

INFANT FEEDING & ALLERGY PREVENTION

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SAFFA Study



Disclosure

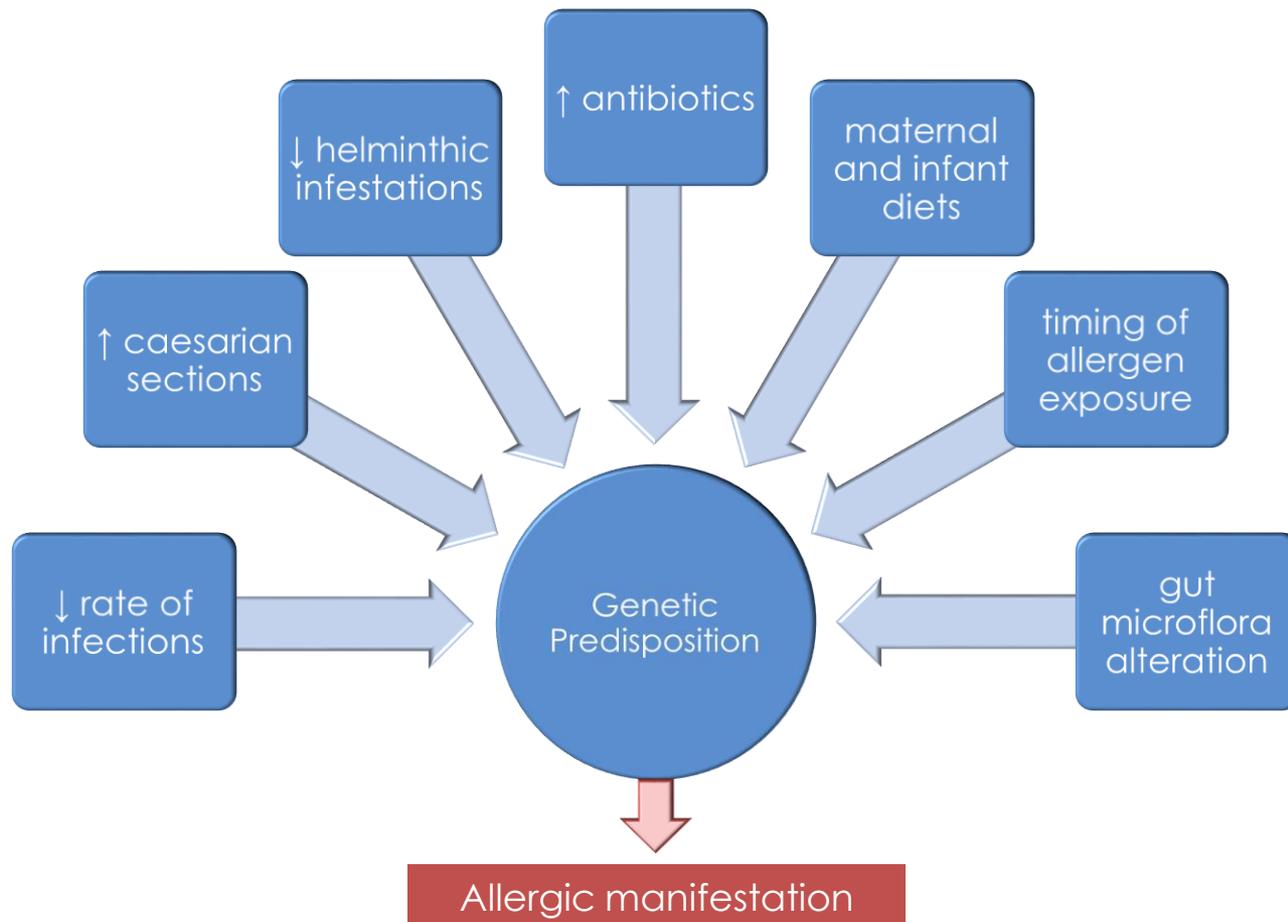
In relation to this presentation, I declare that there are no conflicts of interest.

Aims of this talk

INFANT FEEDING & ALLERGY PREVENTION

1. Review the research literature
2. Considerations for clinical practice

Food allergy prevalence on the rise



Allergy Prevention & Infant Feeding

- Breastfeeding
- Early Introduction of allergenic foods
- Micronutrients e.g. vitamin D
- Hypoallergenic infant formula
- Prebiotics and probiotics

RESEARCH

Allergenic Food Avoidance

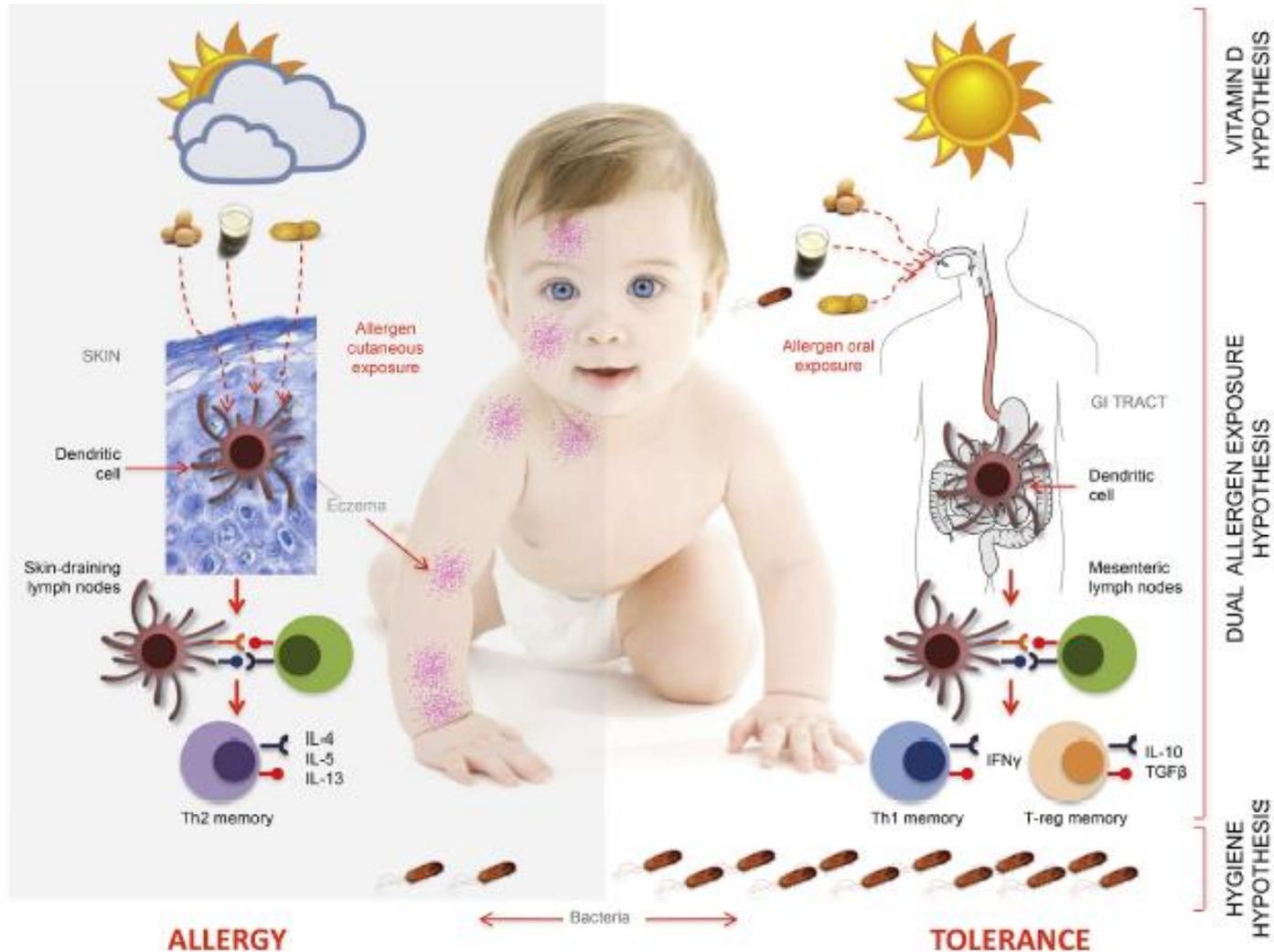
Allergenic Food Avoidance originally advised

- Allergen Exposure => Immunological sensitisation
- Avoidance strategies in pregnancy and infancy
- Until 1990s – national & regional guidelines

Delaying No Longer Advised

- Acquiring tolerance is an active process
- EAACI (2014): *“Current evidence does not justify any recommendations about either withholding or encouraging exposure to potentially allergenic foods after 4 months once weaning has commenced”*

Allergy vs. Tolerance *(Du Toit et al. 2017)*



Observational Studies - Fish



EARLY INTRODUCTION OF FISH

Kull *et al.* (2006)

- A prospective birth cohort of 4089 new-born infants followed for 4 years
- Regular fish consumption during the first year of life was associated with a reduced risk for allergic disease by age 4, OR(adj) 0.76 (95% CI 0.61-0.94) and sensitization, OR(adj) 0.76 (0.58-1.0)

Alm *et al.* (2008)

- Prospective, longitudinal cohort study of infants born in western Sweden in 2003 - 8176 families were randomly selected
- Introducing fish before 9 months of age decreased the risk of eczema at age 1 year (OR 0.76; 95% CI 0.62 to 0.94)

Observational Study - Peanuts

Observational studies cannot determine causality

Randomised Controlled Trials are needed to assess causal relationship between early consumption & allergy development



Early introduction of peanuts into the diet may induce long term tolerance

Observational Study - Hen's Egg



HealthNuts - Koplin *et al.* (2010)

- **Australian cohort** of more than 2500 infants
- **Delaying introduction of egg after 12 months of age** (adjusted odds ratio, 3.4; 95% CI, 1.8-6.5) was **associated with significantly higher risk of egg allergy** compared with earlier introduction at 4 to 6 months of age.

RCTs - Hen's Egg



- **Several RCTs** looking at the early introduction of egg from 4-6 months.
- **Similar designs**
 - Pasteurized raw egg powder
 - Placebo is rice powder
 - The outcome measure was the prevalence of IgE-mediated egg allergy at 12 months of age
- **Different infant population groups** at varying levels of allergy risk



Trial	Population	Study	Outcome
Solids Timing for Allergy Research (STAR) <i>Palmer et al. (2013)</i> Australia	<ul style="list-style-type: none"> ▶ High risk (infants with moderate/severe eczema) ▶ n=86 ▶ Enrolled 4–6 months 	<ul style="list-style-type: none"> ▶ RCT, placebo controlled (consumption of egg powder or placebo until 8 months) ▶ Cooked egg 8-12 mo 	<ul style="list-style-type: none"> ▶ Prevalence of IgE mediated egg allergy at 12 months

- At 12 months, **a lower (but not significant) proportion** of infants in the egg group (33%) were given a diagnosis of IgE-mediated egg allergy compared with the control group (51%) (relative risk, 0.65; 95% CI, 0.38-1.11; $P = 0.11$).
- **Significant adverse events** 31% of infants reacted to the egg powder
- **Already sensitised** - At 4 months of age, before any known egg ingestion, 36% had egg specific IgE levels >0.35 (kUA)/L.

Trial	Population	Study	Outcome
Starting Time for Egg Protein (STEP) <i>Palmer et al. (2016)</i> Australia	<ul style="list-style-type: none"> ▶ Moderate risk (infants without eczema but atopic mothers) ▶ n=820 	<ul style="list-style-type: none"> ▶ RCT, placebo controlled ▶ 4–6 months of age ▶ Consumption of egg powder or placebo until 12 months of age 	<ul style="list-style-type: none"> ▶ Prevalence of IgE mediated egg allergy at 12 months of age

There was **no difference** between groups (**for infants without eczema**) in the percentage of infants with IgE-mediated egg allergy (egg 7.0% vs control 10.3%; adjusted relative risk, 0.75; 95% CI, 0.48-1.17; $P = 0.20$)



Trial	Population	Study	Outcome
Hen's Egg Allergy Prevention (HEAP) Bellach <i>et al</i> (2016), Germany	<ul style="list-style-type: none">▶ General population▶ n~800	<ul style="list-style-type: none">▶ RCT, placebo controlled▶ Enrolled at 4–6 months then consumption of egg powder or placebo until 12 months of age	Prevalence of IgE mediated egg allergy at 12 months of age

- **No evidence** that consumption of hen's egg starting at 4 to 6 months of age prevents hen's egg sensitization or allergy.
- Some 4- to 6-month-old infants were **already allergic to hen's egg**.

Trial	Population	Study	Outcome
Beating Egg Allergy (BEAT) Wei-Liang Tan <i>et al</i> (2016), Australia	<ul style="list-style-type: none">▶ Moderate risk (sibling/parent with allergy)▶ n~290	<ul style="list-style-type: none">▶ RCT, placebo controlled▶ Enrolled at 4 months of age then consumption of egg powder or placebo until 8 months of age	<ul style="list-style-type: none">▶ Egg White sensitisation (SPT) response of 3 mm or greater at age 12 months.▶ Prevalence of IgE mediated egg allergy at 12 months of age

- **Sensitization to Egg White at 12 months** was 20% and 11% in infants randomized to placebo and egg, respectively (odds ratio, 0.46; 95% CI, 0.22-0.95; P = 0.03, x2 test).
- **8.5% of infants** randomized to egg were not amenable to this primary prevention.



Trial	Population	Study	Outcome
<p>Prevention of egg allergy in infants with atopic dermatitis (PETIT)</p> <p>Natsume <i>et al</i> (2016), Japan</p>	<ul style="list-style-type: none">▶ High risk (infants with atopic dermatitis)▶ n=120 Intention to Treat	<ul style="list-style-type: none">▶ DBPCRCT▶ Enrolled at 4–6 months then consumption of egg powder or placebo until 12 months	<ul style="list-style-type: none">▶ Prevalence of IgE mediated egg allergy at 12 months of age

- Randomization to heated egg powder at age 6 months was associated with a **significantly lower rate of egg allergy compared with placebo** until age 12 months (8% vs 38%; P = 0.0001)



SUMMARY

- Mixed results with early introduction of egg
- Different patient risk groups
- Type of egg
- How early is early?
- Identify a window of opportunity

Many more questions to answer...

Enquiring about Tolerance (EAT) Study (2016)

Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants

Michael R. Perkin, Ph.D., Kirsty Logan, Ph.D., Anna Tseng, R.D., Bunmi Raji, R.D., Salma Ayis, Ph.D., Janet Peacock, Ph.D., Helen Brough, Ph.D., Tom Marrs, B.M., B.S., Suzana Radulovic, M.D., Joanna Craven, M.P.H., Carsten Flohr, Ph.D., and Gideon Lack, M.B., B.Ch., for the EAT Study Team*

- **Early introduction (3 months) of common dietary allergens** in exclusively breast-fed infants vs. infants who were exclusively breast-fed for 6 months
- Given common dietary allergens – **Milk, egg, peanuts, sesame, wheat**
- In the **intention to treat analysis** (n=1132), there were no significant differences between the groups in the overall rates of developing any food allergy.
- **Per-protocol (n=732) analysis**, significantly fewer children developed any food allergy with introduction at 3 vs. 6 months (2.4% vs. 7.3%, p=0.01). Fewer children also developed egg allergy (1.4% vs. 5.5%, p=0.009) or peanut allergy (0% vs. 2.5%, p=0.003) with introduction at 3 vs. 6 months.
- The authors hypothesized that Food Allergy prevention through early introduction of allergenic foods may depend on **adherence and dosage**

The SAFFA Study

The South African Food Sensitisation and Food Allergy (SAFFA) Study



- A cross-sectional study to determine the prevalence of sensitization and challenge proven of IgE-mediated food allergy in a South African urban and rural population of 12-36 month olds.
- 1200 South African preschool children and 400 rural preschool children.
- An opportunity to gather data on current infant feeding practices of black African mothers, in rural and urban South African settings

SAFFA – Early Weaning

Age exclusively breastfed	Urban	Rural
Median (mths)	3.0 (0.5-6)	3.0 (1-6)

Age of solid introduction	Urban	Rural	p value
<4 mths	75/357 (21.0)	60/392 (15.3)	0.000
4-6 mths	232/357 (65.0)	218/392 (55.6)	
>6 mths	50/357 (14.0)	114/392 (29.1)	

SAFFA – Late introduction of Allergenic Foods

Median Age of Introduction

Food	Urban	Rural	p value
Egg	12 (8-12)	11 (8-12)	0.000
Peanuts	12 (12-18)	12 (8-12)	0.000
Cow's Milk	7 (6-10)	7 (6-9)	0.022
Tree nuts	18 (12-24)	12 (9-15)	0.000
Soy	12 (10-18)	8 (6-12)	0.000
Wheat	8 (6-12)	11 (7-12)	0.000
Fish	12 (12-18)	12 (9-13)	0.000

SAFFA – Exposure to Allergenic Foods

Food	Urban	Rural	p value
Egg	2.2%	6.4%	0.007
Peanuts	10.3%	53.1%	0.000
Cow's Milk	0.3%	0.8%	0.624
Tree nuts	76.6%	79.3%	0.366
Soy	21.2%	1.3%	0.000
Wheat	0.0%	1.8%	0.016
Fish	7.0%	29.1%	0.000

SAFFA - Unpublished data

CONSIDERATIONS FOR CLINICAL PRACTICE

Considerations for Clinical Practice



1. Guidelines
2. Applicability – SA population
3. Adherence to research principles
4. Nutritional implications
5. Dissemination of information

1. Fit with Existing Guidelines



- **World Health Organization (2002):** infants should be exclusively breastfed for the first six months (26 weeks) and they should receive nutritionally adequate and safe complementary foods while breastfeeding continues for up to two years of age
 - For improved public health and reduced gastrointestinal infections
 - Do not encapsulate guidance regarding allergy prevention
- **Other National Guidelines:** 4-6 months, after 6 months, up to the individual family

1. EAACI Guidelines (2014)

POSITION PAPER

EAACI Food Allergy and Anaphylaxis Guidelines. Primary prevention of food allergy

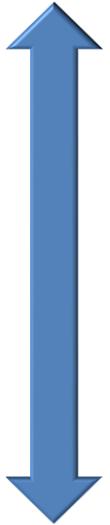
A. Muraro^{1,*}, S. Halken^{2,*}, S. H. Arshad^{3,4,5}, K. Beyer⁶, A. E. J. Dubois⁷, G. Du Toit⁸, P. A. Eigenmann⁹, K. E. C. Grimshaw³, A. Hoest², G. Lack⁸, L. O'Mahony¹⁰, N. G. Papadopoulos^{11,12}, S. Panesar¹³, S. Prescott¹⁴, G. Roberts^{3,4,5}, D. de Silva¹³, C. Venter^{4,15}, V. Verhasselt¹⁶, A. C. Akdis¹⁷ & A. Sheikh^{18,19} on behalf of EAACI Food Allergy and Anaphylaxis Guidelines Group

1. Exclusively breastfeeding for 4 to 6 months of age.
2. Introduction of complementary foods after the age of 4 months according to normal standard weaning practices and nutrition recommendations, for all children irrespective of atopic heredity.
3. No withholding or encouraging of exposure to 'highly allergenic' foods such as cow's milk, hen's egg, and peanuts once weaning has commenced, irrespective of atopic heredity

1. National Institutes of Health (NIH)

National Institutes of Health - 2017 Guidelines for Peanut

High-risk



Normal-risk

- **High-risk babies** (with severe eczema or egg allergies) should have peanut-containing foods introduced into their diet as early as four to six months of age.
- For those kids with **mild to moderate eczema**, peanuts can be added from six months, if they're already a part of the family's existing diet.
- **Infants without eczema or food allergies**, peanut-containing foods can be freely introduced at home in an "age-appropriate manner" together with other solid foods.

1. ASCIA Guidelines (2016)

Australasian Society of Clinical Immunology and Allergy Limited

- When your infant is ready, at around 6 months, but not before 4 months, start to introduce a variety of solid foods, starting with iron rich foods, while continuing breastfeeding.
- All infants should be given allergenic solid foods including peanut butter, cooked egg, dairy and wheat products in the first year of life. This includes infants at high risk of allergy.
- Hydrolysed (partially and extensively) infant formula are not recommended for prevention of allergic disease.

How early is early?

- **No studies suggest prior to infant developmental readiness to eat solid foods**
- **Certainly not before 4 months** – EAT 3 months but in reality few parents before 4 months
- **But we don't have exact window** - LEAP 4-11 months
- **But earlier than compared to the more common age of introduction in most countries at 8–10 months of age.**

2. Applicability – SA population

Application of LEAP to other geographical locations

“Secondary analyses of the LEAP data showed similar levels of prevention in white, black, and Asian (Indian and Pakistani) children, suggesting that these findings were not limited to one racial group and would likely be as efficacious in other geographic locations”

? *Other protective/risk factors in those locations ?*

? *Geographically relevant foods ?*

Du Toit et al. (2016)

3. Adherence

- **LEAP:** The overall rate of adherence to LEAP per-protocol consumption was high at 92.0% BUT *104 telephone calls...*
- **EAT:** Four factors accounted for 78% of the nonadherence in the dominance analysis:
 1. *Nonwhite ethnicity* (odds ratio [OR], 2.21; 95% CI, 1.18-4.14),
 2. *Parentally perceived symptoms to any of the foods* (OR, 1.7; 95% CI, 1.02-2.86),
 3. *Reduced maternal quality of life* (psychological domain),
 4. *Atopic Dermatitis at enrollment* (OR, 1.38; 95% CI, 0.87-2.19).

3. Adherence

The overall rate of adherence to LEAP per-protocol consumption was high at 92.0% BUT *104 telephone calls...*

Reasons for EAT Non Adherence

- Age-related oral motor development
- Food preparation
- Portion sizes
- Number of foods introduced
- Taste might play a role
- Duration of consumption and dose consumed
- Geographically relevant food allergens



Barriers to implementation

Food insecurity

Income

Education

Socioeconomic
position

Knowledge

Culture

Peer pressure

Access to
health care

Other basic
needs

4. Nutritional Implications

Impact of peanut consumption in the LEAP Study: Feasibility, growth, and nutrition



Mary Feeney, MSc, RD,^{a,b*} George Du Toit, MBBCh, FRCPCH,^{a,b*} Graham Roberts, DM,^{c,d} Peter H. Sayre, MD, PhD,^e Kaitie Lawson, MS,^f Henry T. Bahnson, MPH,^f Michelle L. Sever, MSPH, PhD,^f Suzana Radulovic, MD,^{a,b} Marshall Plaut, MD,^g and Gideon Lack, MBBCh, FRCPCH,^{a,b} for the Immune Tolerance Network LEAP Study Team
London, Southampton, and Isle of Wight, United Kingdom, San Francisco, Calif, Chapel Hill, NC, and Bethesda, Md

Consumption and Avoidance Groups equivalent for:

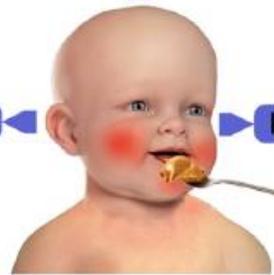
- Weight and length/height
- Body Mass Index
- Waist circumference
- Sub scapular & triceps skin fold thickness

Similarly for the highest peanut consumers

Feasibility:

- Weekly target of 6g peanut protein, achieved within first month
- Sustained to 60 months (median intake 7.9g/week)
- Baseline peanut reactions (n=7) were not severe
- No choking episodes, whole peanuts were avoided
- Sources of peanut changed with age

Feasibility



Growth

Nutrition

Allergy

Nutrition

- Breast feeding duration equivalent
- Energy and protein intakes equivalent (even in highest peanut consumers)
- Peanut consumers had higher fat intakes (accentuated in highest peanut consumers)
- Peanut avoiders had higher carbohydrate intakes
- Micronutrient intakes equivalent
- Peanut products replaced some snack foods, e.g. drinks, spreads and sauces vs diets of peanut avoiders

Peanut Allergy Prevention:

- PA at 60 months, ITT 17.2% in avoidance group and 3.2% in consumption group (p<0.001), represents an 81% relative reduction in PA

4. Nutritional Implications

Dietary Diversity

- **Roduit et al. (2014)** - association between an increased diversity of food within the first year of life and reduced allergic disease outcomes.
- **World Health Organization (WHO) guidelines** – minimum dietary diversity of 4 food groups
- **WHO (2016)** - Few children receive meet the criteria of dietary diversity and feeding frequency that are appropriate for their age
- **Labadarios et al. (2011)** - Black South Africans had the lowest mean dietary diversity of 3.63 (CI: 3.55-3.71)

5. Dissemination of information

Population response to change in infant feeding guidelines for allergy prevention

Dean Tey, MBBS, FRACP,^{a,b,c} Katrina J. Allen, MBBS, BMedSc, FRACP, FAAAAI, PhD,^{a,b,c,d} Rachel L. Peters, MPH,^{b,e} Jennifer J. Koplin, PhD,^{b,e} Mimi L. K. Tang, MBBS, PhD, FRACP, FRCPA, FAAAAI,^{a,b,c} Lyle C. Gurrin, PhD,^{b,e} Anne-Louise Ponsonby, MBBS, FAFPHM, FRACP, PhD,^{b,c} Adrian J. Lowe, PhD,^{b,e} Melissa Wake, MD, FRACP,^{b,c,f} and Shyamali C. Dharmage, MBBS, MSc, MD, PhD,^{b,e} for the HealthNuts study investigators *Parkville and Melbourne, Australia, and Manchester, United Kingdom*

- Updated 2008 guidelines were associated with changes in feeding practice
- Higher socioeconomic status and absence of family history of allergies were associated with better uptake of feeding guidelines.

5. Dissemination of information

ACTA PÆDIATRICA
NURTURING THE CHILD
[Explore this journal >](#)

Introduction of food during the infant's first year: a study with emphasis on introduction of gluten and of egg, fish and peanut in allergy-risk families

J van Odijk, L Hulthén, S Ahlstedt, MP Borres [✉](#)

First published: April 2004 [Full publication history](#)



SWEDEN

- 30-50% of parents did not follow guidance on the introduction of food to infants given by HCP
- Prior to 'Googling'
- Power of the media, celebrities, word of mouth...

SOUTH AFRICA

- Limited access to health care
- Community health workers lack nutrition knowledge
- More pressing health promotion messages

The Bigger Picture: Urban vs. Rural



SAFFA Descriptive Data

	Urban N=359 n, (%)	Rural N=392 n, (%)	p value**
Sex			
Male	192 (53.5)	224 (57.4)	0.281
Female	167 (46.5)	167 (42.6)	
Parental Education			
No education or don't know	3 (0.9)	15 (3.8)	0.000
Primary education	5 (1.4)	55 (14.0)	
Secondary education	218 (60.7)	303 (77.3)	
Tertiary education	113 (37.1)	19 (4.9)	
Household Income			
<R3500	158 (44.0)	339 (86.5)	0.000
R3500-12000	150 (41.8)	44 (11.2)	
>R12000	51 (14.2)	9 (2.3)	
Household Number			
2-3 people	91 (25.4)	26 (6.7)	0.000
4-5 people	152 (42.3)	98 (26.1)	
>6 people	116 (32.3)	267 (68.3)	
Smoking			
Mother (pregnancy)	9 (2.5)	9 (2.3)	0.857
Mother (postpartum)	12 (3.3)	9 (2.3)	0.537
Father	106 (29.5)	89 (22.7)	0.009
Type of Birth			
Normal birth	225 (62.7)	318 (81.1)	0.000
Caesarian section	133 (37.1)	74 (18.8)	
Family History of Allergy			
Mother	73 (20.3)	16 (4.1)	0.000
Father	46 (12.8)	10 (2.6)	0.000
Pet Ownership			
Cat or dog	82 (22.8)	308 (78.6)	0.000

SAFFA Unpublished data

CONCLUSION

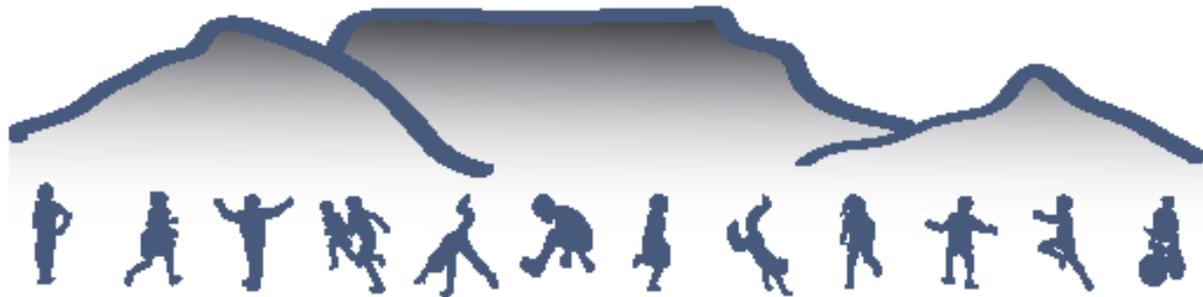
Feeding right from the start

A window of tolerance but it's complicated...

- Any breastmilk exposure
- Time of exclusive breastfeeding
- Mixed feeding
- Overlap of breastfeeding with solids introduction
- Age of solids introduction
- Age of allergenic foods
- Different risk levels of allergy
- Exhaustion, other parental concerns...



The SAFFA Study Team



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