (2021) 17:83 https://doi.org/10.1186/s13223-021-00583-w Allergy, Asthma & Clinical Immunology

LETTER TO THE EDITOR

Canadian food ladders for dietary advancement in children with IgE-mediated allergy to milk and/or egg

Alanna Chomyn^{1*}, Edmond S. Chan¹, Joanne Yeung¹, Timothy K. Vander Leek², Brock A. Williams^{1,3}, Lianne Soller¹, Elissa M. Abrams^{1,4}, Raymond Mak¹ and Tiffany Wong^{1*}

Abstract

Food ladders are clinical tools already widely used in Europe for food reintroduction in milk- and egg-allergic children. Previously developed milk and egg ladders have limited applicability to Canadian children due to dietary differences and product availability. Herein we propose a Canadian version of cow's milk and egg food ladders and discuss the potential role that food ladders may have in the care of children with IgE-mediated allergies to cow's milk and/or egg, as either a method of accelerating the acquisition of tolerance in those who would outgrow on their own, or as a form of modified oral immunotherapy in those with otherwise persistent allergy.

Keywords: Food ladders, Food allergy, Cow's milk allergy, Egg allergy, Oral immunotherapy

HOWEVER...

 Other foods do not change significantly with cooking (some may increase their allergenicity such as peanuts with roasting or shrimps with boiling) so these types of informal or modified desensitization cannot be done

Formal Food Oral Immunotherapy

- Regular ingestion of gradually increasing doses of one's allergen over time, to reduce reactivity and increase reaction threshold
- Initially studied in older age groups (≥ 6yo)
- Goal: prevent reactions to accidental exposures & increase QOL
 - Extensively studied
 - 85-90% success rate for desensitization
- Once started, must continue indefinitely
- Goal ≠ cure
 - Sustained unresponsiveness (?tolerance) may be obtained, but much less frequently

- Burden: allergic rxns, immediate and delayed, can occur during all phases of OIT
 - Must be prepared to tx allergic rxns , willing to use epi
 - May increase anaphylaxis in short term compared with avoidance, appears to decrease over longer time horizon
 - Must take into account cofactors which can change reactivity thresholds
 - Exercise (30-60 minutes before and 2 hours post dose), sleep deprivation, ROH, NSAIDs, fever and viral infections, menses, etc.

- Absolute contra-indications:
 - Poorly controlled asthma
 - Pregnancy
- Relative contra-indications:
 - Active severe AD
 - Pre-existing EoE or EGID
 - Heart disease
 - Use of beta-blockers, ACE inhibitors

- Added degrees of difficulty:
 - Unreliable adherence to protocol
 - Reluctance to use epi
 - Language barrier
 - Severe anxiety
 - Psychiatric barriers
 - Non-collaborative family dynamics
 - Lack of schedule flexibility for dosing
 - Lack of commitment from patient or caregivers

Food, drug, insect sting allergy, and anaphylaxis

Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective

Brian P. Vickery, MD,^a Jelena P. Berglund, PhD,^b Caitlin M. Burk, BA,^a Jason P. Fine, PhD,^a Edwin H. Kim, MD, MHS,^a Jung In Kim, MS,^a Corinne A. Keet, MD, PhD,^c Michael Kulis, PhD,^a Kelly G. Orgel, BS,^a Rishu Guo, MD, PhD,^a Pamela H. Steele, CPNP,^a Yamini V. Virkud, MD, MPH,^d Ping Ye, PhD,^a Benjamin L. Wright, MD,^c Robert A. Wood, MD,^c and A. Wesley Burks, MD^a Chapel Hill and Durham, NC, Baltimore, Md, Boston, Mass, and Scottsdale, Ariz

- 37 PN allergic patients, aged 9-36 months (pos challenge)
- Randomized 1:1 to receive early OIT with 300mg or 3000mg PN protein
- Sustained unresponsiveness at 4weeks = outcome
- ITT 29/37 achieved SU4 (78%)
- Per protocol 29/32 achieved SU4 (91%)

- 19X more likely to consume dietary PN than matched control grp
- 1 pt received epi, overall safe
- Advantages:
 - Less food aversion/fear
 - Immune system possibly more malleable than in older pts

Original Article

First Real-World Safety Analysis of Preschool Peanut Oral Immunotherapy

Lianne Soller, PhD^{a,b}, Elissa M. Abrams, MD^{b,c,d}, Stuart Carr, MD^e, Sandeep Kapur, MD^{f,g}, Gregory A. Rex, MD^{f,g}, Sara Leo, MD^{b,h}, Per G. Lidman, MD^e, Joanne Yeung, MD^{b,i}, Timothy K. Vander Leek, MD^e, Mary McHenry, MD^{f,g}, Tiffany Wong, MD^{a,b}, Victoria E. Cook, MD, MSc^{b,j}, Kyla J. Hildebrand, MD, MScCH (HPTE)^{a,b}, Thomas V. Gerstner, MD^{e,d}, Raymond Mak, MD^b, Nicole J. Lee, MSc^{a,b}, Scott B. Cameron, MD, PhD^{b,j,*}, and Edmond S. Chan, MD^{a,b,*} Vancouver and Victoria, BC, Canada; Winnipeg, MB, Canada; Edmonton, AB, Canada; and Halifax, NS, Canada

JACI In Pr 2019;7:2759-67

- 270 pts 9-71 mo, with PN allergy
- Given PN OIT, daily dosing, increases in hosp Q 2 wks
- Target dose 300mg (=1 peanut)
- 270 pts 243 reached maintenance
 - 27 dropped out
- 67.8% had rxns during build-up
 - 36.3% grade 1
 - 31.1% grade 2
 - 0.4% grade 4

FIGURE 1. Modified World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System.¹⁸ PEF, Peak of

Original Article

First Real-World Effectiveness Analysis of Preschool Peanut Oral Immunotherapy

Lianne Soller, PhD^{a,b}, Elissa M. Abrams, MD^{b,c,d}, Stuart Carr, MD^e, Sandeep Kapur, MD^{g,h}, Gregory A. Rex, MD^{g,h}, Sara Leo, MD^{b,i}, Mary McHenry, MD^{g,h}, Timothy K. Vander Leek, MD^{e,f}, Joanne Yeung, MD^{b,j}, Victoria E. Cook, MD^{b,k}, Tiffany Wong, MD^{a,b}, Kyla J. Hildebrand, MD^{a,b}, Raymond Mak, MD^b, Thomas V. Gerstner, MD^{e,d}, Scott B. Cameron, MD, PhD^{b,k,e}, and Edmond S. Chan, MD^{a,b,e} Vancouver and Victoria, BC, Canada; Winnipeg, MB, Canada; Edmonton, AB, Canada; and Halifax, NS, Canada

JACI In Pr 2021;9:1349-56

- Aim: determine effectiveness of preschool PN-OIT after 1 year of maintenance
- 117 pts successfully completed 1 year of PN-OIT and underwent cumulative 4000mg FU OFC(=13-15 peanuts)
 - 92/117 (=78.6%) had negative OFC
 - 115/117 (=98.3%) tolerated cumulative dose ≥ 1000mg (= 3-4 peanuts) ***This provides 99% protection from accidental exposures ***
 - 25 who reacted increased threshold 3376mg from baseline to FU (2884-3868mg)

• "We hypothesize that once preschoolers have eaten PN regularly post-OIT for roughly a decade before reaching the less-adherent adolescent years, tolerance will probably occur."

Real-world peanut OIT in infants may be safer than non-infant preschool OIT and equally effective

Lianne Soller, PhD^{a,b}, Stuart Carr, MD^c, Sandeep Kapur, MD^{d,e}, Gregory A. Rex, MD^{d,e}, Mary McHenry, MD^{d,e}, Victoria E. Cook, MD^{b,f}, Sara Leo, MD^{b,g}, Tiffany Wong, MD^{a,b}, Timothy K. Vander Leek, MD^h, Thomas V. Gerstner, MD^{i,j}, Joanne Yeung, MD^{b,k}, Elissa M. Abrams, MD^{b,i,j}, Raymond Mak, MD^{a,b}, Kyla J. Hildebrand, MD^{a,b}, Stephanie C. Erdle, MD^{a,b}, Scott B. Cameron, MD, PhD^{b,f,*}, and Edmond S. Chan, MD^{a,b,*}

The U.S. Food and Drug Administration has approved the first ever drug to treat peanut allergy, a life-threatening condition mainly for kids. Aimmune Therapeutics Inc.'s Palforzia [Peanut (Arachis hypogaea) Allergen Powder-dnfp] can now be used to treat patients aged 4 through 17 years.

Approved Jan 2020, \$890US/month (\$11,000/year!!!)

