

Early Allergen Introduction & Prevention of Food Allergy

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(adapted from Sharma 2016)



Discussion Objectives

- Review recent food allergy research studies related to prevention of food allergy and early food introduction
- Understand the implications of these research findings for our patients' health *and* their *health care costs*

When to Introduce Foods?

A Reversal of Recommendations

Year 2000

Delay introduction of highly allergenic foods to
???decrease risk of food allergy:

- Cow's milk until age 1 year
- Egg until age 2 years
- Peanuts, tree nuts, and fish until age 3 years

← This was
WRONG!

Year 2008

- No evidence for delaying introduction highly allergenic foods
- No specific guidelines on when and how to introduce the highly allergenic foods

Timing of Food Introduction: A Reversal of Recommendations

Year 2014

- Recent data suggests delaying introduction of complementary foods increases risk of food allergy
- Early introduction of highly allergenic foods may decrease risk of food allergy (and asthma and eczema)



Year 2015

- LEAP Trial – First randomized clinical trial of early peanut introduction during infancy and risk of peanut allergy in later childhood
- Consensus Communication on Early Peanut Introduction and the Prevention of Peanut Allergy in High-Risk Infants



Year 2016

- NIAID Update to Food Allergy Guidelines – coming soon!

Case 6

- A 3 month old breastfed girl has severe atopic dermatitis.
- Her parents tell you they saw something on TV about babies with eczema and peanut allergy.
- They want to know when they should start introducing peanut and other potentially allergenic foods??

Learning Early About Peanut Allergy

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

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Helen A. Brough, M.B., B.S., Deborah Phippard, Ph.D., Monica Basting, M.A.,
Mary Feeney, M.Sc., R.D., Victor Turcanu, M.D., Ph.D.,
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Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the LEAP Study Team*

Impact of Peanut Allergy & Rationale for a Trial of Early Introduction

Peanut allergy:

- Prevalence has more than tripled in the past 1-2 decades in the US
 - Affects 1-3% of general population
 - Nearly 100,000 new cases annually!!
- Most common cause of fatal food-induced anaphylaxis

Rationale for early introduction:

- Prior studies had shown the risk of peanut allergy was 10 times higher for Jewish children in the United Kingdom versus Jewish children in Israel
 - Could not be explained by: atopy, genetics, SES, peanut allergenicity
 - Only significant difference was timing of peanut introduction

LEAP Trial Study Design

- Purpose: To determine whether early introduction of peanut to high-risk infants decreases later risk of peanut allergy.
- Population: 640 infants at “high risk” for food allergy between ages 4-11 months:
 - severe atopic dermatitis and/or
 - IgE-mediated egg allergy
- Randomized into two groups:
 - Peanut consumption group until 5 years of age
 - Peanut avoidance group until 5 years of age
- Included 542 infants with negative skin prick test (SPT) to peanut, but also 98 infants with a small positive SPT
- **Excluded those with SPT >4mm**

Peanut Consumption in the LEAP Trial

- Consumed 6 grams of peanut protein weekly (or 2 grams 3 times/week)



Box 2. Examples of peanut-containing foods used in the LEAP trial

- Smooth peanut butter (1 teaspoon) mixed with milk or with mashed or pureed fruit
- Bamba snack* (Osem; approximately two thirds of a 1-oz (25 g) bag; 21 sticks of Bamba)
 - For young infants (<7 months), softened with 20 to 30 mL water or milk and mixed with milk or with mashed or pureed fruit or vegetables
- Peanut soup
- Finely ground peanuts mixed into other foods, such as yogurt

*Other foods more customary to particular nations/cultures can be substituted.

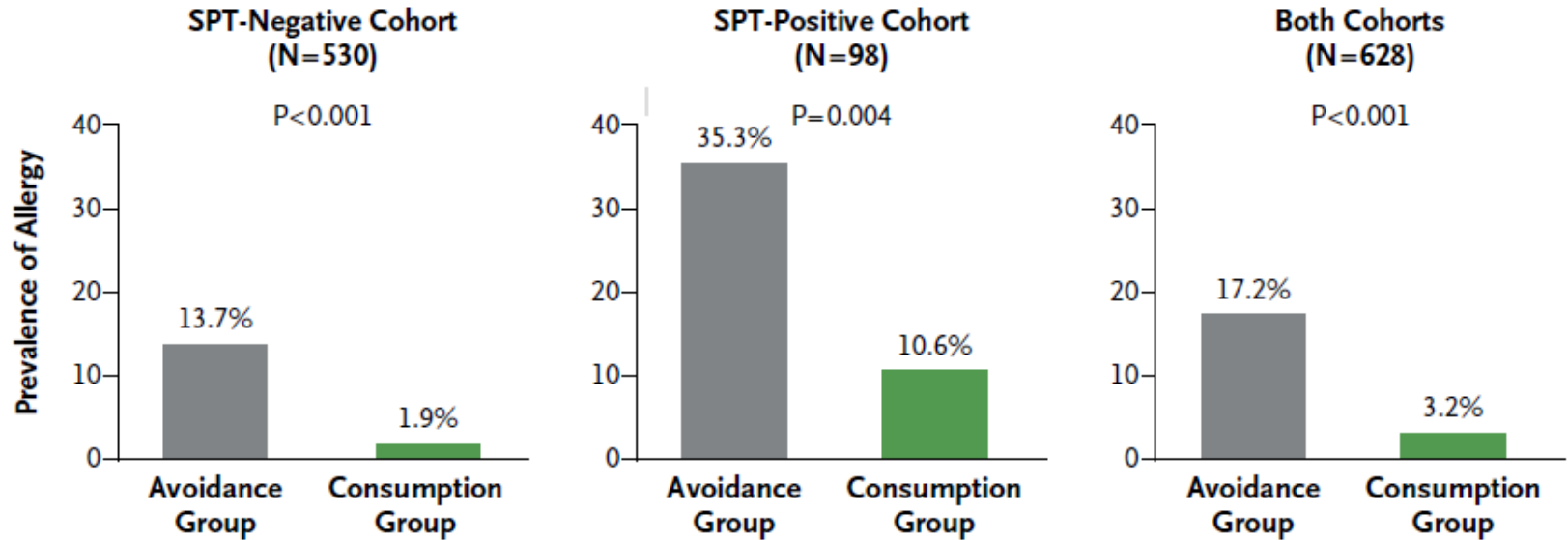
Whole peanut is not recommended for introduction because this is a choking hazard in children less than 4 years of age.



- At age 5 years, underwent peanut oral food challenges and peanut skin testing and specific IgE and IgG testing

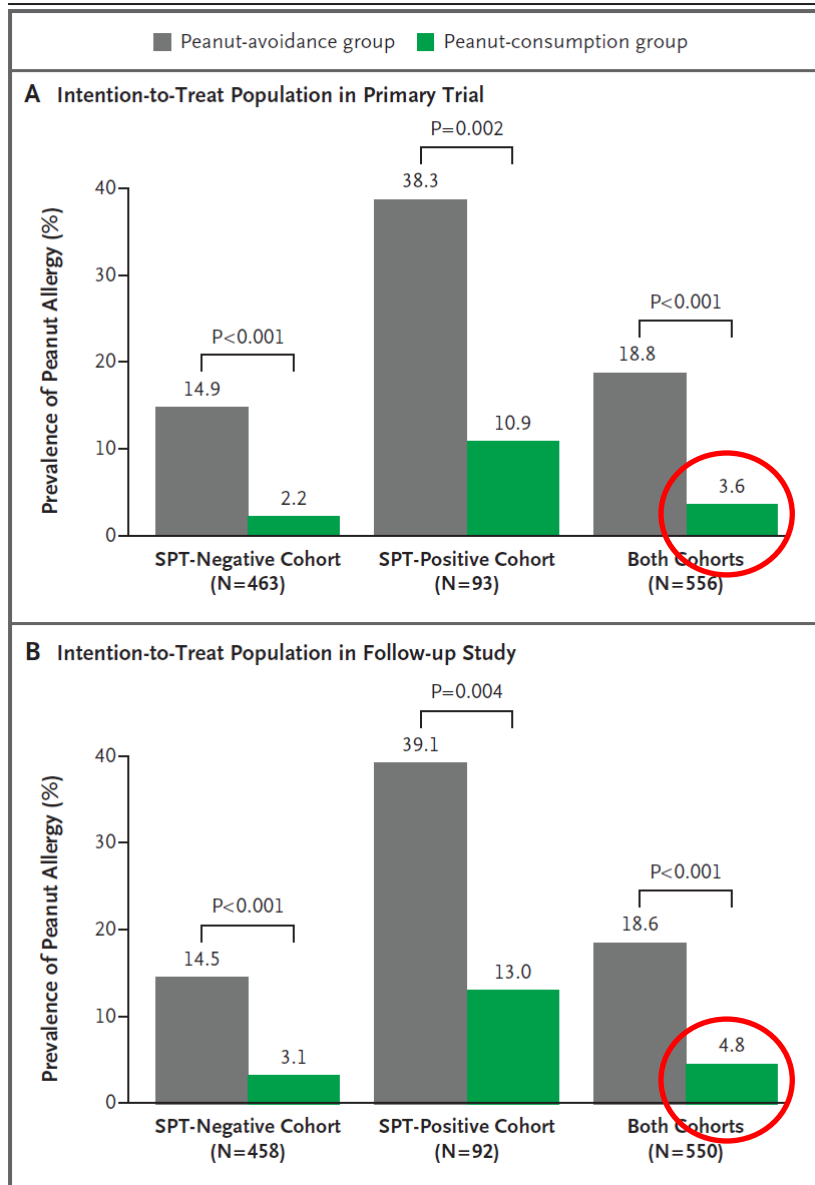
LEAP Trial Results

A Intention-to-Treat Analysis



	SPT Negative	SPT Positive	Combined
Relative risk reduction	86.1%	70.0	81.3%
Absolute risk reduction	11.8%	24.7	14.0%
Number needed to treat (NNT)	8.5	4	7.1

LEAP-ON Trial: Results



- After 12 months of avoidance, there was no significant increase in the prevalence of allergy among consumption group (3.6% [10 of 274 participants] at 60 months and 4.8% [13 of 270] at 72 months, $p = 0.25$)
- Among children at high risk for allergy in whom peanuts had been introduced in the first year of life and continued until 5 years of age, a 12-month period of peanut avoidance was *not* associated with an increase in the prevalence of peanut allergy

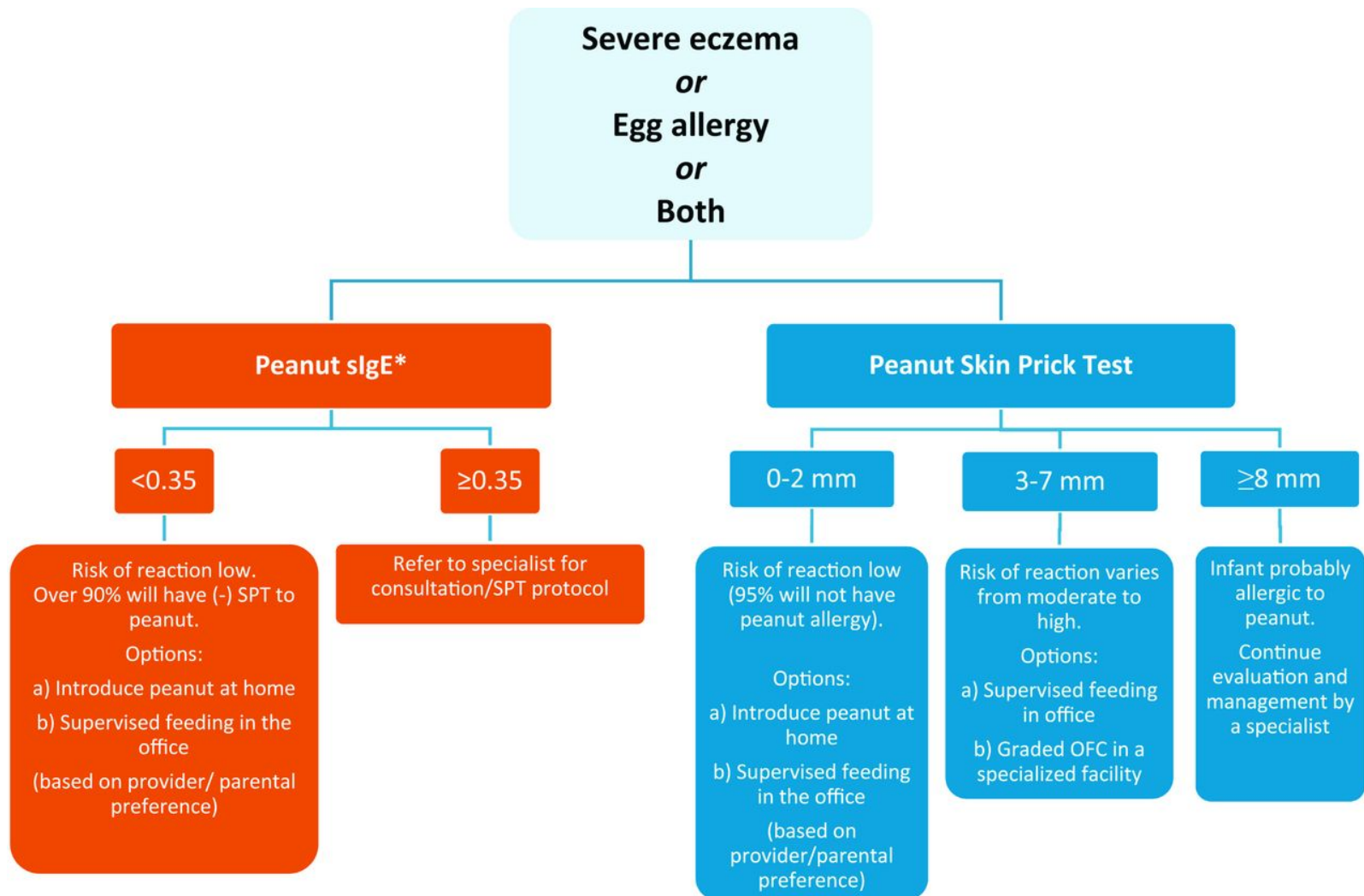
Consensus Communication on Early Peanut Introduction and the Prevention of Peanut Allergy in High-risk Infants

- Health care providers should recommend introducing peanut-containing products into the diets of “high-risk” infants early (between 4 and 11 months of age) because delaying the introduction of peanut can be associated with an increased risk of peanut allergy
- Infants with early-onset atopic disease, such as severe eczema or egg allergy in the first 4 to 6 months of life, might benefit from evaluation by an allergist
 - Evaluation of such patients might consist of performing peanut skin testing, in-office observed peanut ingestion, or both

2017 Addendum guidelines for the prevention of peanut allergy in the United States: Report of the NIAID expert panel

TABLE I. Summary of addendum guidelines 1, 2, and 3

Addendum guideline	Infant criteria	Recommendations	Earliest age of peanut introduction
1	Severe eczema, egg allergy, or both	Strongly consider evaluation by sIgE measurement and/or SPT and, if necessary, an OFC. Based on test results, introduce peanut-containing foods.	4-6 months
2	Mild-to-moderate eczema	Introduce peanut-containing foods	Around 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods	Age appropriate and in accordance with family preferences and cultural practices



* To minimize a delay in peanut introduction for children who may test negative, testing for peanut-specific IgE may be the preferred initial approach in certain health care settings. Food allergen panel testing or the addition of sIgE testing for foods other than peanut is not recommended due to poor positive predictive value.

Implementing the Guidelines

- Retrospective study of the feasibility of implementation of the guidelines
- Infant under 12 months evaluated for peanut allergy
- Observed feeding of graded OFC to peanut offered if SPT < 8 mm
- Reaction rates were low and mild

Low-dose Infant Peanut Challenges at Children's

- All infants who are high risk for PN allergy 0-13 months of age
- High Risk (one of the following criteria)
 - Mod-severe atopic dermatitis
 - Egg allergy
 - Prior peanut reaction
 - Prior positive PN-IgE
 - Sibling with food allergy
- LEAP used exclusion cutoff of >4 mm
- Typical 95% PPV for SPT is 8mm (12 month and older)

Low dose infant PN-OFCs

- Overall a safe procedure for infants in this setting
- Consider IV placement for very high risk (depending on SPT size and Ara h2)
- Attempt to OFC all infants regardless of SPT to prevent PN allergy in many
- If unable to safely OFC, then strict avoidance suggested
- Regular follow up with families 1 month post OFC and every 3 months
- Keep PN in the diet regularly and increase amount as age appropriate/ ad lib up to age 4 or 5 years
- Continue to carry epinephrine for at least a year

Physician Side Gigs...

the simplest way to introduce your baby to allergenic foods



COMING SOON



A Gradual Way To Introduce Your Infant To Peanuts

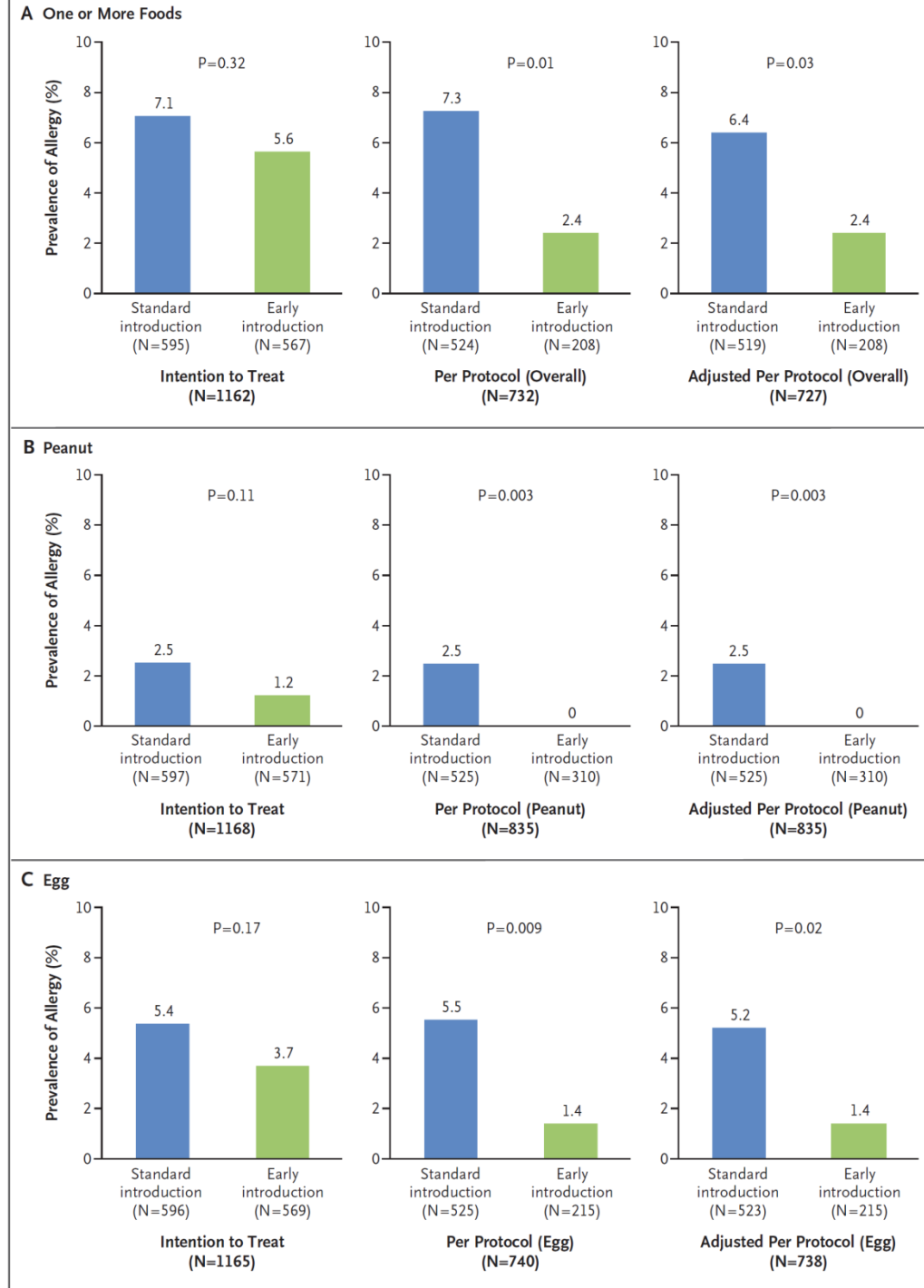


EAT (Enquiring About Tolerance) Trial: Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants

- Purpose: To determine whether the early introduction (3 to 6 months age) of allergenic foods (peanut, cooked egg, cow's milk, sesame, whitefish, and wheat) in the diet of breast-fed infants would protect against the development of food allergy
- Population: 1303 exclusively breast-fed infants 3 months of age
 - Randomly assigned to early introduction of all 6 allergenic foods or to exclusive breast-feeding to approximately 6 months of age
 - Primary outcome - food allergy to one or more of the six foods between 1 year and 3 years of age

EAT Trial: Results

- The early introduction of all six foods was not easily achieved (**adherence** = 42%) but was safe
- No significant difference in intention to treat analysis
- In per-protocol analysis, prevalence of any food allergy was significantly lower in early-introduction vs standard introduction group, as was the prevalence of:
 - peanut and egg allergy
 - no significant effects with respect to milk, sesame, fish, or wheat
- Efficacy was related to duration and **dose** of foods consumed between 3 and 6 months



Sample Food Introduction Timeline

Adjust based on child's developmental skills and family/cultural preferences

Starting at 4-6 months (fruits, veg, dairy, oat, wheat)

- yogurt
- avocado
- pureed:
 - peas
 - carrots
 - plums
 - peaches
 - squash
 - sweet potato
 - Other fruits/veggies
- - could mix fruits with yogurt
- - oatmeal and wheat cereals thinned - could add fruit purees that were already tolerated

starting 6-9 months add the following (eggs, nuts, legumes, sesame, soy, fish, shellfish)

- scrambled eggs cut up small
- soft well done cut up macaroni (wheat)
- mix 1/4 teaspoon of peanut, almond, or cashew butter with fruit purees or oatmeal
- grind up nuts individually to a fine powder and mix into other foods (purchase peanut powder/flour)
- new vegetables: pureed cauliflower, broccoli
- berries (can sometimes be too acidic when fresh (these can flare eczema too))
- smoothies with blended fruits, vegetables, nut butters or ground nuts, yogurt
- small pieces of soft tofu mixed with vegetables or eggs
- lentil soup
- hummus
- soft fish and shellfish like salmon and crab
- soft thinned ground or tiny shredded pieces of poultry, beef, pork (can mix with vegetable purees)

Conclusions

- *Growing evidence for role of early food introduction in preventing food allergy*
- *There is strong evidence that early peanut introduction (4-11 months age) in high-risk infants decreases risk of later peanut allergy, and protective effect is not lost after peanut avoidance 5-6 years of age*
- *Potential of preventing food allergy by means of early introduction of multiple allergenic foods in normal breast-fed infants may depend on adherence and dose*
- *Prevention of food allergy has significant health care cost implications*

Immunomodulatory Therapies under Investigation for Peanut Allergy

- Food allergen-specific therapy
 - Oral immunotherapy (OIT)
 - Sublingual immunotherapy (SLIT)
 - Epicutaneous immunotherapy (EPIT)
- Non-specific therapy
 - Monoclonal anti-IgE
 - Traditional Chinese Medicine

Allergen Immunotherapy:

Potential Outcomes

Immunotherapy relies on the delivery of gradually increasing doses of specific allergens to induce:

- **Desensitization**

- *Temporary* increase in the reaction threshold to a food allergen during active therapy
- Achieved after only months of therapy and requires ongoing therapy

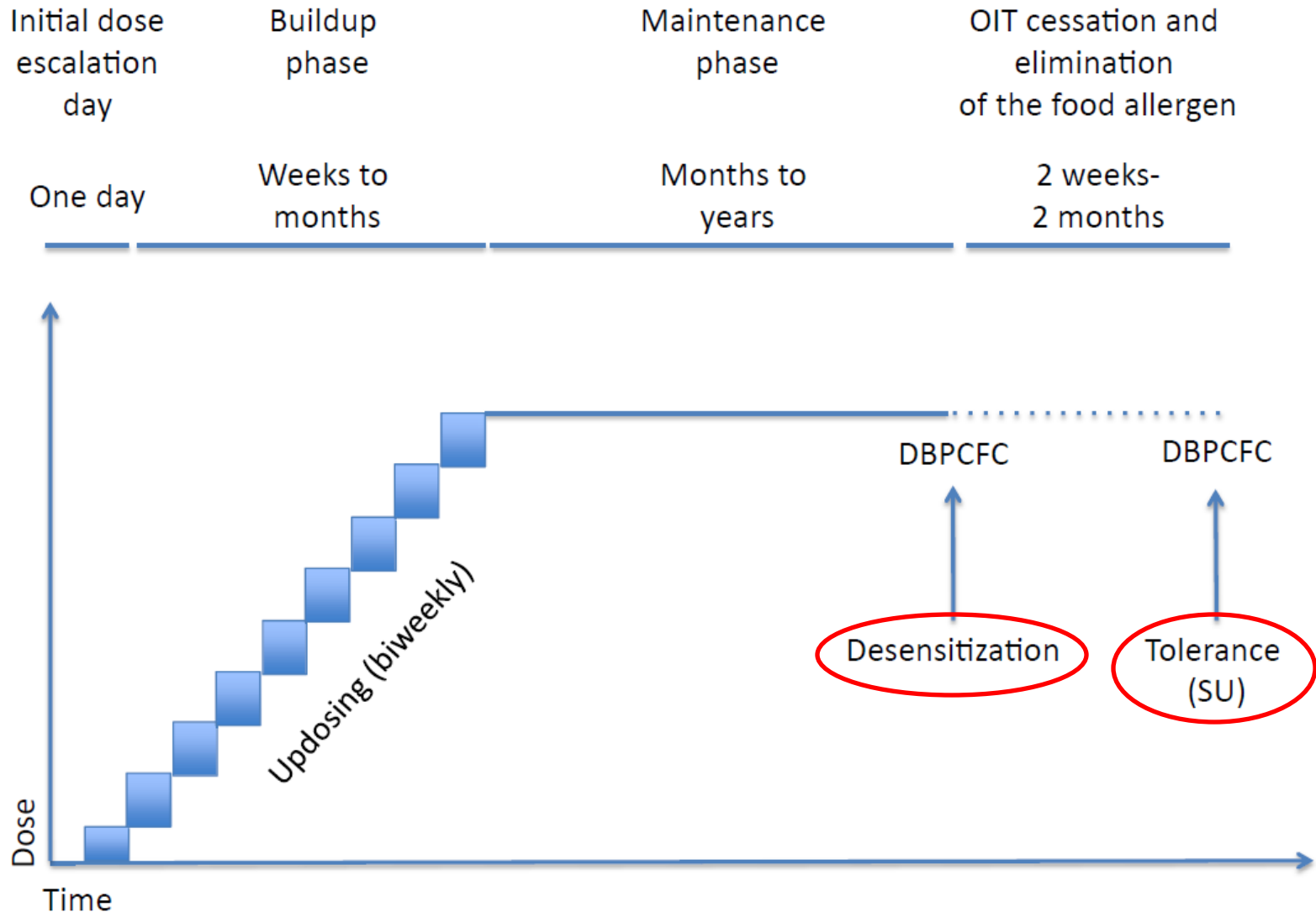
- **Tolerance**

- Ability to ingest food allergen without symptoms despite prolonged periods of avoidance or irregular intake

- **“Sustained unresponsiveness”**

- Used in studies as a surrogate for permanent oral tolerance as the exact period of food avoidance after treatment defining tolerance is unknown
- Requires years of therapy and has been seen only in subgroups of patients

Typical OIT Dosing Protocol



Children's National Food Allergy Program



- Children's National Food Allergy Program

- Inaugural FARE (Food Allergy Research and Education) Clinical Network Center of Excellence
- > 1,100 new and > 2,000 returning food-allergic patients treated annually
 - Immediate appointment availability throughout region
- > 500 oral food challenges performed annually
- One of <5 programs in the US to have a dedicated Food Allergy Psychology Program
- Multidisciplinary clinics: Eosinophilic Esophagitis clinic (Allergy/GI/Nutrition)
- NIAID-CNMC Pediatric Allergy Immunology Fellowship Program
- Clinical trials program for novel food allergy immunotherapies



Novel Food Allergy Research at Children's National



Adora Lin, MD PhD

B cell responses to IL-10 and regulation of IgE/IgG4 production in peanut-allergic, sensitized and non-allergic children

Karen Robbins, MD

Nutritional implications of food allergy in children
Gastrointestinal and nutritional effects of early peanut introduction



Amaziah Coleman, MD

Access to food allergy care among underserved children
Racial differences in food allergy morbidity and burden

Linda Herbert, PhD

Identification of factors affecting psychosocial functioning and adherence in children and adolescents with food allergy



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Safety and efficacy of early peanut introduction to high-risk, peanut-sensitized infants

Will Sheehan, MD

Relationship of home environmental peanut exposure to pediatric asthma morbidity



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