

# Nutrizione e dermatite atopica nei primi tre anni di vita

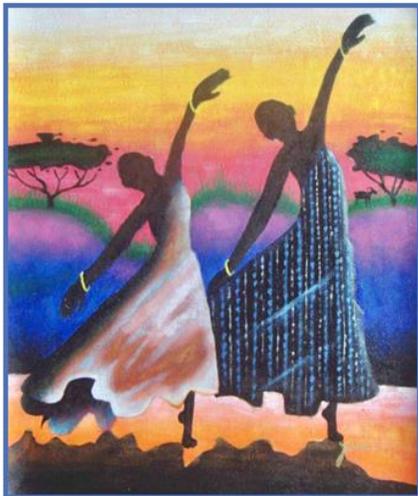
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Dermatologia  
per il Pediatra

*Dermatologia in movimento*



- ✓ **DA & AA come e perchè**
- ✓ Misure dietetiche ..
- ✓ Gli errori da non fare..
- ✓ In conclusione

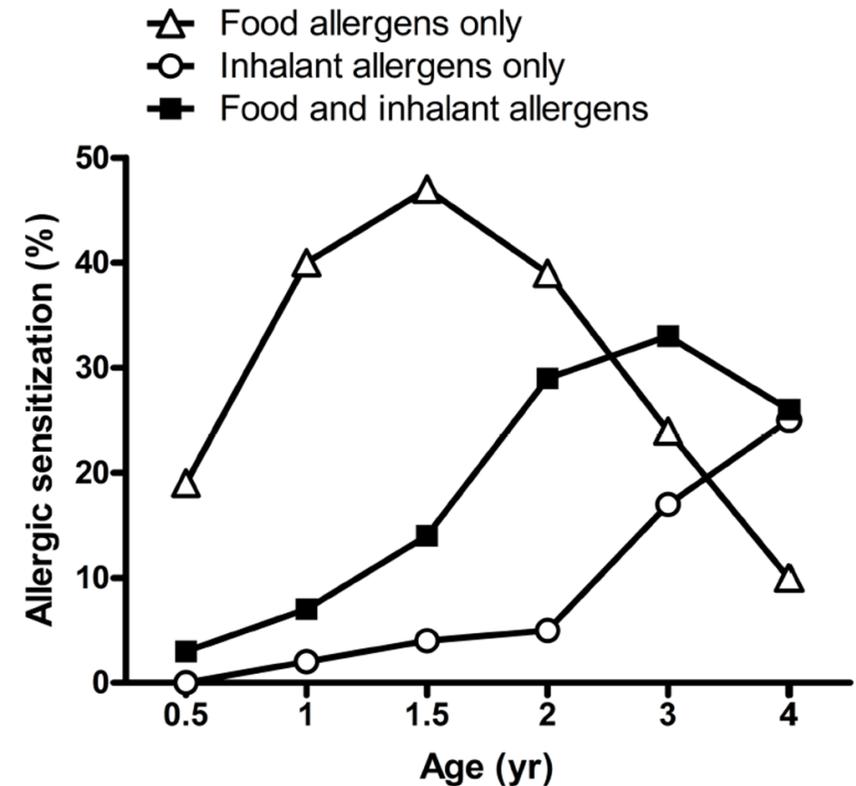
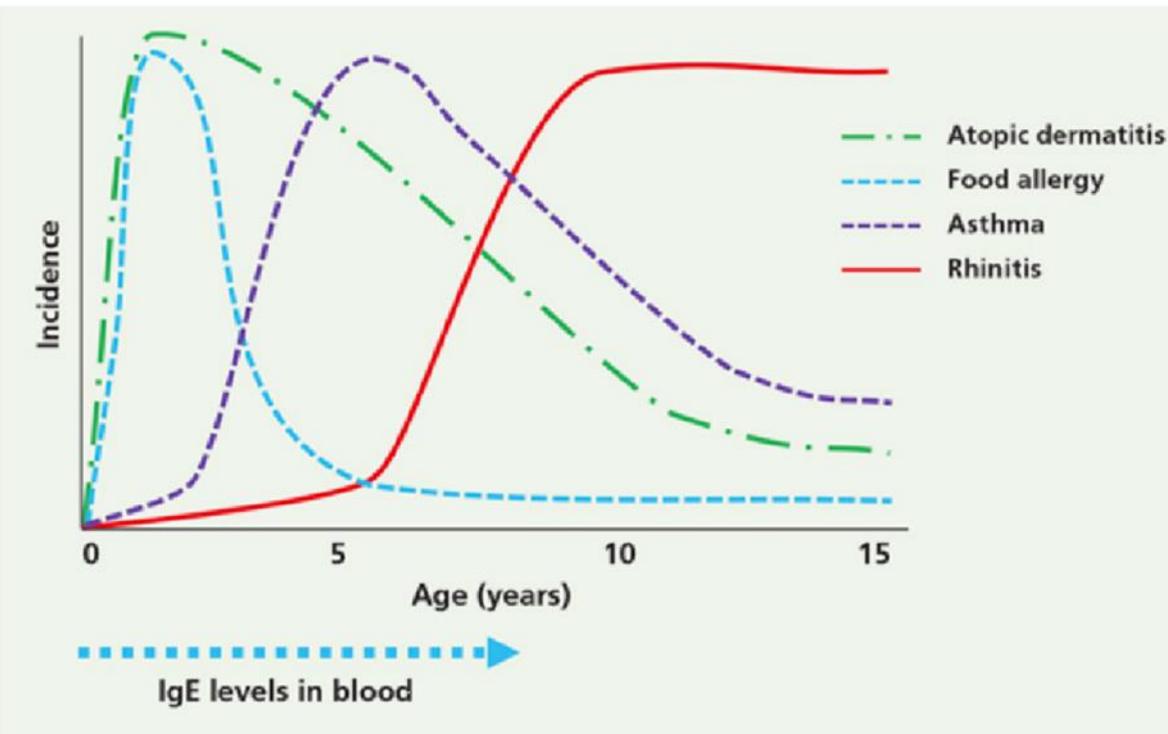
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# Epidemiology of Atopic Dermatitis and Atopic March in Children.

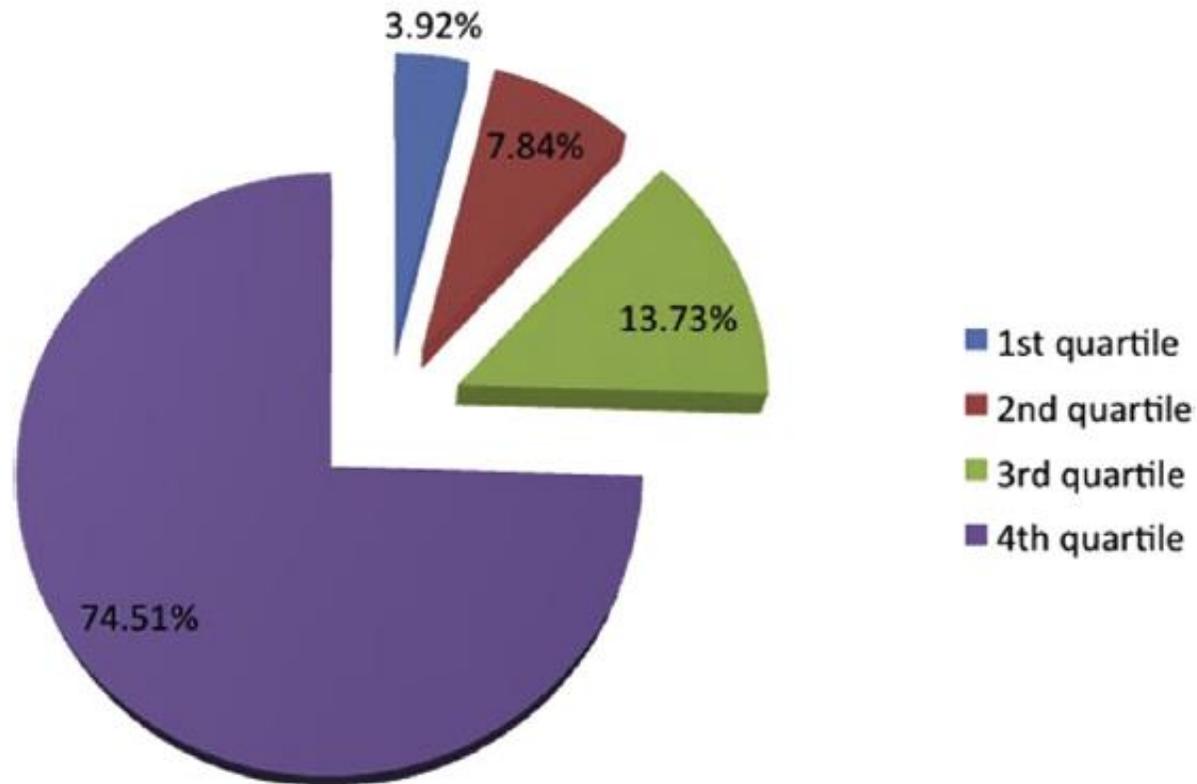
Spergel, Immunol Allergy Clin N Am 30 (2010) 269

The natural history of AD is also associated with the development of other atopic diseases. About 30% of the patients may develop asthma, whereas nearly 66% develop allergic sensitization and symptoms of allergic rhinitis. The studies have also consistently found about a 2- fold increase in OR for development of asthma, which increases with AD severity.



# Skin barrier impairment at birth predicts food allergy at 2 years of age. Kelleher, JACI 2016, 137:1111.

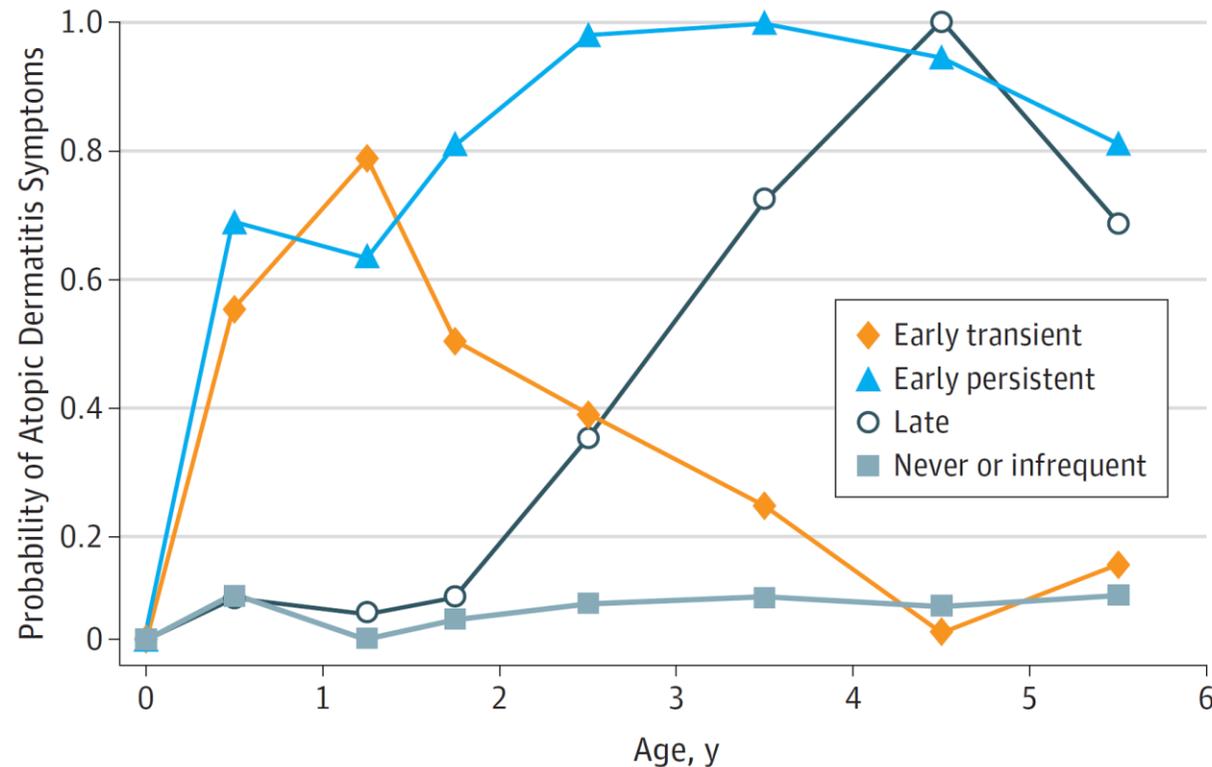
Food Allergy at 2 years by TEWL quartile at day 2 of life



**Clinical implications: A skin barrier signal for the development of FA is seen in infants soon after birth, even in those infants who do not go on to have AD.**

# Phenotypes of Atopic Dermatitis Depending on the Timing of Onset and Progression in Childhood. C. Roduit, JAMA Pediatr 2017

Figure 1. Estimated Probabilities of Atopic Dermatitis Symptoms at Each Time Point From Birth to 6 Years of Age for Each Atopic Dermatitis Phenotype in the 4-Class Model



The prevalences of the phenotypes are 9.2% for early transient (n = 96), 6.5% for early persistent (n = 67), 4.8% for later (n = 50), and 79.5% for never/infrequent (n = 825).

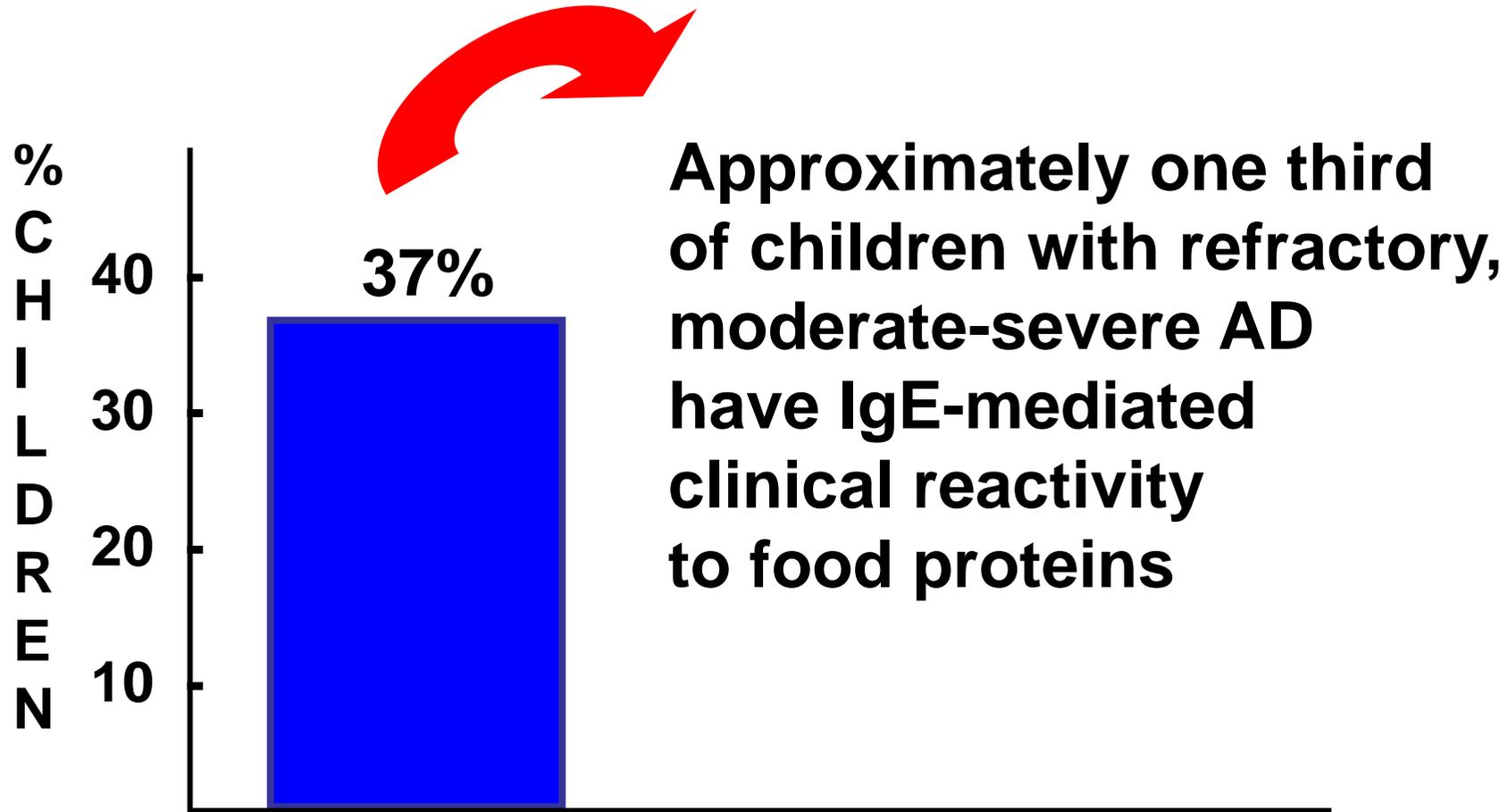
# Phenotypes of Atopic Dermatitis Depending on the Timing of Onset and Progression in Childhood. C. Roduit, JAMA Pediatr 2017

Table 3. Association Between Atopic Dermatitis Phenotypes and Other Allergic Diseases up to 6 Years of Age (Asthma, Food Allergy, and Allergic Rhinitis) and Sensitization to Food and Inhalant Allergens at 6 Years (Cutoff: 0.7 IU/mL)

Variable	No./Total No. (%)	OR (95% CI)	OR <sup>a</sup> (95% CI)
<b>Asthma</b>	78/923 (8.5)	NA	NA
Early transient	10/86 (11.6)	1.62 (0.79-3.315)	1.60 (0.77-3.305)
Early persistent	10/57 (17.5)	2.62 (1.26-5.475)	2.87 (1.31-6.315)
Late	3/48 (6.3)	0.82 (0.25-2.735)	0.83 (0.25-2.805)
Never/infrequent	55/732 (7.5)	1 [Reference]	1 [Reference]
<b>Food allergy</b>	78/864 (9.0)	NA	NA
Early transient	16/80 (20.0)	3.8 (2.02-7.13)	3.69 (1.93-7.035)
Early persistent	19/56 (33.9)	7.8 (4.13-14.72)	7.08 (3.59-13.975)
Late	1/48 (2.1)	0.32 (0.04-2.4)	0.32 (0.04-2.395)
Never/infrequent	42/680 (6.2)	1 [Reference]	1 [Reference]
<b>Allergic rhinitis</b>	73/921 (7.9)	NA	NA
Early transient	9/86 (10.5)	1.82 (0.86-3.88)	1.90 (0.88-4.115)
Early persistent	12/57 (21.0)	4.16 (2.05-8.42)	4.04 (1.82-8.955)
Late	8/48 (16.7)	3.12 (1.38-7.07)	3.23 (1.37-7.615)
Never/infrequent	44/730 (6.0)	1 [Reference]	1 [Reference]

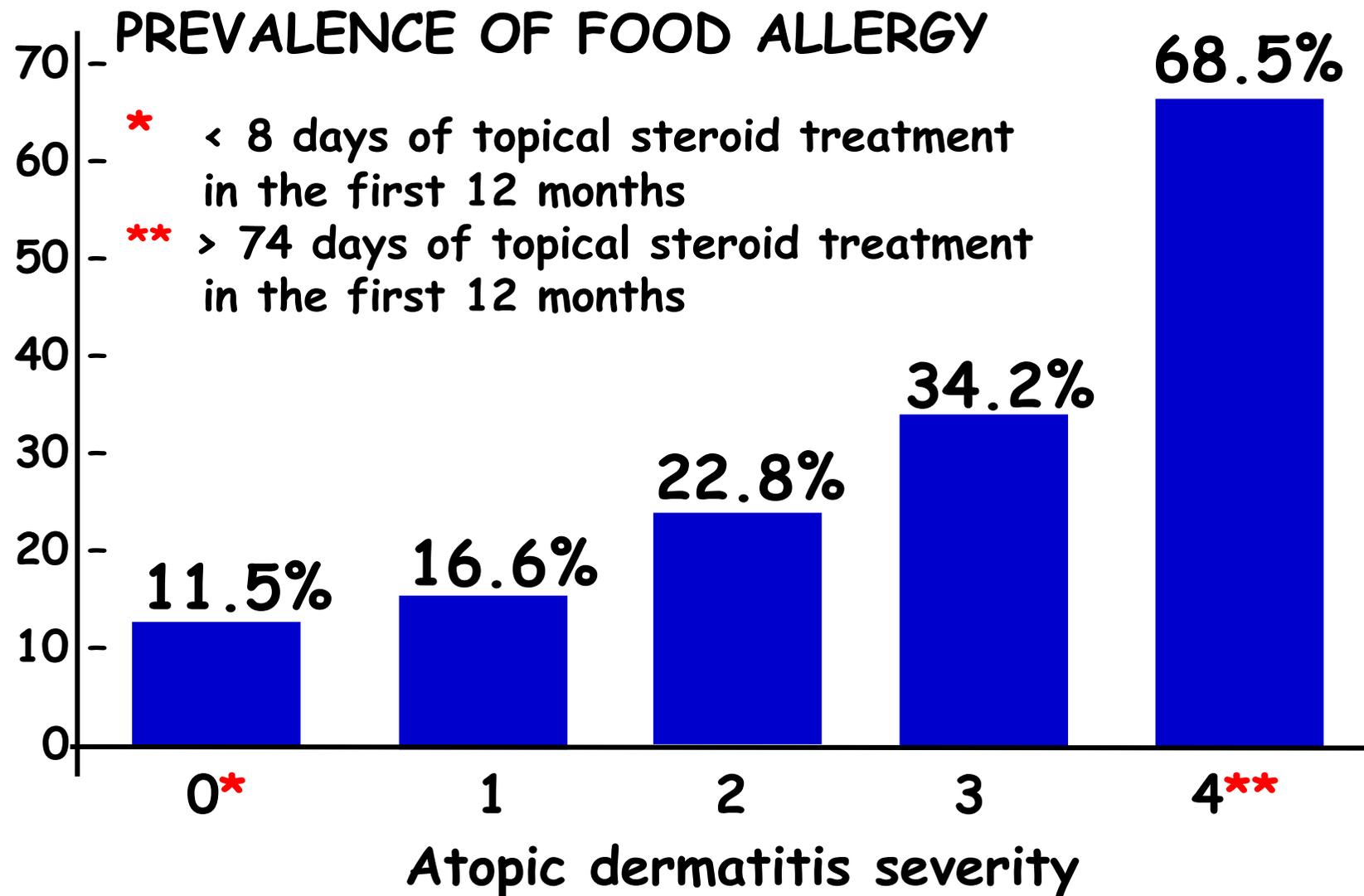
# Prevalence of IgE-mediated food allergy among Children with atopic dermatitis

*Eigenmann Pediatrics 1998; 101: E8*



# FOOD ALLERGY AND ATOPIC DERMATITIS IN INFANCY: AN EPIDEMIOLOGIC STUDY

Hill *Pediatr. Allergy Immunol.* 2004; 15: 421



# Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I.

A. Wollenberg, JEADV 2018, 32, 657

Three different clinical reaction patterns in patients with AE have been described, depending on the type of symptoms and their time of onset.

1. **Immediate-type**, non-eczematous reactions are usually IgE-mediated, occur within 2 h after the administration of the allergen, with skin manifestations such as urticaria, angio-oedema

2. **Isolated eczematous delayed-type reactions** typically occur 6-48 h after the administration of the allergen with flares of eczema on predilection sites of AE, suggestive for a non-anaphylactic pattern.

3. **A combination of the two above-mentioned patterns** with an immediate-type reaction followed by an eczematous delayed type reaction has been described in approximately 40% of children.

# AD TRIGGERS

*Jones Imm All CNA; 2002; 22: 55*

✓ food allergens (most common)

77% of (+) SPT to food  
are clinically irrelevant

peanut

soy

wheat

shellfish

fish

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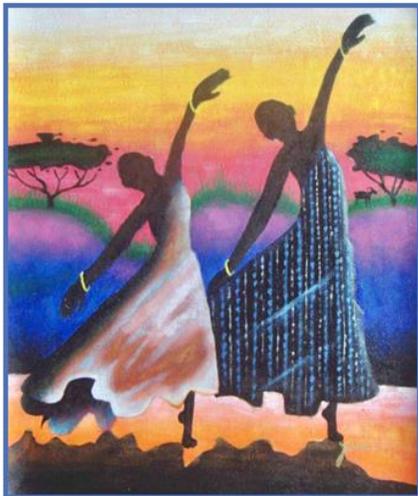
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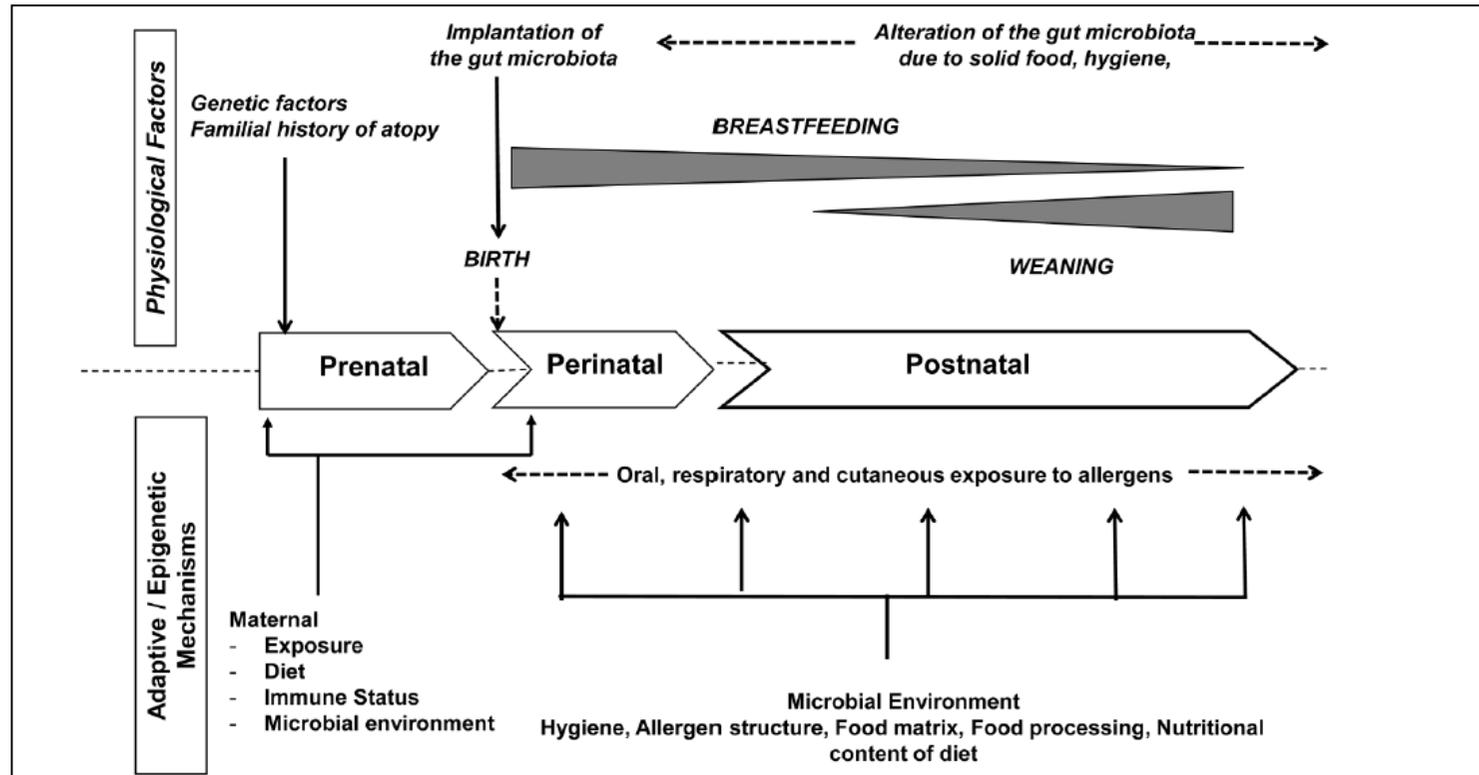
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# Modifying the infant's diet to prevent food allergy.

Grimshaw K, Arch Dis Child 2016

## Intervention trials with food allergy as a primary or secondary outcome



**MATERNAL AVOIDANCE OF HIGHLY ALLERGENIC FOODS FOR PRIMARY PREVENTION OF ALLERGIC DISEASE IN THE CHILDREN**

**Maternal avoidance of highly allergenic foods during pregnancy**

Maternal avoidance of cow's milk and egg during pregnancy does not affect the incidence of allergic disease.

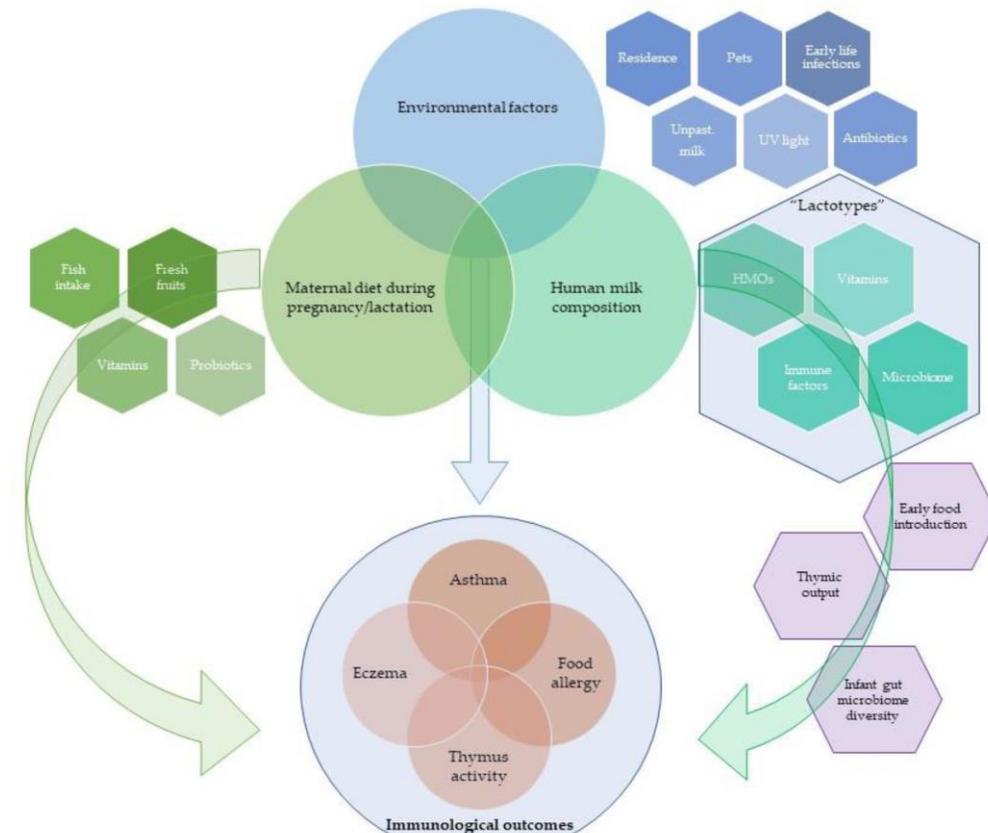
Studies found no association between maternal peanut avoidance during pregnancy and lactation and the incidence of subsequent peanut allergy in their children.

Review

# Human milk and allergic diseases: an unsolved puzzle

Daniel Munblit <sup>1,2,3,§,\*</sup>, Diego G. Peroni <sup>3,4,§</sup>, Alba Boix-Amorós <sup>3,5,§</sup>, Peter S. Hsu <sup>3,6,§</sup>, Belinda Van't Land <sup>7,8,§</sup>, Melvin C.L. Gay <sup>3,9,§</sup>, Anastasia Kolotilina <sup>2,§</sup>, Robert J. Boyle <sup>1,3,§</sup>, Maria Carmen Collado <sup>3,5,§</sup>, Johan Garssen <sup>7,10,§</sup>, Donna T. Geddes <sup>3,9,§</sup>, Ralph Nanan <sup>11,§</sup>, Carolyn Slupsky <sup>12,§</sup>, Ganesa Wegienka <sup>3,13,14,§</sup>, Anita L Kozyrskyj <sup>15,§</sup> and John O. Warner <sup>1,3,16,§</sup>

The impact of human milk composition on allergic disease development in children is still a matter of discussion as studies continue to produce conflicting results. In view of the vast number of crucial components in human milk, investigation of a single or limited range of constituents may well lead to confusing outcomes.

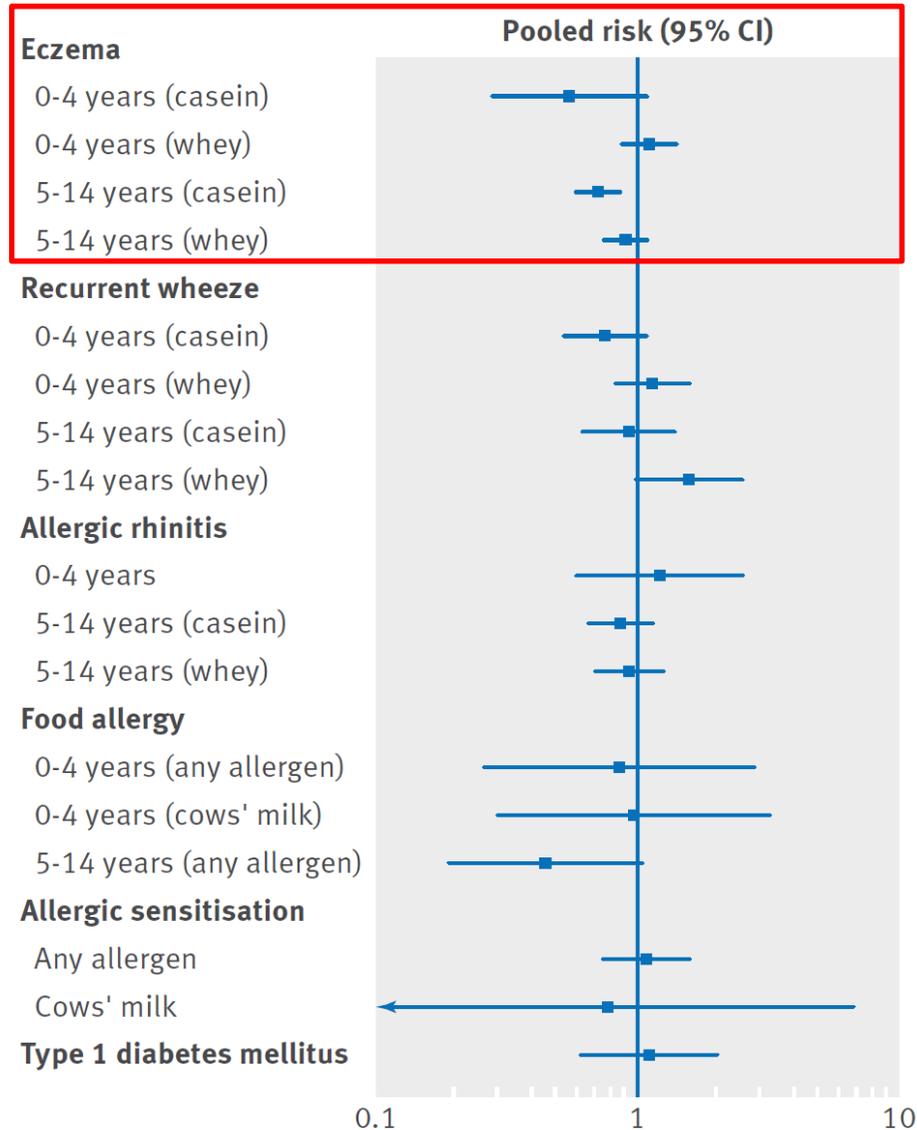


# Hydrolysed formula and risk of allergic or autoimmune disease: systematic review and meta-analysis. Boyle R, BMJ 2016;352:i974

Current infant feeding guidelines in North America, Australasia, and Europe recommend the use of hydrolysed formula in the first 4-6 months of life in place of a standard cows' milk formula for the primary prevention of allergic diseases in childhood

Systematic review commissioned by the UK Food Standards Agency to inform guidelines on infant feeding.

## Summary of treatment effects of hydrolysed formula on different outcome measures

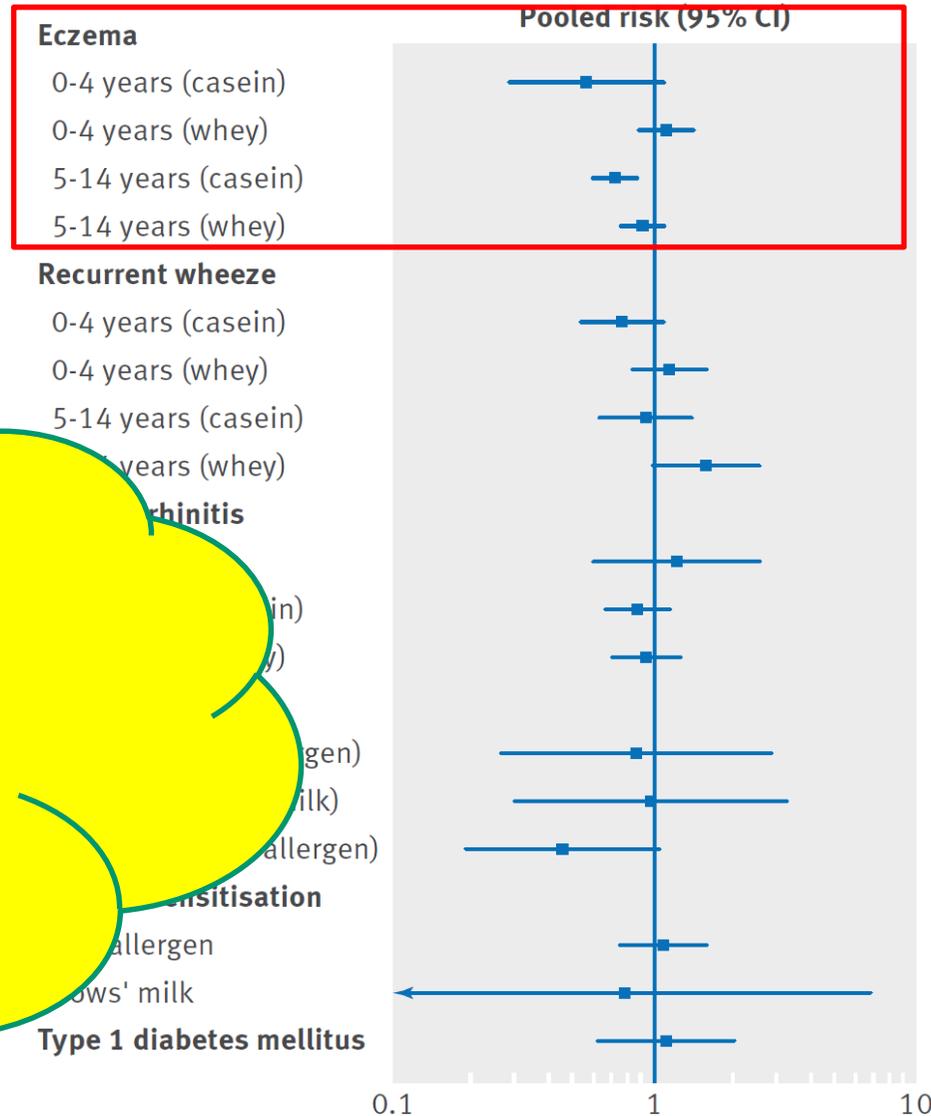


# Hydrolysed formula and risk of allergic or autoimmune disease: systematic review and meta-analysis. Boyle R, BMJ 2016;352:i974

## Summary of treatment effects of hydrolysed formula on different outcome measures

Current infant feeding guidelines in North America, Australasia, and Europe recommend the use of hydrolysed formula in high risk infants.

These findings do not support current guidelines that recommend the use of hydrolysed formula to prevent allergic diseases in high risk infants



# Randomized trial of peanut consumption in infants at risk for peanut allergy. Du Toit G, N Engl J Med 2015;372:803

## The LEAP Study (Learning early about Peanut)

530 high risk infants

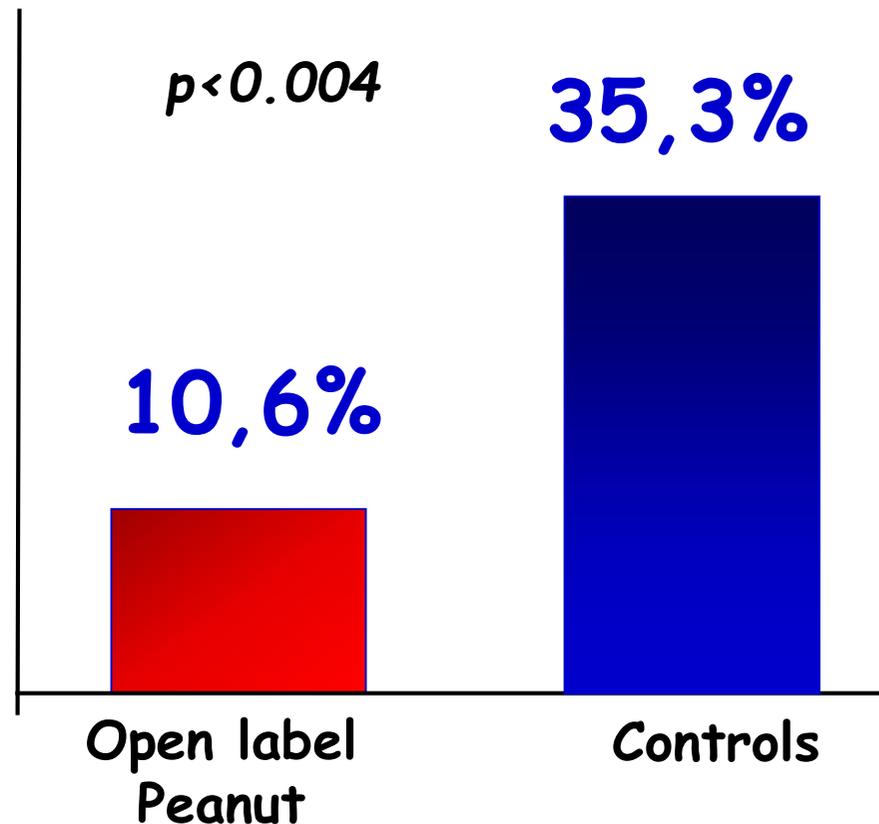
moderate/severe eczema  
and/or egg allergy

Aged 4-11 mo.

Open label peanut  
consumption or placebo

At 5 yrs DBPCC

## Peanut allergy in 98 with SPT peanut positivity

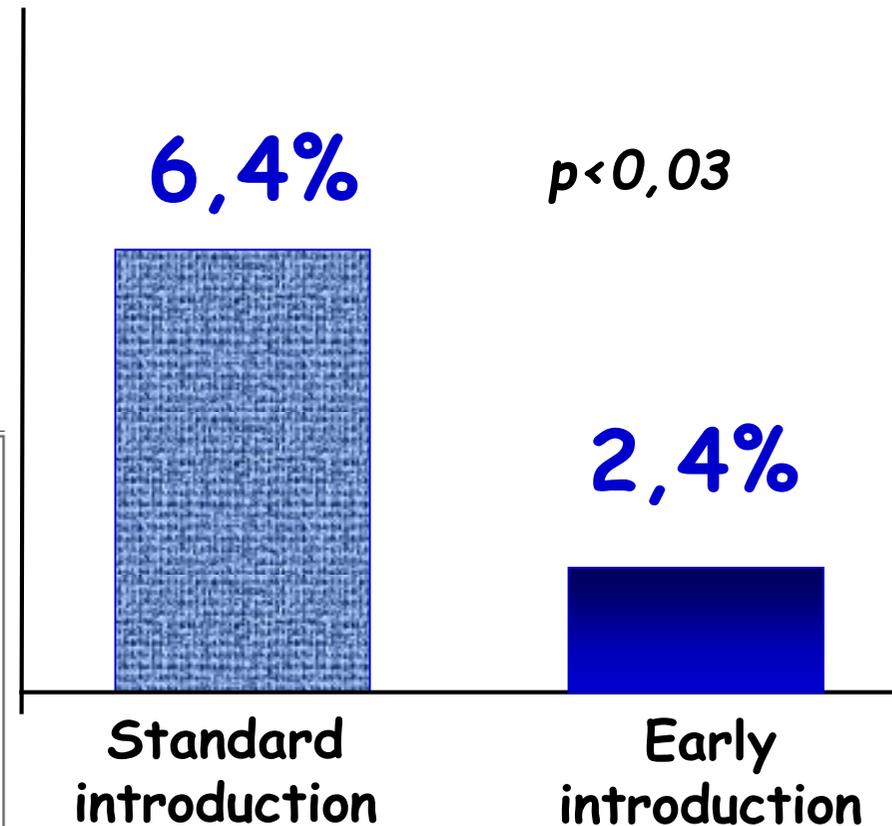
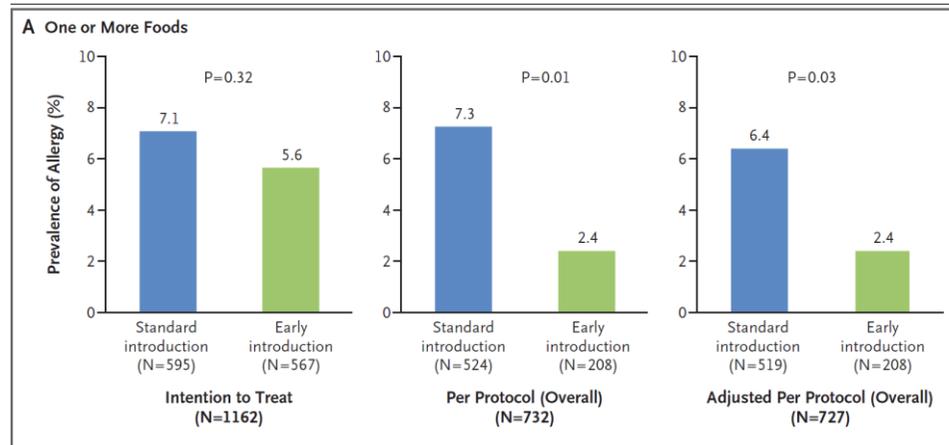


# Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants. Perkin, N Engl J Med 2016;374:1733

Enquiring about Tolerance (EAT) Study.

However, when the analysis was adjusted for adherence to early introduction ..

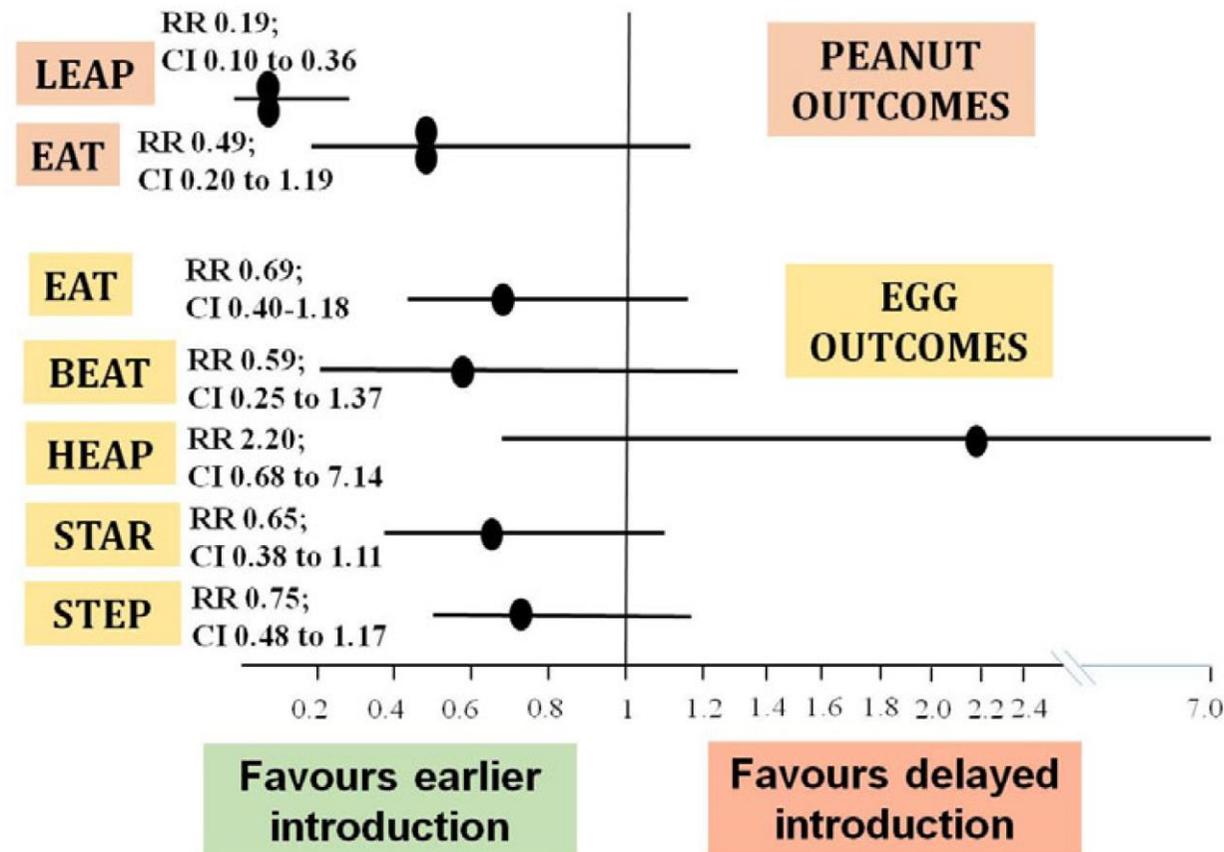
Food allergy at 1 of the 6 foods between 1-3 yrs



# Early introduction of food reduces food allergy - Pro. Palmer PAI 2017

Findings from randomised controlled trials investigating the timing of commencement of regular inclusion of peanut and/or egg in infant diets on food allergy outcomes:

Enquiring About Tolerance (EAT), Learning Early About Peanut Allergy (LEAP), Beating Egg Allergy Trial (BEAT), Hen's Egg Allergy Prevention(HEAP), Solids Timing for Allergy Reduction (STAR), and Starting Time of Egg Protein (STEP) trials.



# Preventing Food Allergy in Infancy — Early Consumption or Avoidance?

Gary W.K. Wong, M.D.

In the EAT trial, the rate of adherence was the highest for dairy products in the form of yogurt, as opposed to textural food such as egg. This difference may well be due to the rather immature oral motor skills of young infants at 3 to 4 months of age and also to concerns of the parents about choking.

**If feeding these foods is safe,**

- What is the minimal amount needed for inducing tolerance to these foods?
- Will the regimen be as effective if we introduce these foods at a later age but early enough before sensitization may occur?
- How can we improve the preparation of foods to make them easier for parents to administer?

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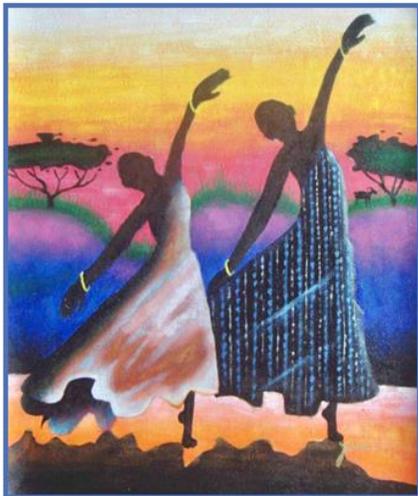
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# Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I.

A. Wollenberg, JEADV 2018, 32, 657

Food sensitization occurs in about **50% of children with severe AE.**

The relevance can be evaluated by **oral provocation tests**, best performed as double-blind placebo-controlled food challenge. (1a)

**Food allergy plays a role for disease exacerbation in 30% of AE children**, most often against basic foods such as hen's egg or cow's milk.

Pollen-associated food allergy can occur in all ages. (2a)

**Food elimination diets represent a major impairment in quality of life and are not easy to perform.** (2a)

# Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I.

A. Wollenberg, JEADV 2018, 32, 657

There is evidence that elimination of basic foods in food allergic children can improve the AE. (1a)

The persistence of food allergy can be evaluated by oral provocation after 1 or 2 years. (3a)

There are no long-term studies to the effect of food elimination diets in AE. (-)

# Dietary intervention: Food allergens



- Among food allergens, cow's milk, hen's egg, wheat, soy, tree nuts and peanuts are most frequently responsible for eczema or exacerbation in infancy.

*Werfel T, Curr Opin Allergy Clin Immunol 2004; 4: 379-385.*



- In older children, adolescents and adults pollen related food allergy should be taken into account.

*Breuer K, Allergy 2004; 59:988-994.*

*Reekers R, J Allergy Clin Immunol 1999; 104: 466-472.*



- Patients with moderate to severe AE should observe a diet eliminating those foods that elicited clinical early or late reactions upon controlled **oral provocation tests**.

*Guidelines for treatment of atopic eczema (atopic dermatitis) Part I*

*J. Ring, JEADV 2012, 26, 1045-1060*



Clinical presentation	DRACMA <sup>3</sup>	BSACI Guidelines <sup>9</sup>	NIAID US Guidelines <sup>14</sup>	ESPGHAN <sup>13,95</sup>
Anaphylaxis	AAF	AAF	No specific recommendation	AAF
Acute urticaria or angioedema	EHF	EHF	No specific recommendation	EHF
Atopic eczema/AD	EHF	EHF	No specific recommendation	EHF
EoE	AAF	AAF	The NIAID guidelines acknowledge that trials in EoE have shown symptom relief and endoscopic improvement in almost all children on AAF/elemental diet, though no specific recommendation on formula choice is made	AAF (as specified by current ESPGHAN guidelines on EoE)
Gastroesophageal reflux disease	EHF	EHF	No specific recommendation	EHF
Cow's milk protein–induced enteropathy	EHF	EHF unless severe in which case AAF	No specific recommendation	EHF but AAF if complicated by faltering growth
FPIES	EHF	AAF	Hypoallergenic formulas are recommended	EHF
Proctocolitis	EHF	EHF	No specific recommendation	EHF
Breast-feeding with ongoing symptoms (already on maternal elimination diet) or requiring a top-up* formula	No specific recommendation	AAF	No specific recommendation	With severe symptoms that are complicated by growth faltering, a hypoallergenic formula up to 2 wk may be warranted. In many countries, AAF is used for diagnostic elimination in extremely sick exclusively breast-fed infants. Although this is not evidence based, it is aimed at stabilizing symptoms

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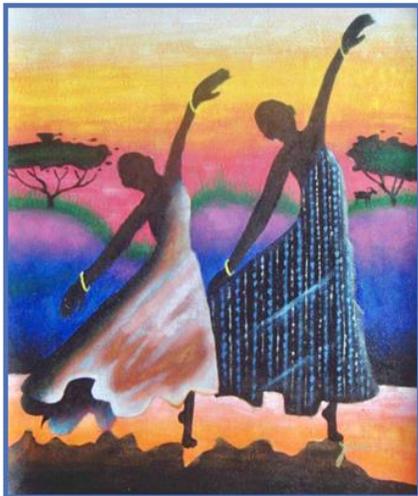
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# The Role of Elimination Diets in Atopic Dermatitis—A Comprehensive Review.

Lim N, Ped Dermatol. 2017; 5, 516

## Efficacy of

- Specific Exclusion Diets in Unscreened Patients
- Specific Exclusion Diets in Preselected Patients
- General Elimination Diets
- Tailored Elimination Diets
- Strict Elimination Diets
- Caloric Restriction

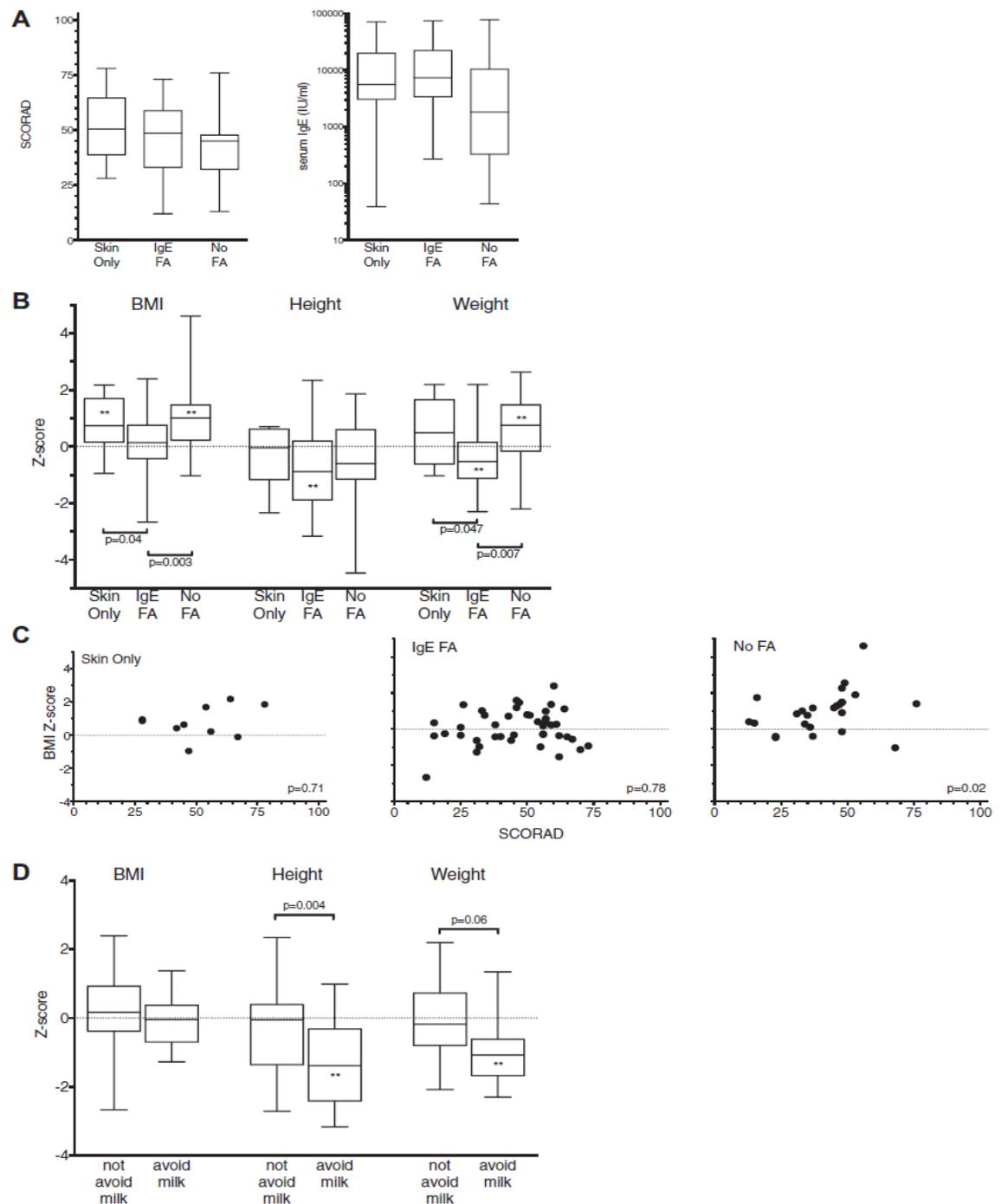
**Results:** Trials varied in type, duration, and the AD patient populations studied. Overall, there is some level I evidence to support specific exclusion diets in preselected patients but insufficient evidence for strict elimination diets (diets that are typically limited to six to eight foods). Data supporting other interventions are mixed and based on small, poorly designed studies.

**Conclusions:** A comprehensive literature review reveals some promising results and several areas in need of further study. More evidence is needed to form a strong foundation for recommendations regarding the utility and role of elimination diets in AD management, but current evidence suggests that strict diet management is not effective in the treatment AD in the vast majority of patients.

# Impact of food allergy on the growth of children with moderate-severe atopic dermatitis.

Jhamnani, JACI 2018

The growth of children with AD may be significantly impaired by the simultaneous presence of IgE FA, particularly milk allergy. In contrast, patients with moderate-severe AD alone are often more likely to have elevated BMI and weight. These data suggest that all children with moderate-severe AD may benefit from close nutritional follow-up.



# Misdiagnosed Food Allergy Resulting in Severe Malnutrition in an Infant

*Alvares M, Pediatrics 2013;132:e229*

- As food allergies become increasingly prevalent and testing methods to identify "food allergy" increase in number, the importance of careful diagnosis has become even more critical.
- Misdiagnosis of food allergy and inappropriate of unproven testing modalities may lead to a harmful food-elimination diet.
- This case is an example of an infant who was placed on an overly restrictive elimination diet at the recommendation of her health care providers, resulting in **kwashiorkor** and **acquired acrodermatitis enteropathica**.

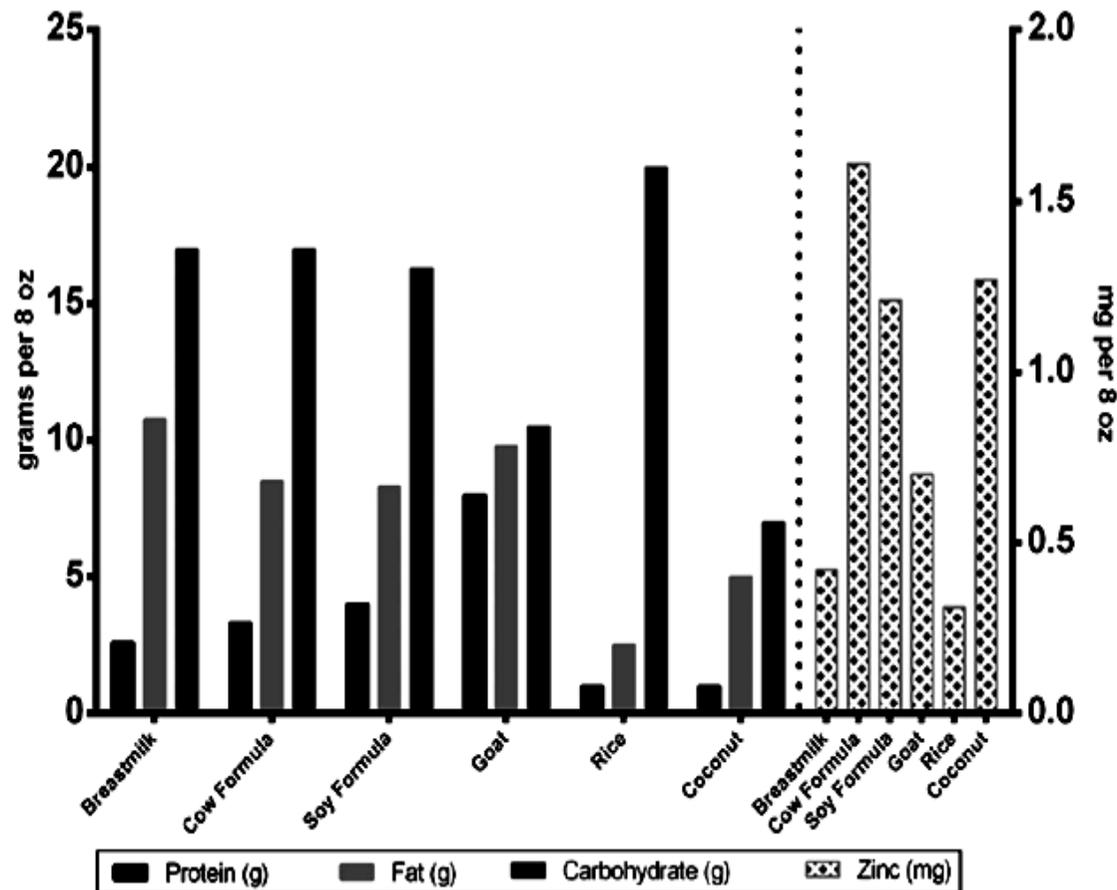


# Misdiagnosed Food Allergy Resulting in Severe Malnutrition in an Infant

*Alvares M, Pediatrics 2013;132:e229*

Comparison of nutritional content among breast milk, infant formulas, and milk substitutes occasionally given to toddlers

8 oz = 236 mL



# BSACI guideline for the diagnosis and management of cow's milk allergy

Luyt D, CEA 2014;44:642

## Recommendations on the use of alternative 'milk' beverages

1. They are **not suitable** for infants as a main drink **under 1 year of age**. A nutritionally complete formula should always be chosen, preferably to 2 years of age (although they can be used for cooking).
2. Their use in children should be under the close guidance of a dietitian as shortfalls in energy, protein, calcium, riboflavin, vitamin A and D, and essential fatty acids are likely without an alternative dietary source. Weight and growth should be regularly monitored.
3. They are not available on prescription and therefore should not be suggested to families with financial constraints where a more suitable complete formula can be prescribed.



# FOOD INTOLERANCE TEST

Con F.I.T. puoi scoprire  
gli alimenti che mettono  
in difficoltà il tuo organismo



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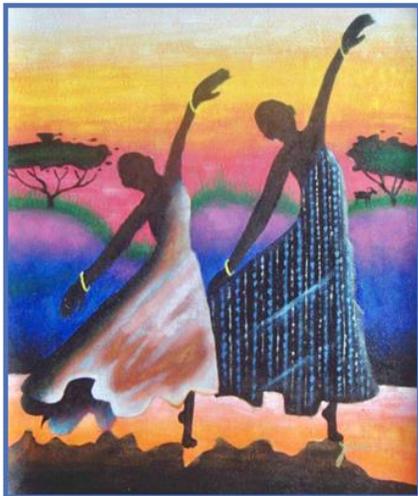
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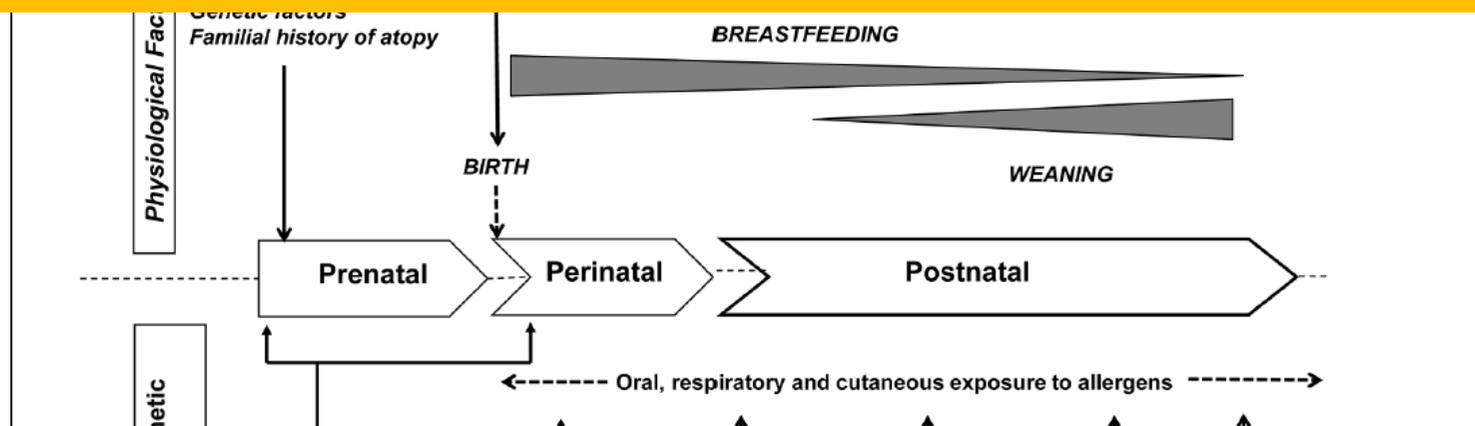
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# What can you tell parents to do to decrease the risk

- Recommend Moms eat a healthy, diverse diet
- Have babies born by vaginal delivery
- Breastfeed for a variety of benefits
- Recommend daily use of a moisturizer on infants
- Introduce a variety of healthy, diverse foods, including all major allergens, starting around 6 months of ag, but within the first year of life



Parental confusion may result when primary health care professionals show heterogeneity in their knowledge, attitudes, and perceptions regarding infant nutrition, food allergy, and atopic dermatitis.

Yrjänä JMS, Allergol Immunopathol 2018

Only 35% of all the professionals recognized either severe airway or cardiovascular symptoms as potential food allergy-related symptoms.

Moisturizers and emollients were thought to be adequate treatment for atopic dermatitis by 56%.

Among 248 one-year-old children, the incidence of food allergy was 4% and atopic dermatitis 13%.

During this period, parents intentionally avoided giving at least one food to 23% of the children, yet more than 80% of these restrictions can be regarded as unnecessary.