Eat Up, Baby! The Impact of Early Diet on Food Allergy Prevention

Presented by:
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November 2020

Today's Presenter

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Disclosure

General:

- Advisory board member to FARE

Provided and reviewed education material for:

- Danone
- Abbott
- Reckitt Benckiser Group
- DBV Technologies

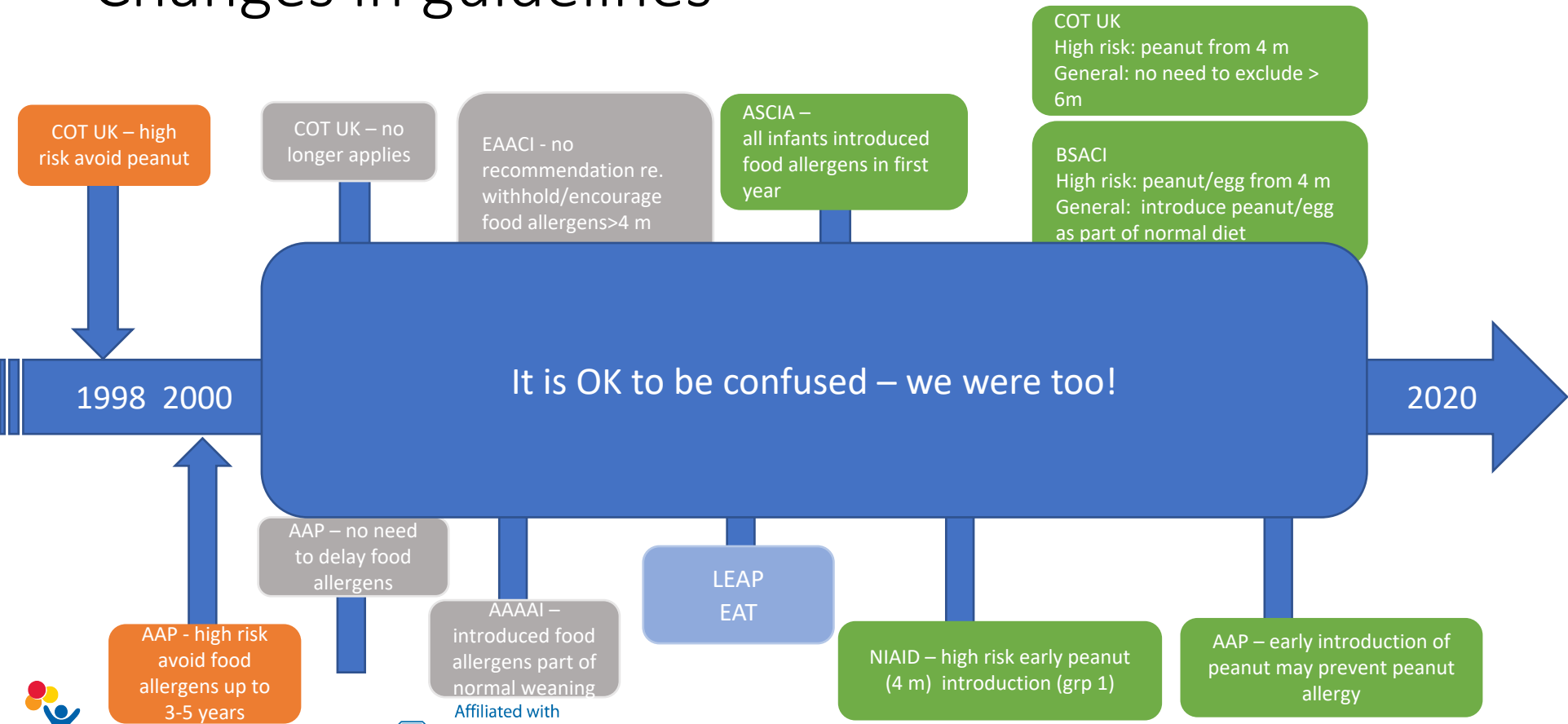
Research support:

- Reckitt Benckiser Group
- National Peanut Board US

Objectives

- To provide an overview of current guidelines (and their evolution) for food allergy prevention
- Another “U-turn”
  - Breastfeeding and concurrent allergen introduction
- What is new?
  - Diet diversity
  - Diet indices
- A few remaining questions regarding food allergen introduction in infancy

Changes in guidelines



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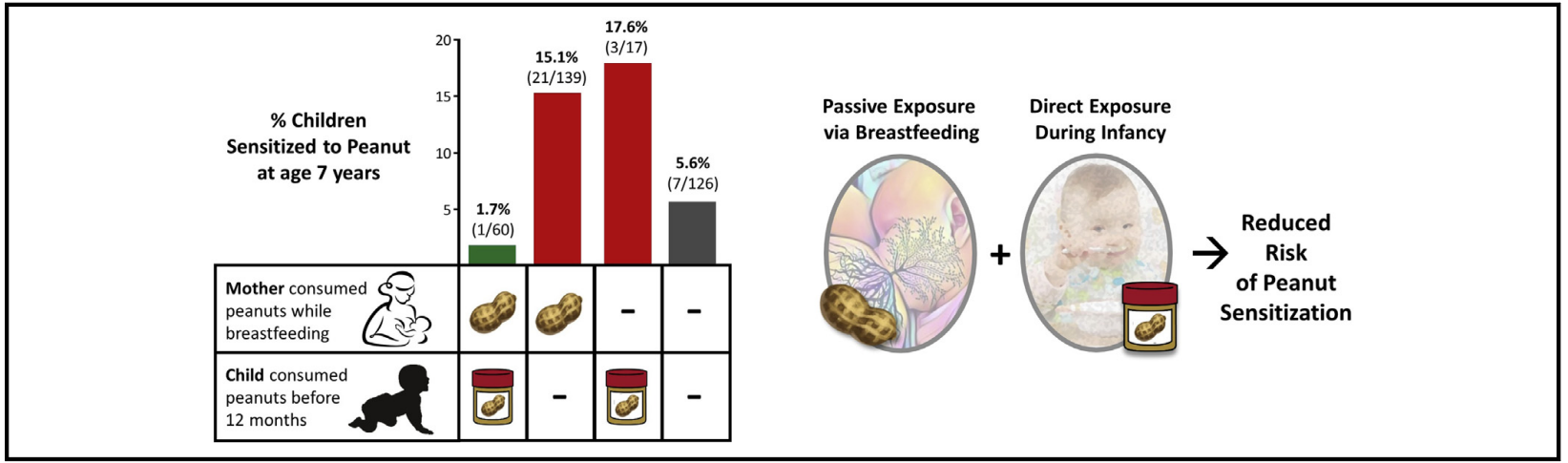
Shroer, Groetch, Mack, Venter https://www.jaci-inpractice.org/article/S2213-2198(20)31182-X/abstract

Breastfeeding and early introduction

GRAPHICAL ABSTRACT



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Pitt TJ et al. J Allergy Clin Immunol. 2018;141(2):620-5 e1

One study showing that introducing cow's milk while breastfeeding prevents ALL food allergies

Another study showing that is it not the case….

There is no need to feel guilty…

- Southampton UK: Introduction of cow's milk while breast feeding significantly reduce ALL food ies
- Wight UK: Introduction of cow's milk while breast feeding significantly reduce ALL food allergies

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Venter C, et al. J Nutr Sci. 2016;5:e40.

Grimshaw K, et al. Pediatrics. 2013;132(6):e1529-38

Definitions

- Dietary diversity: can be defined as the number of different foods or food groups consumed over a given reference period.

- Dietary quality: no official definition in the literature. Definitions vary widely, and many different measurement tools are used. Diet quality may reflect nutrient adequacy, but this is not always the case (use of a diet index, e.g., Mediterranean diet index)

Venter C et al. *Allergy.* 2020;75(3):497-523.

What does diet diversity mean in relation to allergy outcomes?

EAACI position paper on diet diversity in pregnancy, infancy and childhood: Novel concepts and implications for studies in allergy and asthma

Carina Venter, Matthew Greenhawt, Rosan W. Meyer, Carlo Agostoni, Imke Reese , George du Toit, Mary Feeney, Kate Maslin, Bright I. Nwaru, Caroline Roduit, Eva Untersmayr, Berber Vlieg-Boerstra, Isabella Pali-Schöll, Graham C. Roberts, Peter Smith, Cezmi A. Akdis, Ioana Agache, Miriam Ben-Adallah, Stephan Bischoff, Remo Frei, Holger Garn, Kate Grimshaw, Karin Hoffmann-Sommergruber, Nonhlanhla Lunjani, Antonella Muraro, Lars K. Poulsen, Harald Renz, Milena Sokolowska, Catherine Stanton, Liam O'Mahony

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Venter C et al. Novel concepts and implications for studies in allergy and asthma. *Allergy*. 2020;75(3):497-523.

Diet diversity (DD) in infancy vs. allergy outcomes

Allergy outcome	Increased risk with higher DD	Reduced risk with higher DD	No effect
Sensitization		+ (4.5 yrs) [food + (6 yrs) [food] + (up to 15 yrs) [aero-allergens] +(yrs 5)	+ (4.5 yrs) [inhalant] + (6 yrs) [inhalant]
Food Allergy		**+ (up to 6 yrs)**	
Atopic Dermatitis (eczema)	+(2 yrs) + (6 yrs) + (2 yrs) + (3 yrs) + (10 yrs)	+ (2 yrs) + (1 yr) + (5 yrs) + (4 yrs) +(2 yrs)	+ (4 yrs) + (6 yrs)
Asthma/Wheeze		+ (6 yrs) + (5 yrs)	
Rhinitis (seasonal allergies/hay fever)		+ (5 yrs)	+(6yrs)

Venter C et al. *Allergy*. 2020;75(3):497-523.

The association between four different measures of DD during infancy and development of FA over the first 10 years of life

DD was defined using four measures:

1) the WHO definition of minimum diet diversity at 6 m;

2) number of foods introduced: food diversity (FD) at 3, 6 and 9 m;

3) number of food allergens introduced: food allergen diversity (FAD) at 3, 6, 9 and 12 m; and

4) number of fruit and vegetables introduced: fruit and vegetable diversity (FVD) at 3, 6 and 9 m.

Venter C et al. *J Allergy Clin Immunol Pract* 2020; 8(6):2017 – 2026

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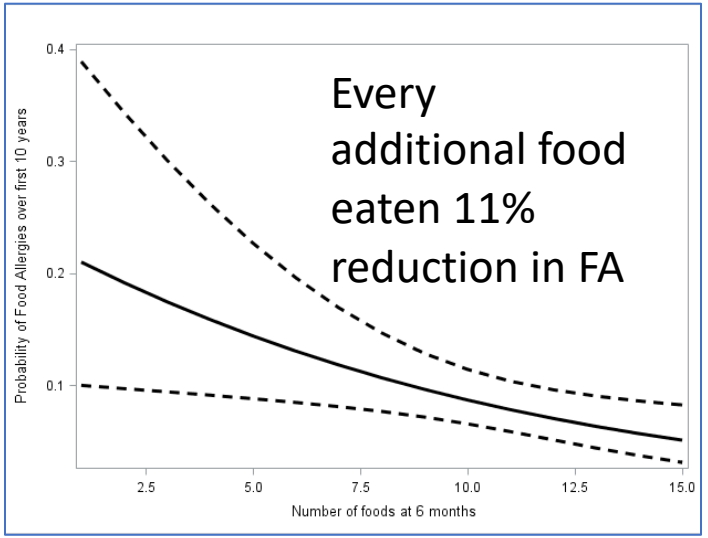
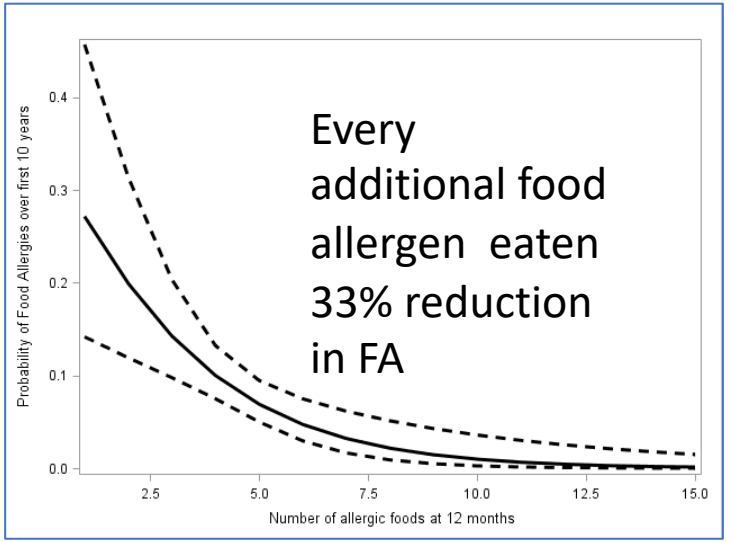
Food Diversity at 6 months/food allergen diversity at 12 months vs. food allergy





- Multivariate analysis showed that food diversity at 6 m (p=0.0111) and FAD at 12 m (p=0.0005) significantly reduced the odds of food allergy over first 10 years

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Venter C et al. *J Allergy Clin Immunol Pract.* 2020; 8(6):2017 – 2026

Just how many foods did the babies eat?

Age range	Median WHO DD score (IQR, minimum – maximum)	Median Food DD score (IQR, minimum – maximum	Median FAD score (IQR, minimum – maximum	Median FVD score (IQR, minimum-maximum
By 3 months*	NA	0 (0, 0-15)	0 (0, 0-3)	0 (0, 0-4)
By 6 months*	5 (3-4; 0-5)	11 (9-13, 0-21)	2 (2-3; 0 -6)	3 (3-4, 0-5)
By 9 months*	NA	16 (14 – 17; 5-21)	4 (1-8; 3-4)	5 (4-5, 1-5)
By 12 months**	NA	NA	5 (4-6; 0-8)	NA

Warren CM, et al. *J Allergy Clin Immunol Pract.* 2020; 8(6):2017 – 2026

Association between food allergy outcomes, family history of allergic disease, maternal history of allergic disease, maternal history of food allergy, parity and eczema in the first year of life

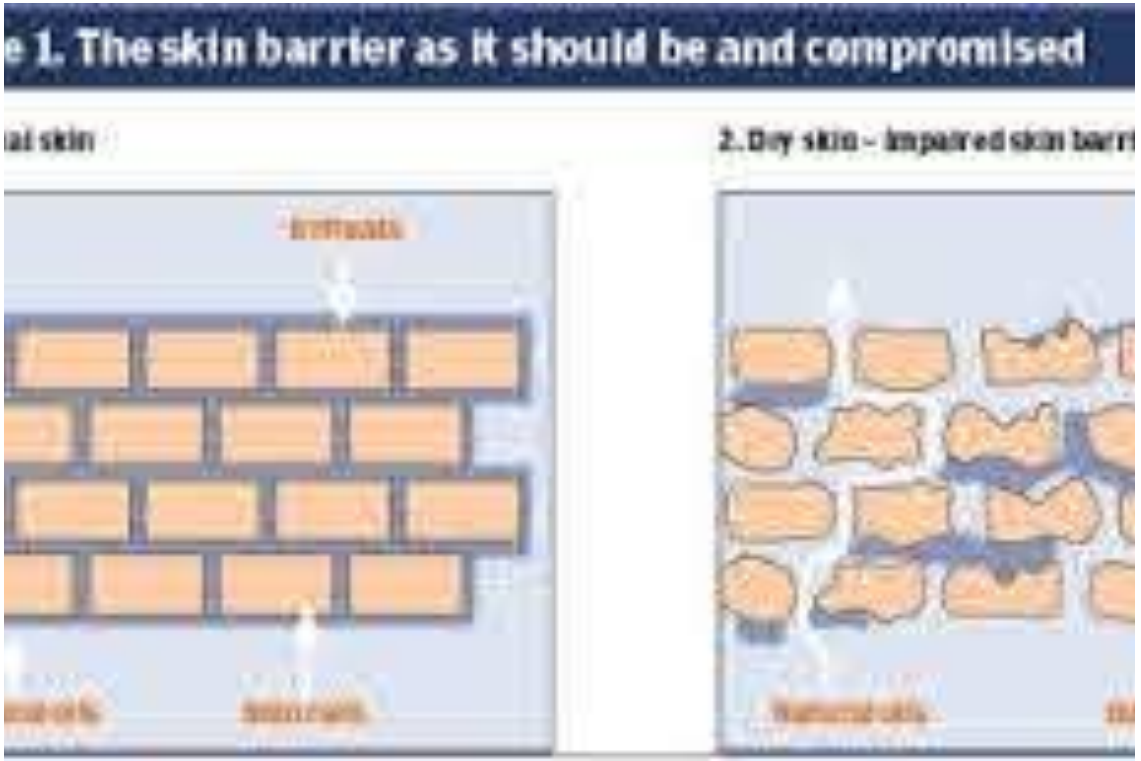
Demographic factor	Association with food allergy in the child
Family history of allergic disease	No
Maternal history of allergic disease	No
Maternal history of FA	YES At 10 years: 3.06 (1.4 - 6.5); p=0.004
Parity	No
Breastfeeding duration (days)	No
Age of introduction of solid foods (weeks)	YES Over the first 10 years: 1.16 (1.1- 1.3); p = 0.002
Any eczema in first year of life	YES Over the first 10 years: 2.82 (1.5 - 5.5); p =0.002

Vazquez-Ortiz M, et al. *J Allergy Clin Immunol Pract.* 2020; 8(6):2017 – 2026

Other factors of interest

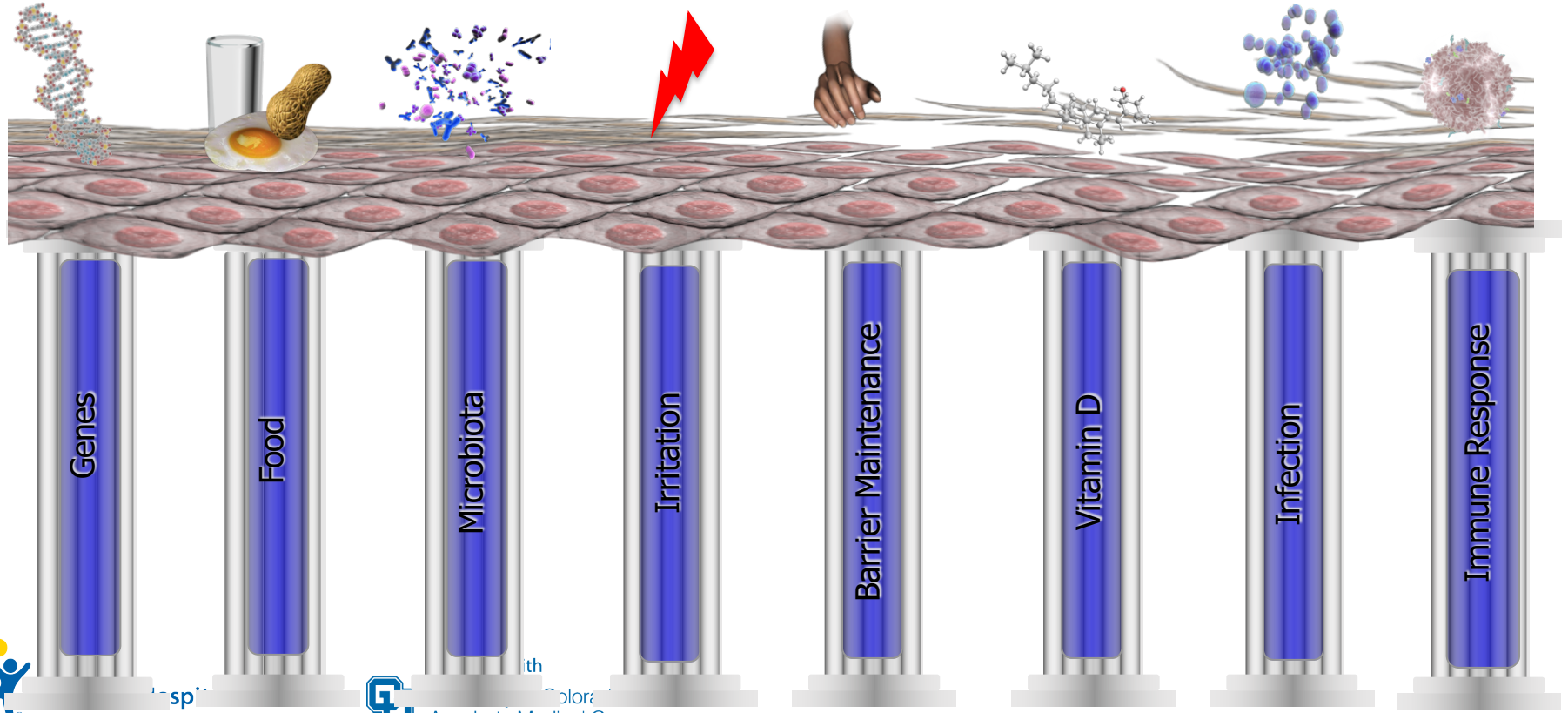
Factor	Association
Did eczema lead to delayed introduction of solid foods?	No (14.9 vs. 15 weeks)
Did eczema lead to fewer allergens introduced by 1 year?	Negative association (p=0.04) i.e. having eczema did not reduce number of food allergens introduced.
Is the filaggrin loss-of-function mutation associated with increased food allergy outcomes?	YES (4 times more likely to have a food allergy)
Is the filaggrin loss-of-function mutation associated with increased eczema outcomes?	No (underpowered)

Venter C et al. *J Allergy Clin Immunol Pract.* 2020; 8(6):2017 – 2026



Loss-of-function mutations within the filaggrin gene (FLG-LOF) lead to reduced protein expression resulting in epidermal barrier dysfunction, making the skin more permeable to environmental allergens and increasing trans-epidermal water loss. If those same food proteins enter the body through a broken skin barrier due to eczema, the signaling to the immune system says, “These proteins are in the wrong place,” so that the immune system learns to defend against those proteins, and that’s what an allergic reaction is.

Pillars of Atopic Dermatitis



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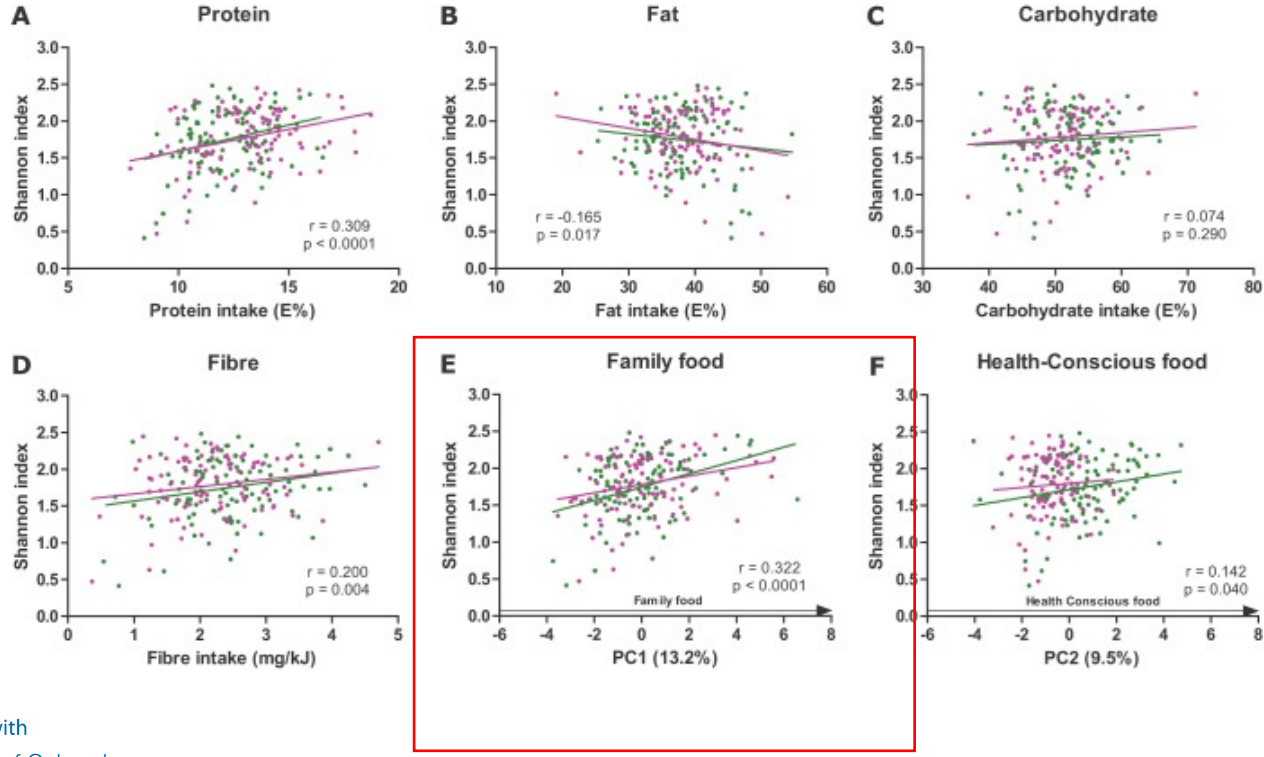
Source: Prof Pete Smith

Diet diversity in infancy and infant microbiome

The transition to family foods with higher protein and fiber content correlates with increased gut microbiota diversity.



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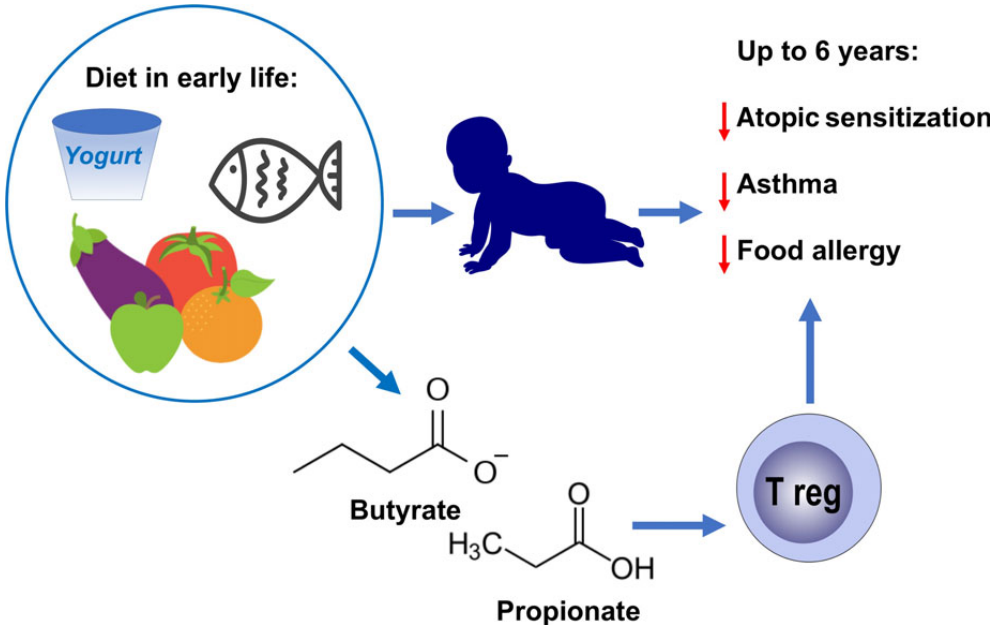
Laursen et al. mSphere. 2016;1(1).

Early life diet increases butyrate production



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Should we just eat ghee?

Mukkada 2010; Furuta 2018

Barriers to diet diversity

- Prolonging time between new foods may negatively affect diet diversity, which has been shown to affect food allergy outcomes
- From a recent paper by Ruchi Gupta's group in JAMA Network Open: *Out of 563 pediatric practitioners, 217 (39%) recommended waiting 3 days or longer before introducing new foods; however, for infants at risk for developing food allergy, 259 (66%) recommended waiting.*
- Although the American Academy of Pediatrics and the Centers for Disease Control and Prevention recommend waiting 3 to 5 days between the introduction of new complementary foods (solid foods introduced to infants <12 months of age), with advances in the understanding of infant food diversity, **these may need to be reviewed.**

Samady W. *JAMA Netw Open.* 2020;3(8):e2013070.

Results Sixty-five per cent of mothers had avoided peanuts during pregnancy. Forty-two per cent of the mothers had heard about the government advice, and half modified their diet as a consequence. Neither maternal nor family history of atopy had any significant effect on peanut consumption. Parity did play a role, and mothers having their first child were twice as likely to change their diet ($P < 0.001$). Mothers of 77% of the children sensitized to peanuts had avoided peanuts during pregnancy. In this cohort study maternal consumption of peanut during pregnancy was not associated with peanut sensitization in the infant.

	Unadjusted		Adjusted	
Exposure (predictor)	OR (CI)	*P*-value	OR (CI)	*P*-value
First child	2.03 (1.42–2.92)	<0.001	1.97 (1.37–2.84)	<0.001
Maternal atopy	0.92 (0.65–1.29)	0.615	0.92 (0.65–1.30)	0.639
Paternal atopy	1.10 (0.78–1.55)	0.598	1.04 (0.73–1.48)	0.820

RESEARCH PAPER

Government advice on peanut avoidance during pregnancy – is it followed correctly and what is the impact on sensitization?

T. Dean,*† C. Venter,*† B. Pereira,* J. Grundy,* C. B. Clayton* & B. Higgins†

*The David Hide Asthma and Allergy Research Centre, St Mary's Hospital, Newport, Isle of Wight, UK; †School of Health Sciences and Social Work, University of Portsmouth, Portsmouth, UK

When public health messages go wrong...

- Dean T, Venter C, et al. *J Hum Nutr Diet.* 2007;20(2):95-99.

In the U.S.

- Recent research shows that only 30% of pediatricians fully implemented the NIAID guidelines on food allergy prevention
- 1781 pediatricians were surveyed between June 1, 2018, and December 1, 2018
- 93% of pediatricians reported being aware of the guidelines
- Yet only 30% reported full implementation and 1105 64% reported partial implementation
- Common barriers included
  - parental concerns about allergic reactions – about 33%
  - uncertainty in understanding and correctly applying the guidelines – 33%
  - conducting in-office supervised feedings – 32%
  - BUT 65% (two thirds) of pediatricians **reported a need for further training** on the guidelines.

Johnson JL, Gupta RS, Blaiser LA, et al *J Allergy Clin Immunol*. 2020;146(4):875-883.

CLINICAL COMMENTARY REVIEW | ARTICLES IN PRESS

Practical challenges and considerations for early introduction of potential food allergens for prevention of food allergy

Brian Schroer, MD • Marion Groetch, MS, RDN • Douglas P. Mack, MSc, MD • Carina Venter, PhD RD

Published: October 27, 2020 • DOI: https://doi.org/10.1016/j.jaip.2020.10.031

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https://www.jaci-inpractice.org/article/S2213-2198(20)31182-X/abstract

Practical implication of the U.S. Department of Agriculture draft guidelines

- 4-6 months: 1 g in total per week for 4 allergens OR 2 g per week for 2 allergens
- 7-8 months: 2 g in total per week for 7 allergens or 2 g per week for 2 allergens and then 1 g per week for 5 allergens
- 9-12 months: 2 g in total per week for 7 allergens or 2 g per week for 2 allergens and then 1 g per week for 5 allergens

Mukkada 2010; Furuta 2018

Let the babies eat!

Mukkada 2010; Furuta 2018

Introducing allergens – Peanut

Food	Choose healthy infant foods	How much/how often (based on allergy/healthy eating guidelines)
Peanut	Choose peanut flour or thinned peanut butter that has no added ingredients (salt, sugar, oils) for the healthier options! Peanut butter should be thinned with breast milk, water or formula or mixed into a pureed food, e.g., 2 tsp of peanut butter mixed with 2-3 tsp liquid.	About 1-2 teaspoons peanut butter/powder per serving, served 2-3 times per week as tolerated

Shroer, Groetch, Mack, Venter accepted JACI IP 2020

https://www.niaid.nih.gov/diseases-conditions/guidelines-clinicians-and-patients-food-allergy

Introducing allergens – Egg

Food	Choose healthy infant foods	How much/how often (based on allergy/healthy eating guidelines)
Egg	Egg should be **well-cooked**, e.g., boiled or scrambled until no visible liquid remains. Serve eggs mashed with pureed foods or chopped and served as finger foods.	About 1/3 of a well-cooked egg, 2 times per week

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Introducing allergens - Other

Food	Choose healthy infant foods	How much/how often (based on healthy eating guidelines)
Wheat	Infant iron-fortified wheat cereals; whole wheat toast, pasta or crackers for older infants	½- 1 ounce total grains per day. ½ ounce wheat serving includes: ¼ cup fortified infant wheat cereal, ¼ cup pasta, ½ slice bread
Sesame	Tahini is sesame paste typically served as an ingredient in hummus or as tahini dipping sauce for finger foods like vegetables (blended with water, lemon juice, olive oil, and herbs for flavoring).	> or = ½ ounce seeds/any nuts per week (or 3 teaspoons)
Cow's Milk	Plain, full-fat yogurt can be mixed into pureed fruit or vegetable; cow's milk should not substitute for breast milk or infant formula.	2-4 fluid ounces per day

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Introducing allergens - Other

Food	Choose healthy infant foods	How much/how often (based on healthy eating guidelines)
Seafood	Cooked shrimp, lobster, crab – modified to appropriate infant texture Low-mercury finfish	1 ounce per serving, 3 times per week (See U.S. Food and Drug Administration link for frequency and type of fish; varies between countries)
Tree nuts	e.g., Almond, cashew, hazelnut, pistachio, walnut-smooth, thinned nut butters	> or = ½ ounce seeds/any nut per week (or 3 teaspoons)
Soy	Soft tofu	4 tablespoons per serving as part of protein recommendations

Once in – keep it in…

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Tree nut butter…can be a seed and nut butter…suggested home-made recipes

Nut (Total g wt per nut)	Gram of protein per nut	2 grams protein per serving
Almond (1.2 g)	0.254	8 nuts (2.032 g)
Peanut (0.9g)	0.219	9 kernels (1.917
Cashew (app. 1.5 g)	0.273	8 (Whole nuts 2.1 g)
Pistachio (0.7 g)	0.141	14 nuts (1.974 g)
Macadamia (2.6 g)	0.202	10 nuts (2.02 g)
Brazil nut (5 g)	0.716	3 nuts (2.139 g)
Walnut (4g whole = 2 halves)	0.609	3.5 whole or 7 halves (2.13 g)
Pecan (4 g whole = 2 halves)	0.348	6 whole or 7 halves (2.088)
Hazelnut (app 1.4 g)	0.234	9 nuts (2.11 g)
https://ndb.nal.usda.gov/		
4 types of nuts (approx. 1/3 cup) plus 2 tablespoons of oil – grind and mix with blender 9 types of nuts (almost 1 cup) plus 4 tablespoons of any type of oil – grind and mix with blender Keep in fridge and eat as is or mix with any preferred food such as applesauce or yogurt. Oil will separate from nut butter during storage; mix well before using.		

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Problems with adherence

- In the Enquire About Tolerance (EAT) study, a qualitative analysis of the parental reporting of problems feeding their infant the allergenic foods identified three main themes:
  - infant refusal (swallowing issues, dislike of the taste and infant illness)
  - concerns about reactions (digestive or skin issues and actual allergy)
  - practical problems (lifestyle convenience and food preparation issues)

Voorheis P, Bell S, Cornelsen L, Quaife M, Logan K, Marrs T, et al. Challenges experienced with early introduction and sustained consumption of allergenic foods in the Enquiring About Tolerance (EAT) study: A qualitative analysis. J Allergy Clin Immunol. 2019;144(6):1615-23.)

Home-cooked foods

Food	Serving	Calories	Protein (g)	Fat (g)	Added Sugar (g)	Sodium (mg)	Cost per 4 weeks (USD)
Egg- hard boiled, well-cooked scrambled	1/3 egg	24.8	2.08	1.67	0	21.6	Large organic eggs $3.49 Conventional eggs $1.18 portions of 3 eggs per week/4 weeks
Peanut butter national brand	1 teaspoon	32	1.17	2.67	0.5	23	$0.44 3 teaspoons per week/4 weeks
Peanut butter "healthy" brand (just ground peanuts)	1 teaspoon	33	1.33	2.67	0	15	$0.52 3 teaspoons per week/4 weeks
Powdered peanut butters (e.g., PB2)	1 teaspoon	10	1.0	<0.5	<0.5	15	$0.86 3 teaspoons per week/4 weeks
Bamba	0.35 ounce (about 10 sticks)	55	1.0	3.5	0.5 g	40	$5.25 3 servings per week/4 weeks

Shroer, Groetch, Mack, Venter accepted JACHP 2023

Points to consider – so many new commercial options!

Features	Commercial	Conventional
Cost	More expensive	Less expensive
Convenience	More convenient for families spending little time preparing foods	Can be convenient to families cooking and preparing most of their meals
Additional ingredients	These foods can act as food allergens too	Ability to use a pure source of the food allergen only
Nutritional composition	Generally low in calories and lacking a wider nutritional profile	Rich sources of other nutrients
Dose of food allergen	Some products contain far less food allergen compared to doses used in research and those recommended by international guidelines	A desired dose can be chosen from allergen-containing foods
Degree of heating	Degree of heating/cooking of the allergen may be not similar to those used in research and those recommended by international guidelines	A desired degree of cooking/heating can be chosen from allergen-containing foods

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Summary

Diet intake	Outcome
Guidelines keep changing	They all agree – let the babies eat! No reason to withhold or delay allergens
Practical dilemmas for food allergen introduction	When infant is developmentally ready. Take randomized controlled trial outcomes and general guidance on introduction of solid foods into account.
Diet diversity in infancy and allergy outcomes	Associations with reduced food allergy promising

Question & Answer

Thank you!