

OIT PROTOCOLS

Hugh H. Windom, M.D.
Food Allergy Center of Florida
Sarasota, Florida

A Precursor to OIT: Milk and Egg Ladder

Gradual introduction of partially denatured protein

- ▶ Heated milk tolerant kids 28x more likely to become tolerant to unheated milk over 5 years
- ▶ Eating heated milk accelerates milk tolerance
- ▶ Casein IgG₄ increased over 5 yrs in heated milk tolerant kids

Kim JS. *J Allergy Clin Immunol* 2011; 128:125-31

Baked Milk OFC

- ▶ 41 patients, 3 -18 yo, milk sIgE > 5 kU/L, + history
- ▶ 11 of 41 (27%) passed baked milk (BM) challenge
- ▶ 18 of 30 (60%) + OFC treated with epi
- ▶ No predictors of BM tolerance, median casein IgE in these patients was 22.7 KU/L

Dantzer JA. J Allergy Clin Immunol 2020;146:1434-37

Milk/Egg Allergy Management

	Under 6-8 years old	> 6-8 years old
Low level suspicion	OFC whole food	OFC whole food
Moderate level suspicion	Muffin challenge*	OFC whole food vs OIT
Strong history and tests	Muffin challenge**	Oral immunotherapy

* milk casein <1, can introduce muffins at home (96% negative muffin OFC)

**~~milk casein >20~~ recent baked reaction, go directly to OIT

Help Wanted - Dietary Instructions

Each ladder step:

- baked muffin
- pancake
- whole egg/milk

Need listing of allowed foods, i.e. those with same or less allergenic potency

OIT Protocol Overview

The gradual introduction of a food to a person previously intolerant

- ▶ 12-20 visits to increase the amount of food from ~0.1 mg protein to ~1 gm, a minimum of 1 week apart
- ▶ Top dose is 1-8 peanuts, 2-4 cashews, 1-2 walnuts, 2-3 oz milk, ½ egg, ⅔ Tbsp sesame seeds, 1/3 wheat bagel
- ▶ Maintenance dosing is indefinite, going from daily to 1-2 days/week

Clinic OIT Process

- ▶ Confirm diagnosis – history, diagnostic testing, +/- OFC
- ▶ Pre-study visit – confirm ST and sIgE in past year, spirometry in asthma pts, consent form discussed/sign
- ▶ **Day One** – plan 3-5 hours, dosing q 20 minutes, STOP at first sign of a reaction
- ▶ **Build Up** – continue highest dose tolerated Day One at home QD, return 1-2 weeks for next higher dose
- ▶ **Maintenance** – 300 mg -2 gm protein

Dosing Goals

- ▶ A conversation with patient/family pre-OIT is critical
- ▶ Bite-proof vs free eating
- ▶ We focus on safety, aiming for 0.5 – 1 gm protein
- ▶ Staple foods different, most want to eat normally
- ▶ Egg and milk so common in diet, scheduled dosing becomes less important

Typical Protocol

- ▶ **Day One:** Starting dose: 0.01 - 0.1 mg protein

Top dose: 1-5 mg protein

- ▶ **Build Up:** Dose increment: 25 - 100%

Frequency of visits: 1 - 2 weeks

- ▶ **Maintenance:** Top dose: 300 mg - 2 grams

Frequency of dosing: QD – 2 times a week

Walter Reed SCIT Schedule

Schedule 1	Schedule II	Schedule III	Schedule IV
0.1 ml	0.1 ml	0.05 ml	0.05 ml
0.2	0.2	0.1	0.1
0.4	0.3	0.15	0.15
0.6	0.4	0.2	0.2
	0.5	0.3	0.25
		0.4	0.3
		0.5	0.4
			0.5

Palforzia	Windom Allergy
Day 1 Top Dose: 3 mg peanut protein	2.5 mg peanut protein
6	4.5
12	7.5
20	12.5
40	20
80	33
120	55
160	90
200	150
240	250
300 (~1 peanut)	425
	750 (~ 3 peanuts)

Palforzia	Windom Allergy
Day 1 Top Dose: 3 mg peanut protein	2.5 mg peanut protein
6 (100%)	4.5 (80%)
12 (100%)	7.5 (67%)
20 (67%)	12.5 (67%)
40 (100%)	20 (60%)
80 (100%)	33 (65%)
120 (50%)	55 (61%)
160 (33%)	90 (64%)
200 (25%)	150 (67%)
240 (20%)	250 (67%)
300 (25%)	425 (70%)
	750 (76%)

Dallas	Hartford	Sarasota
Day 1	Day 1	Day 1
mg protein	mg protein	mg protein
0.1	0.1	0.05
0.2	0.2	0.15
0.4	0.4	0.5
1	0.8	1.25
2	1.5	2.5
	3	

Dallas	Hartford	Sarasota
4 mg peanut protein	3 mg peanut protein	4.5 mg peanut protein
6	4.5	7.5 (1 st fragment)
8	6	12.5
10	9	20
15	12	33
20	18	55
26 (1 st fragment)	25	90
53	35	150
79	50	250
105	75 (1 st flour in cup)	425
158	100	750 (~ 3 peanuts)
250	125	
500	165	
750	225	
1000	300	
1500	400	
2000	2.5 peanuts	
2500	3 peanuts	
3000		

Dallas	Hartford	Sarasota
4 mg peanut protein	3 mg peanut protein	4.5 mg peanut protein
6 (50%)	4.5 (50%)	7.5 (1 st fragment)
8 (33%)	6 (33%)	12.5
10 (25%)	9 (50%)	20
15 (50%)	12 (33%)	33
20 (33%)	18 (50%)	55
26 (1 st fragment) 30%	25 (39%)	90
53 (104%)	35 (40%)	150
79 (50%)	50 (43%)	250
105 (30%)	75 (1 st flour in cup) 50%	425
158 (50%)	100 (33%)	750 (~ 3 peanuts)
250 (58%)	125 (25%)	
500 (100%)	165 (32%)	
750 (50%)	225 (36%)	
1000 (33%)	300 (33%)	
1500 (50%)	400 (33%)	
2000 (33%)	2.5 peanuts (56%)	
2500 (20%)	3 peanuts (20%)	
3000 (20%)		

Canadian pre-school	Sarasota < 3 y.o.
Day 1 Top Dose: 6 mg peanut protein	3.5 mg peanut protein
12 (PB2)	7 mg (flour)
25 (PB2)	10 (0.08 gm Bamba)
50 (PB2)	17 (0.13 gm Bamba)
~80 (1 Bamba)*	29 (0.22 gm Bamba)
~120 (1.5 Bamba)*	49 (0.36 gm Bamba)
~ 160 (2 Bamba)*	83 (0.6 gm Bamba)
~240 (3 Bamba)*	141 (1 gm Bamba)
~320 (4 Bamba)*	234 (1.7 gm Bamba)
	400 (3 gm Bamba)
	668 (4 gm Bamba)
*next slide	

Protein Variability

Bamba protein content:

Osem – 4 gm PP/28 gm, 14.3% protein

Gratify – small bag 15% protein, large bag 17.6%

Trader Joe's – 5 gm PP/30 gm, 16.7% protein

Canada – 5 gm PP/28 gm, 17.9% protein

Bamba stick weight:

Osem/Trader Joe's – 700-900 mg

Canada – 400-500 mg

M&M's:

30-80% of an average peanut

Soller L. J Allergy Clin Immunol Pract 2019; 7:2759-67

Protein goal	Amount of Food X
-	e.g. <u>20</u> % protein
Day 1 Top Dose – 3 mg	$3 \text{ mg} / 0.2 = 15 \text{ mg}$
Updose in <u>60</u> % increments	-
$3 \times 0.6 = 1.8, 3 + 1.8 = 4.8$	$4.8 \text{ mg} / 0.2 = 24 \text{ mg}$
$4.8 \times 0.6 = 2.9\dots = 7.7$	38
12.3	61
19.7	98
32	157
50	252
81	403
...	...

An Accelerated Protocol (or OFC roll-over into OIT)

- ▶ Day One is an oral food challenge (OFC)
- ▶ 1st buildup dose is 1-2 doses back from provocative dose
- ▶ 9/11 patients were successfully up dosed to 8 peanuts
- ▶ Very similar to Day One dosing by Mansfield since 2005

Bird JA. *J Allergy Clin Immunol Pract* 2015; 3:433-5

Multi-Food OIT

- ▶ Saves time and money to combine foods vs sequential single food OIT
- ▶ Typically no more than 3 foods, may choose not to combine sIgE > 100 foods and in older pts
- ▶ Same protocol, just cut Day 1 doses by 1/extra food
- ▶ Can always drop a food(s) if trouble building up

Conclusions

- ▶ The life of an Allergist, more art than science
- ▶ Minimum requirements – consistent food source with known protein content
- ▶ Plug and play
- ▶ Keep Day One < 5 mg protein, adjust buildup if issues arise
- ▶ Remain vigilant