Early Allergen Introduction & Prevention of Food Allergy

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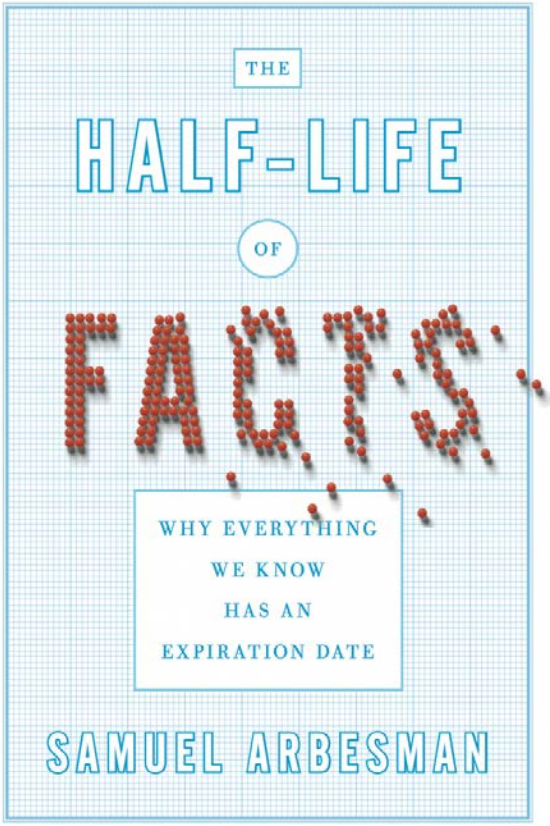
Discussion Objectives

- 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*

The Short Half-Life of Medical Knowledge

- Medical knowledge is always evolving - half-life of just 5-7 years!!
- Current evidence has limitations, and drawing incorrect conclusions from current knowledge can have adverse consequences
- Importance of staying up to date with events like Future of Pediatrics!



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!

Learning **E**arly **A**bout **P**eanut Allergy

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

George Du Toit, M.B., B.Ch., Graham Roberts, D.M., Peter H. Sayre, M.D., Ph.D., Henry T. Bahnson, M.P.H., Suzana Radulovic, M.D., Alexandra F. Santos, M.D., 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., Michelle L. Sever, M.S.P.H., Ph.D., Margarita Gomez Lorenzo, M.D., Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the LEAP Study Team*

Du Toit. NEJM 2015; 372: 803.

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

Du Toit. JACI 2008; 122: 984.

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

LEAP Study Design: Further Definition of "High Risk"

Egg allergy: Children with either –

1) a SPT wheal diameter ≥6 mm from exposure to raw hen's egg white and no history of previous egg tolerance,

or

2) a SPT wheal diameter ≥3 mm from exposure to pasteurized hen's egg white and allergic symptoms related to exposure to hen's egg.

Severe eczema: An eczematous rash that –

1) requires the application of topical creams and/or ointments containing corticosteroids or calcineurin inhibitors, and if the participant is <6 months of age, lasted for at least 12 out of 30 days on two occasions, or if >6 months of age, lasted for at least 12 out of 30 days on two occasions in the last 6 months

or

2) is currently or was previously graded ≥ 40 using the modified SCORAD evaluation

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

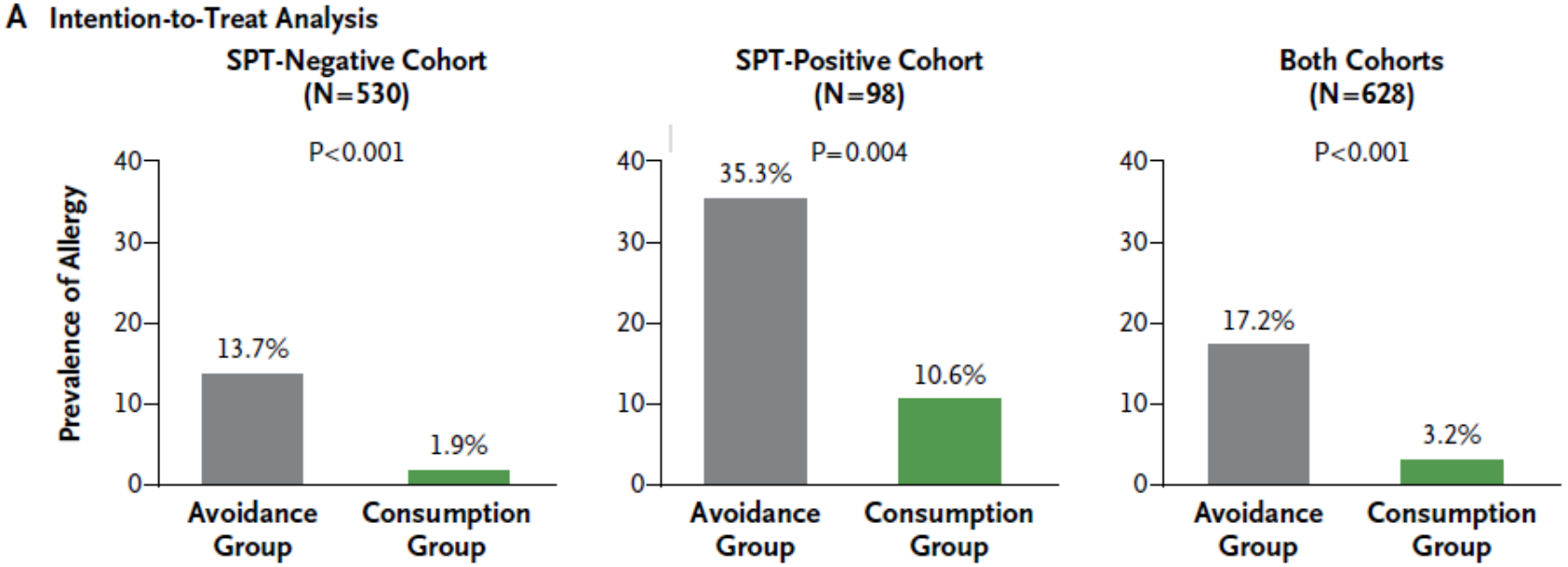
- Smooth peanut butter (1 teaspoon) mixed with milk or with mashed or pureed fruit
- Bamba snack* (Osem; approximately two thirds of a 1-oz (25 g) bag; 21 sticks of Bamba)
  - For young infants (<7 months), softened with 20 to 30 mL water or milk and mixed with milk or with mashed or pureed fruit or 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



	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 Trial Results

- Peanut consumption by infants was feasible
  - Adherence = 92%
- Similar results by Race:
  - Subgroup analysis showed similar results in White, Black and South Asian children
- Safety:
  - No deaths
  - Similar safety outcomes between consumption and avoidance groups
  - Risk of food challenge was low – only 7/319 children randomized to the consumption group reacted to peanut at the baseline food challenge → peanut food challenge and introduction, even in minimally SPT positive infants, are safe and feasible
- 6/320 children in the consumption group still developed peanut allergy → peanut allergy can still develop even with attempts to introduce early

LEAP Trial Implications

- *Early introduction of peanut significantly reduces the risk of peanut allergy up to 80% in high-risk children*
- *Prevention of peanut allergy has significant health care cost implications*
  - *Cost of food allergy = $4184 per year per child!*

Table 5. Comparison of WTP and Total Reported Costs

	Annual Costs, US$			
			95% CI	
Characteristic	Total (in Billions)	Per Child	Total (in Billions)	Per Child
WTP[a]	20.8	3504	15.7-25.7	2652-4344
Total costs borne by families	20.5	3457	16.7-24.9	2816-4208
Out-of-pocket costs for treatment[b]	5.5	931	4.7-6.4	793-1080
Lost labor productivity	0.77	130	0.53-1.00	89-175
Opportunity costs[b,c]	14.2	2399	10.5-18.4	1771-3104
Total direct medical costs	4.3	724	2.8-6.3	472-1063
Total reported costs	24.8	4184	20.6-29.4	3475-4960

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

- New Update to NIAID Food Allergy Guidelines coming soon

Remaining Questions… And Follow-up Studies

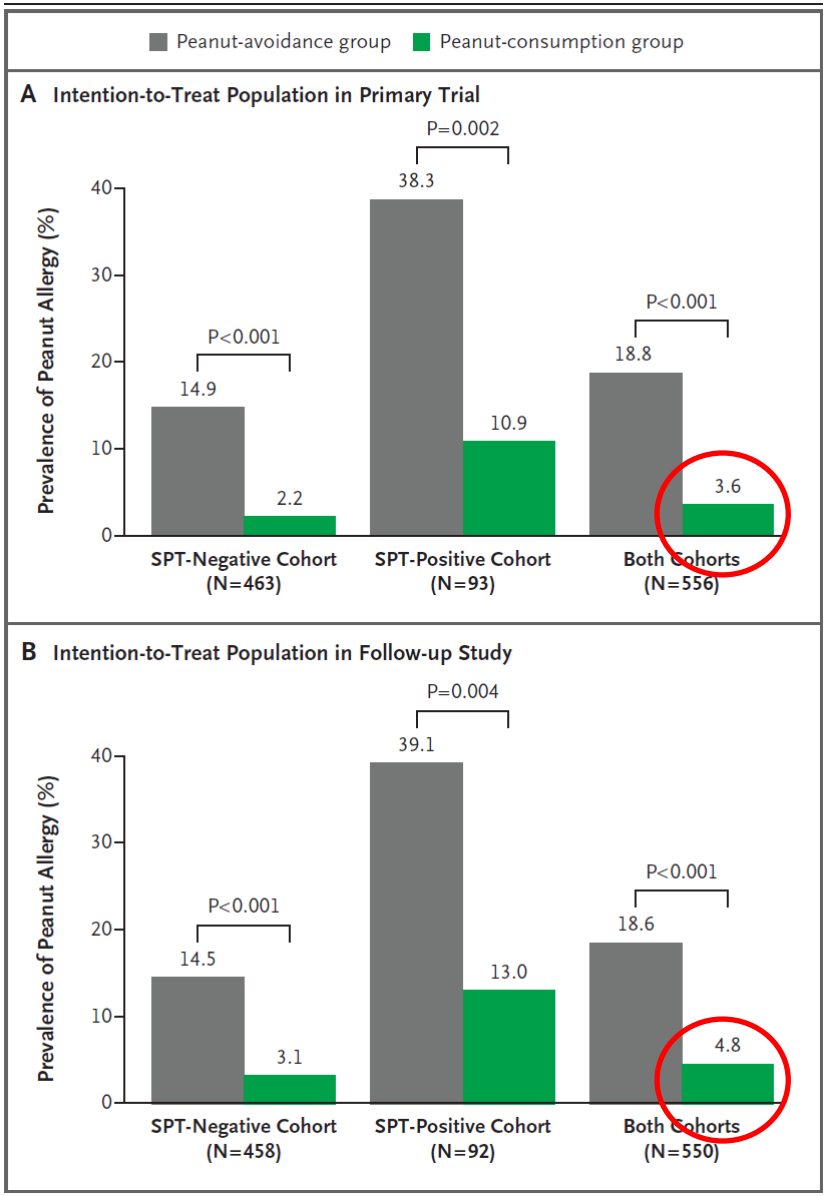
- *Questions:*
  - *Would different doses or length of peanut introduction affect the outcomes?*
  - ***What happens if peanut is stopped? → LEAP ON Study***
  - *Do the findings apply to infants at low risk for peanut allergy?*
  - ***What about food allergens other than peanut? → EAT Study***

LEAP-ON Trial:
Effect of Avoidance on Peanut Allergy after Early Peanut Consumption

- Purpose: To determine whether the rate of peanut allergy remained low after 12 months of peanut avoidance among participants who had consumed peanuts during the primary trial

- Population: 550 children from primary trial in consumption and avoidance groups
  - Avoidance of peanut from 5 to 6 years age
  - Peanut food challenge at 6 years age

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

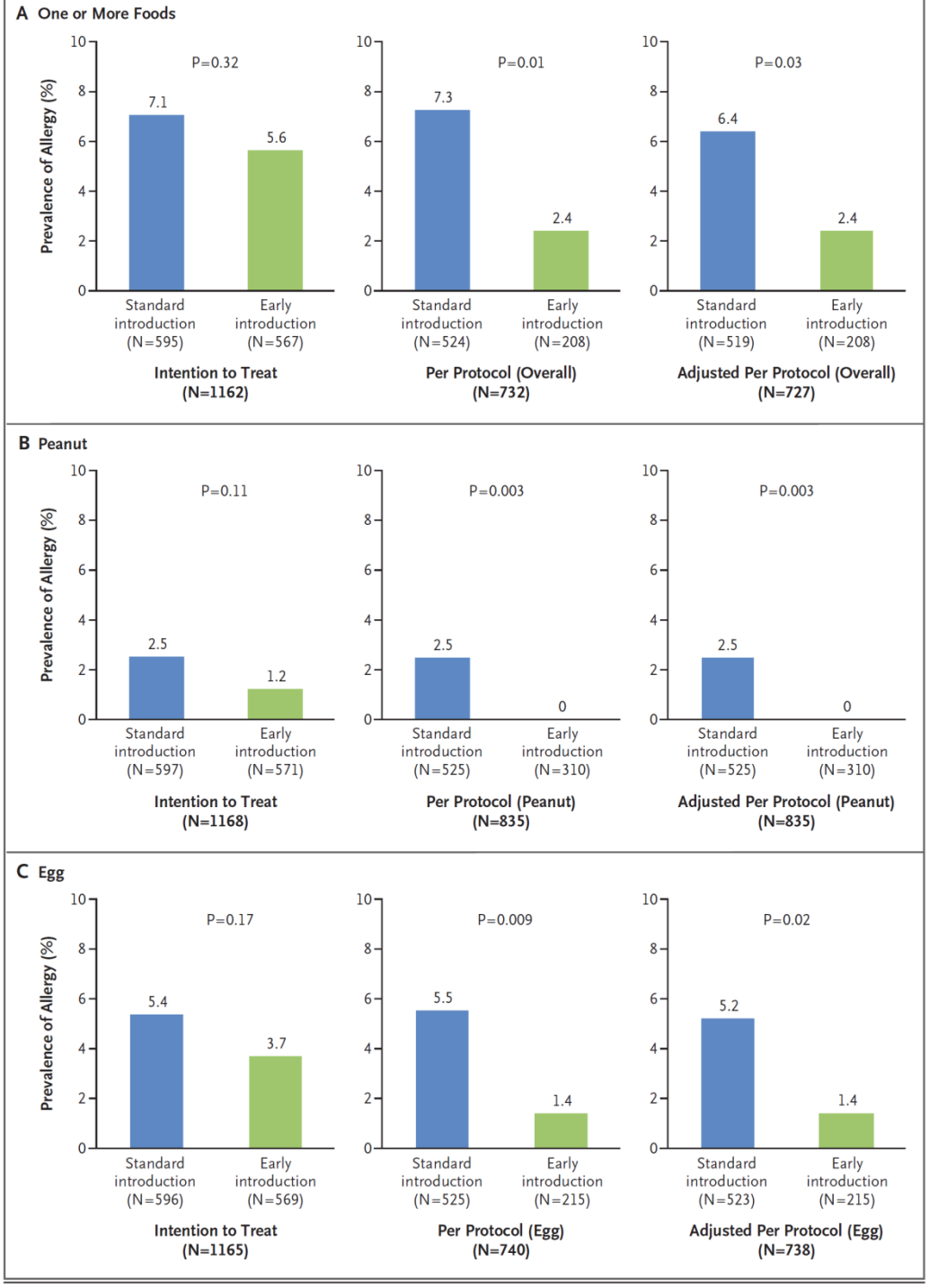
EAT (Enquiring About Tolerance) Trial: Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants

- 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



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*

Thank you!!

Children's National Health System