Alessandro Fiocchi

May 8th, 2010

Diagnosis & Rationale for Action against CMA:

DRACMA

MELLONI PAEDIATRIA

Quale latte

Chi è il bambino allergico al latte di mucca

Come si diagnostica

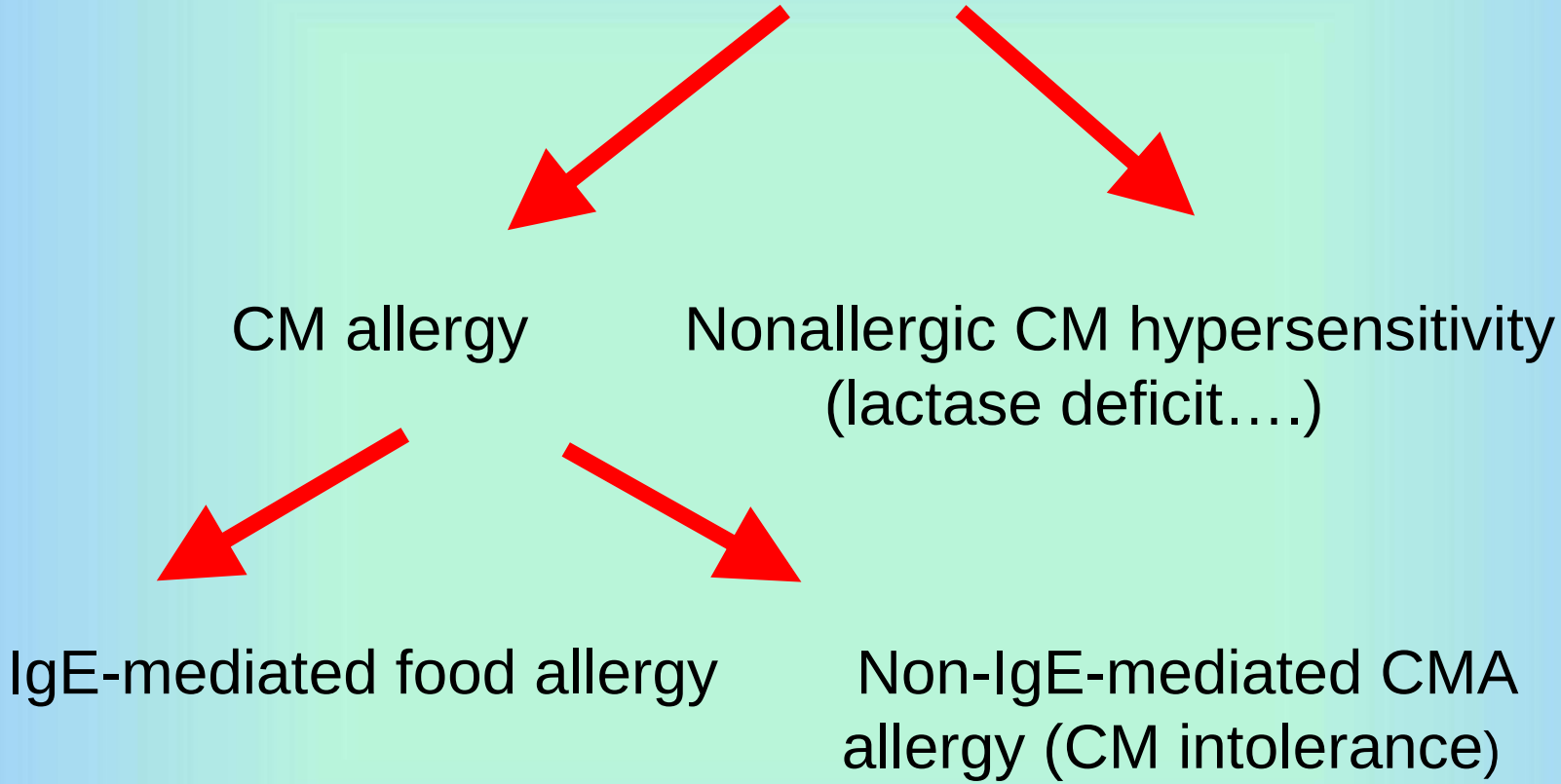
DRACMA

Esiste una prima scelta?

implementazione delle linee-guida

Scelta della formula e storia naturale della APLV

CM hypersensitivity



Johansson SG. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization. J Allergy Clin Immunol. 2004 ;113:832-6

Definitions

Adverse reactions after the ingestion of cow's milk can occur at any age from birth and even among infants fed exclusively at the breast, but not all such reactions are of an allergic nature. A revision of the allergy nomenclature was issued in Europe in 2001[9] and was later endorsed by the WAO[10] under the overarching definition of "milk hypersensitivity," to cover nonallergic hypersensitivity (traditionally termed "cow's milk intolerance") and allergic milk hypersensitivity (or "cow's milk allergy"). The latter definition requires the activation of an underlying immune mechanism to fit. In DRACMA, the term "allergy" will abide by the WAO definition ("*allergy is a hypersensitivity reaction initiated by specific immunologic mechanisms*"). In most children with CMA, the condition can be immunoglobulin E (IgE)-mediated and is thought to manifest as a phenotypical expression of atopy, together with (or in the absence of) atopic eczema, allergic rhinitis and/or asthma. A subset of patients, however, have non-IgE mediated (probably cell-mediated) allergy and present mainly with gastro-intestinal symptoms in reaction to the ingestion of cow's milk.

WORLD ALLERGY ORGANIZATION

Fiocchi A, Schunemann H. Diagnosis and Rationale for Action against Cow's Milk Allergy. The WAO DRACMA guideline. WAO Journal & Pediatr Allergy Immunol 2010; *S1 (April), 1-105.*

Immediate allergic reactions

I- anaphylaxis	
II - GI	OAS
	Immediate GI (vomting, bloody stools)
	CMA in short bowel syndrome
III-respiratory	After ingestion
	After ihalation
IV-cutaneous	Acute urticaria
	Contact urticaria

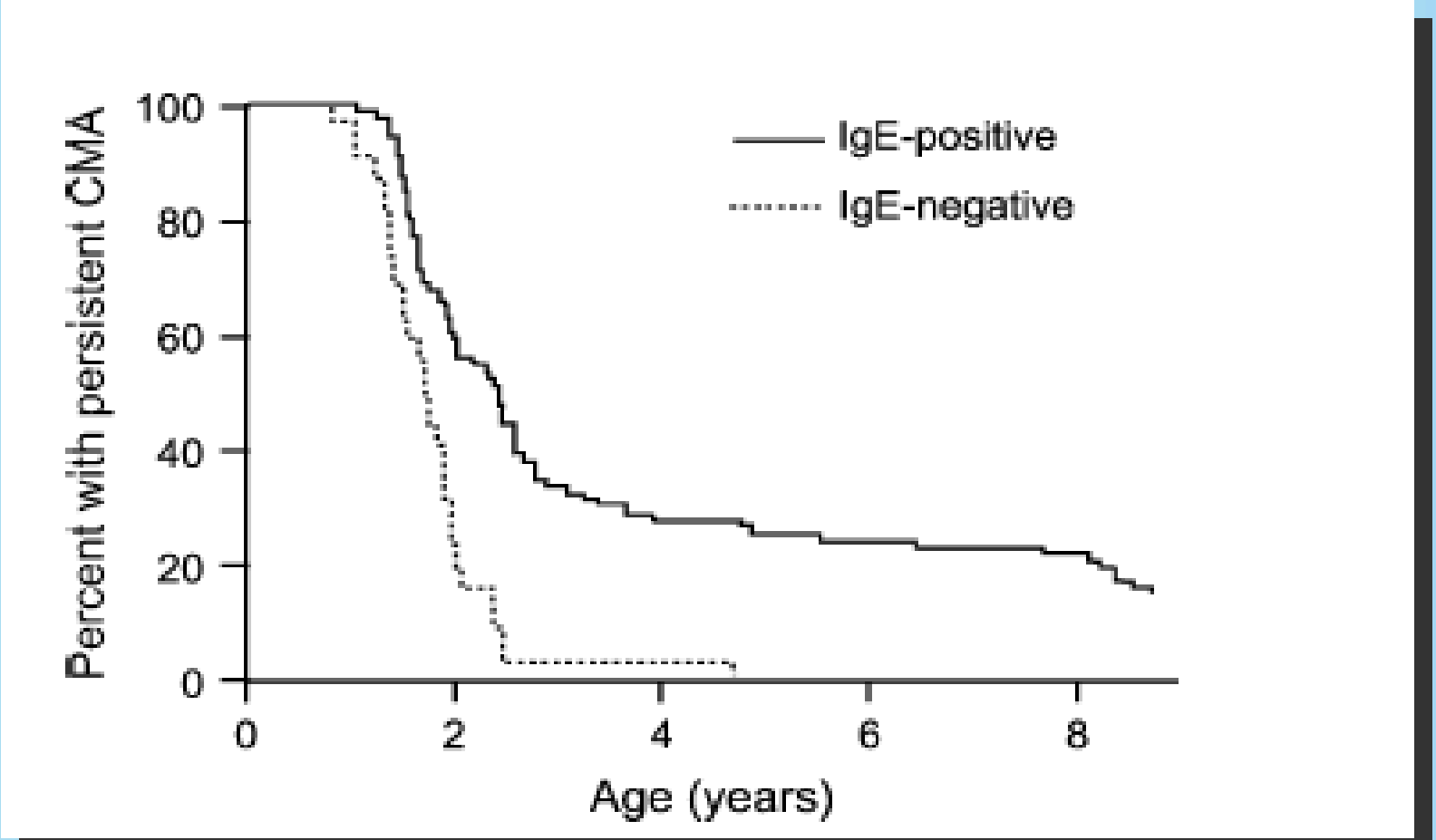
Fiocchi A, Schunemann H. Diagnosis and Rationale for Action against Cow's Milk Allergy. The WAO DRACMA guideline. WAO Journal & Pediatr Allergy Immunol 2010; *S1 (April), 1-105*.

Delayed allergic reactions

I- Cutaneous	Atopic dermatitis
II - GI	GERD
	Cryco-pharyngeal spasm
	Pyloric stenosis
	Allergic Eosinophil Oesophagitis
	FPIES
	Cow's Milk Protein-Induced Enteropathy
	Constipation
	Severe Irritability (Colic)
	Food Protein-Induced Gastroenteritis and Proctocolitis
III-respiratory	Milk-Induced Chronic Pulmonary Disease (Heiner's Syndrome)

Fiocchi A, Schunemann H. Diagnosis and Rationale for Action against Cow's Milk Allergy. The WAO DRACMA guideline. WAO Journal & Pediatr Allergy Immunol 2010; *S1 (April), 1-105*.

Proportion of children with persistent CMA: IgE-positive vs. IgE-negative



Saarinen KM. Clinical course and prognosis of cow's milk allergy are dependent on milk-specific IgE status. J Allergy Clin Immunol. 2005;116:869-75

Quale latte

Chi è il bambino allergico al latte di mucca

DRACMA

Come si diagnostica

Esiste una prima scelta?

implementazione delle linee-guida

Scelta della formula e storia naturale della APLV

No recent guidelines on diagnosis and treatment of CMA

Høst A. Dietary products used in infants for treatment and prevention of food allergy. Joint Statement of the European Society for Paediatric Allergology and Clinical Immunology (ESPACI) Committee on Hypoallergenic Formulas and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition. Arch Dis Child. 1999;81:80-4.

American Academy of Pediatrics Committee on Nutrition. Hypoallergenic Infant Formulae. Pediatrics 2000:106:346-9

Kemp AS; Australian consensus panel. Guidelines for the use of infant formulas to treat cows milk protein allergy: an Australian consensus panel opinion. Med J Aust. 2008;188:109-12

POSITION STATEMENT

Guidelines for the use of infant formulas to treat cows milk protein allergy: an Australian consensus panel opinion

Andrew S Kemp,* David J Hill,* Katrina J Allen, Kym Anderson, Geoffrey P Davidson, Andrew S Day, Ralph G Heine, Jane E Peake, Susan L Prescott, Albert W Shugg and John K Sinn

ABSTRACT

- Three types of infant formula (soy, extensively hydrolysed and amino acid) may be appropriate for treating cows milk protein allergy.
- Selection of a formula depends on the allergy syndrome to be treated.
- Extensively hydrolysed formula is recommended as first choice for infants under 6 months of age for treating immediate cows milk allergy (non-anaphylactic), food protein-induced enterocolitis syndrome, atopic eczema, gastrointestinal symptoms and food protein-induced proctocolitis.
- Soy formula is recommended as first choice for infants over 6 months of age with immediate food reactions, and for those with gastrointestinal symptoms or atopic dermatitis in the absence of failure to thrive.
- Amino acid formula is recommended as first choice in anaphylaxis and eosinophilic oesophagitis.
- If treatment with the initial formula is not successful, use of an alternative formula is recommended.

MJA 2008; 188: 109–112

Kemp AS. Med J Aus 2008; 188:109-112

Guidelines for the diagnosis and management of cow's milk protein allergy in infants

Yvan Vandenplas, Martin Brueton, Christophe Dupont, David Hill, Erika Isolauri, Sibylle Koletzko, Arnold P Oranje, Annamaria Staiano

Arch Dis Child 2007;**92**:902–908. doi: 10.1136/adc.2006.110999


Nutramigen
LIPIL
Hypoallergenic
Infant Formula Powder
Iron Fortified
Enfamil
infant
Neocate
Enhanced with DNA and ARA
Nestlé
Nutrition
Althéra
Similac
Isomil
ADVANCE
SOY Formula
with IRON

Goat's milk

26 children with CMA

SPT with goat's milk: 100% positive

Challenge with goat's milk: 24/26 positive

Blotting cross-inhibition: 100%

Bellioni-Businco B. Allergenicity of goat's milk in children with cow's milk allergy.
J Allergy Clin Immunol 1999;103:1191-4
Muraro MA. Soy formulas and nonbovine milk.
Ann Allergy Asthma Immunol. 2002; 89 (6 Suppl 1):97-101.


WAO
WORLD ALLERGY ORGANIZATION

Restani P, Gaiaschi A, Plebani A, Beretta B, Cavagni G, Fiocchi A, Poiesi C, Velonà T, Ugazio AG, Galli CL. Cross reactivity between milk proteins from different animal species. Clin Exper Allergy 1999; 29:997-1004


WAO
WORLD ALLERGY ORGANIZATION

The pediatrician faces CMA

- Time pressure
- Fatigue
- Lack of expertise
- Hostile patients or families
- Societal lack of the figure of the paediatric allergist
- Dominance by individuals with powerful personalities in scientific policy forums

Jaeschke R, Guyatt GH, Dellinger P, Schünemann H, Levy MM, Kunz R, Norris S, Bion J; GRADE Working Group. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive. BMJ. 2008 Jul 31;337:a744.


WAO
WORLD ALLERGY ORGANIZATION
AMERICAN ACADEMY OF ALLERGY ASTHMA & IMMUNOLOGY
ACAAI American College of Allergy, Asthma & Immunology
Follow the Leader Into the Future
ICAAI
ascia
australasian society of clinical immunology and allergy
SLaai
ALLSA
ARCTIC OCEAN
NORTH PACIFIC OCEAN
NORTH ATLANTIC OCEAN
SOUTH PACIFIC OCEAN
SOUTH ATLANTIC OCEAN
INDIAN OCEAN
Equator
Greenland (DEN.)
ICELAND
RUSSIA
U.S.
MEXICO
CANADA
CHINA
MONGOLIA
KAZAKSTAN
AUSTRALIA
NEW ZEALAND
Antarctica
Scale 1:134,000,000
Robinson Projection
standard parallels 38° N and 38° S
January 1997
Boundary representation is not necessarily authoritative.
802543 (R00352) 1-97

WAO guidelines

Recommendations for standardization of clinical trials with Allergen Specific Immunotherapy for respiratory allergy. A statement of a World Allergy Organization (WAO) taskforce

Allergy 2007: 62: 317–324

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WAO Special Committee on Food Allergy

Lead by Prof. Alessandro Fiocchi, the WAO Special Committee on Food Allergy brings together experts in the field from all over the world.

WAO Food Allergy Special Committee

- **Chair**: Alessandro Fiocchi, Italy
- Sami Bahna, USA
- Barbara Ballmer-Weber, Switzerland
- Martin Bozzola, Argentina
- Chng Hiok Hee, Singapore
- Motohiro Ebisawa, Japan
- Maria Antonieta Guzman, Chile
- Ralf Heine, Australia
- Gideon Lack, United Kingdom
- Haiqi Li, China
- Hugh Sampson, USA
- Stefan Vieths, Germany

The WAO Food Allergy Special Committee is in the process of developing an evidence-based document:

Cow's Milk Allergy (CMA) in infancy and childhood: from suspicion to treatment

Why this document and why now?

A new CMA Document is necessary because:

- The current documents on CMA treatment are not global in scope
- The existing documents are not up-to-date
- Much of the existing research is not evidence-based

Format & Methodology:

This will be an evidence-based document using GRADE methodology. The authors of the document are supported by the WAO Evidence Based Medicine Special Committee. The GRADE methodology ensures the best grading of evidence and

CM allergy diagnosis and treatment

- Method: GRADE guidelines
- Setting; WAO
- Targets: Allergist, Paediatric allergist, General Paediatrician, Gastroenterologist, Dermatologist, Dietician, Food Chemist.
- Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA)

World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines

Alessandro Fiocchi, (Chair), Holger Schünemann, (Chair), Sami L. Bahna, Andrea von Berg, Kirsten Beyer, Martin Bozzola, Julia Bradsher, Jan Brozek, Enrico Compalati, Motohiro Ebisawa, Maria Antonieta Guzman, Haiqi Li, Ralf G. Heine, Paul Keith, Gideon Lack, Massimo Landi, Alberto Martelli, Fabienne Rancé, Hugh Sampson, Airton Stein, Luigi Terracciano, and Stefan Vieths.

WORLD ALLERGY ORGANIZATION

Fiocchi A, Schunemann H. Diagnosis and Rationale for Action against Cow's Milk Allergy. The WAO DRACMA guideline. WAO Journal & Pediatr Allergy Immunol 2010; *S1 (April), 1-105*.

DRACMA: the document

1.	Introduction and CMA epidemiology
2.	CM allergens
3.	Mechanisms of CMA
4.	Clinical presentation (history and symptoms)
5.	What do preceding guidelines say?
6.	Milk elimination in the diagnostic process of CMA
7.	GRADE questions on diagnosis
8.	When and how should oral food challenges be performed?
9.	Natural history
10.	What do preceding guidelines say?
11.	When can milk proteins be eliminated from the diet without substitute?
12.	GRADE questions on treatment
13.	Other milks (goat's, ewe's, mare's, donkey's, camel's, …)
14.	Nutritional considerations
15.	Which is the 1st choice formula?
16.	GRADE questions on OIT
17.	Unmet needs. Recommendations for research. Recommendation for the implementation of the DRACMA guidelines. Periodical update of DRACMA.

The DRACMA worked with the GRADE members on this panel the clinical questions and their scope after various fine-tuning stages. The GRADE panelists independently searched the relevant literature for sections 9, 14, 18. Their analysis was independent of the other panel lists. For question formulation, guideline panel members explicitly rated the importance of all outcomes on a scale from 1–9, where the upper end of the scale (7–9) identifies outcomes of critical importance for decision making, ratings of 4–6 represent outcomes that are important but not critical and ratings of 1–3 are items of limited importance. Evidence summaries were prepared following the GRADE Working Group's approach[1–6] based on systematic reviews done by an independent team of the GRADE Working Group members (JLB and HJS supported by 5 research associates).

WORLD ALLERGY ORGANIZATION

Fiocchi A, Schunemann H. Diagnosis and Rationale for Action against Cow's Milk Allergy. The WAO DRACMA guideline. WAO Journal & Pediatr Allergy Immunol 2010; *S1 (April), 1-105*.

vodafone
Santander
Mobil 1
Mercedes-Benz
BRIDGESTONE
SAP

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Come si diagnostica

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Scelta della formula e storia naturale della APLV

Guidelines for diagnosis

- **Question 1.** Should **skin prick tests** be used to exclude IgE-mediated CMA in patients with low pre-test probability of CMA?
- **Question 2.** Should **in vitro specific IgE determination** be used to exclude IgE-mediated CMA in patients with low pre-test probability of CMA?
- **Question 3.** Sh sed to exclude IgE-mediated CMA and a positive result of a skin p
- **Question 4.** Sh rmination be used to confirm the di high pre-test probability of CMA?
- **Question 5.** Should ***allergen microarrays*** be used to *confirm or* exclude IgE-mediated CMA in patients with low pre-test probability of CMA?
- **Question 6.** Should ***component-resolved diagnostics*** be used to *confirm or* exclude IgE-mediated CMA in patients with low pre-test probability of CMA?

Records identified through database searching (all study designs)
EMBASE = 2203
MEDLINE = 2261
Total n = 4464

Records identified through database searching (all study designs) EMBASE = 2203 MEDLINE = 2261 Total n = 4464

Additional records identified through other sources (n = 0)

Records after duplicates removed (n = 3877)

Records screened (n = 3877)

Records excluded (n = 3619)

Full-text articles assessed for eligibility (n = 258)

Full text articles awaiting assessment (n = 15)

Full-text articles excluded, with reasons (n = 207)

Studies included in qualitative synthesis (n = 36)

Studies included in quantitative synthesis (meta-analysis) (n = 31)

CMA diagnosis

PRISMA diagram

Should skin prick tests be used for the diagnosis of IgE-mediated CMA in patients suspected of CMA?

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

Questions of diagnosis

Should skin prick tests be used for the diagnosis of IgE-mediated CMA in patients suspected of CMA?

Should in vitro specific IgE determination be used for the diagnosis of IgE-mediated CMA in patients suspected of CMA?

Should in vitro specific IgE determination be used for the diagnosis of IgE-mediated CMA in patients suspected of CMA and a positive SPT?

Should in vitro specific IgE determination be used for the diagnosis of IgE-mediated CMA in patients suspected of CMA and a negative SPT?

Should allergen microarrays or component resolved diagnostics be used for the diagnosis of IgE-mediated CMA?

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

Recommendation 1. 1

- In settings where oral food challenge is considered a requirement for making a diagnosis of IgE-mediated cow's milk allergy, we recommend using oral food challenge with cow's milk as the only test without performing a skin prick test as a triage or an add-on test to establish a diagnosis (strong recommendation | very low quality evidence).

Underlying values and preferences

- This recommendation places a relatively high value on avoiding resource consumption and the risk of anaphylactic reactions at home in patients who would be misclassified by a skin prick test alone. It places a lower value on anaphylactic reactions in a controlled setting that can be managed by experienced personnel when oral food challenge is performed. This recommendation also places a high value on avoiding any unnecessary treatment in patients who would be incorrectly classified by a skin prick test as allergic to cow's milk.

Remark

- This recommendation applies to clinical practice settings. In research settings there may be compelling reasons to perform skin prick tests even though a food challenge test with cow's milk is always being done.

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; in press

APPENDIX 2-1. Question 1, Profile 1. Should Skin Prick Tests Be Used for the Diagnosis of IgE-Mediated CMA in Patients Suspected of CMA? Cut-Off ≥3 mm/All Populations

			Limitations							
Outcome	No. of Studies	Study Design	Limitations	Indirectness	Inconsistency	Imprecision	Reporting Bias	Final Quality	Effect Per 1000*	Importance
True positives (patients with CMA)	23 studies (2302 patients)	Consecutive or nonconsecutive series	Serious†	None	Serious‡	None	Unlikely	⊕⊕OO low	Prev 80%: 536 Prev 40%: 268 Prev 10%: 67	Critical
True negatives (patients without CMA)	23 studies (2302 patients)	Consecutive or nonconsecutive series	Serious†	None	Serious‡	None	Unlikely	⊕⊕OO low	Prev 80%: 108 Prev 40%: 324 Prev 10%: 486	Critical
False positives (patients incorrectly classified as having CMA)	23 studies (2302 patients)	Consecutive or nonconsecutive series	Serious†	Serious§	Serious‡	None	Unlikely	⊕OOO very low	Prev 80%: 92 Prev 40%: 276 Prev 10%: 414	Critical
False negatives (patients incorrectly classified as not having CMA)	23 studies (2302 patients)	Consecutive or nonconsecutive series	Serious†	None	Serious‡	None	Unlikely	⊕⊕OO low	Prev 80%: 264 Prev 40%: 132 Prev 10%: 33	Critical
Inconclusive¶	1 study (310 patients)	Nonconsecutive series	—	—	—	—	—	—	—	Important
Complications	Not reported	—	—	—	—	—	—	—	—	Not important
Cost	Not reported	—	—	—	—	—	—	—	—	Not important

*Based on combined sensitivity of 67% (95% CI: 64–70) and specificity of 74% (95% CI: 72–77).

†Most studies enrolled highly selected patients with atopic eczema or gastrointestinal symptoms, no study reported if an index test or a reference standard were interpreted without knowledge of the results of the other test, but it is very likely that those interpreting results of one test knew the results of the other; all except for one study that reported withdrawals did not explain why patients were withdrawn.

‡Estimates of sensitivity ranged from 10 to 100%, and specificity from 14 to 100%; we could not explain it by quality of the studies, tests used or included population.

§There is uncertainty about the consequences for these patients; in some a diagnosis of other potentially serious condition may be delayed.

¶One study in children <12 months of age reported 8% inconclusive challenge tests but did not report number of inconclusive skin prick tests.

Recommendation 1. 2

- In settings where oral food challenge is not considered a requirement in all patients suspected of IgE-mediated cow's milk allergy, in patients with **high pre-test probability** of CMA we suggest using a skin prick test with a cut-off value of ≥3 mm as a triage test to avoid oral food challenge in those in whom the result of a skin prick test turns out positive (weak recommendation | low quality evidence).

Underlying values and preferences

- This recommendation places a relatively high value on avoiding burden, resource use and very likely anaphylactic reactions during the oral food challenge test (~50–70% food challenges avoided). It places a lower value on unnecessary treatment of around 1 in 20 patients misclassified as allergic to cow's milk (5–6% false positive results).

Remark

- A high pre-test probability of CMA (~80%) can be estimated based on the history and would represent, for instance, patients who experienced an anaphylactic reaction in the past.

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; in press

If SPT positive:

unnecessary treatment of
1 in 20 patients
misclassified as CMA
(5–6% false positive results).

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

Recommendation 1. 4

- In settings where oral food challenge is not considered a requirement in all patients suspected of IgE-mediated cow's milk allergy, in patients with **low pre-test probability** of CMA we suggest using a skin prick test with a cut-off value of ≥3 mm as a triage test to avoid oral food challenge in those in whom the result of a skin prick test turns out negative (weak recommendation | low quality evidence).

Underlying values and preferences: This recommendation places a relatively high value on avoiding burden and resource use with an oral food challenge test (~70% challenges avoided). It places a lower value on avoiding an allergic reaction (possibly a mild one) in around 1 in 25–50 patients misclassified as not having cow's milk allergy while they would actually be allergic to cow's milk (2–4% false negative results).

Remark: A low pre-test probability of CMA (~10%) can be estimated based on the history and would represent, for instance, patients with unexplained gastrointestinal symptoms (e.g. gastroesophageal reflux).

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; in press

If SPT negative: allergic reaction (possibly mild) in 1 in 25–50 patients misclassified as not having cow's milk allergy while they would actually be allergic to cow's milk (2–4% false negative results).

Fiocchi A, Schunemann H. WAO Special Committe or Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; 3(April): 1-105

Recommendation 1. 3

- In settings where oral food challenge is not considered a requirement for making a diagnosis of IgE-mediated cow's milk allergy, in patients with **average pre-test probability** of CMA we suggest using an oral food challenge test with cow's milk as the only test without performing a skin prick test with a cut-off value of ≥3 mm as a triage or an add-on test to establish a diagnosis

Underlying values and preferences

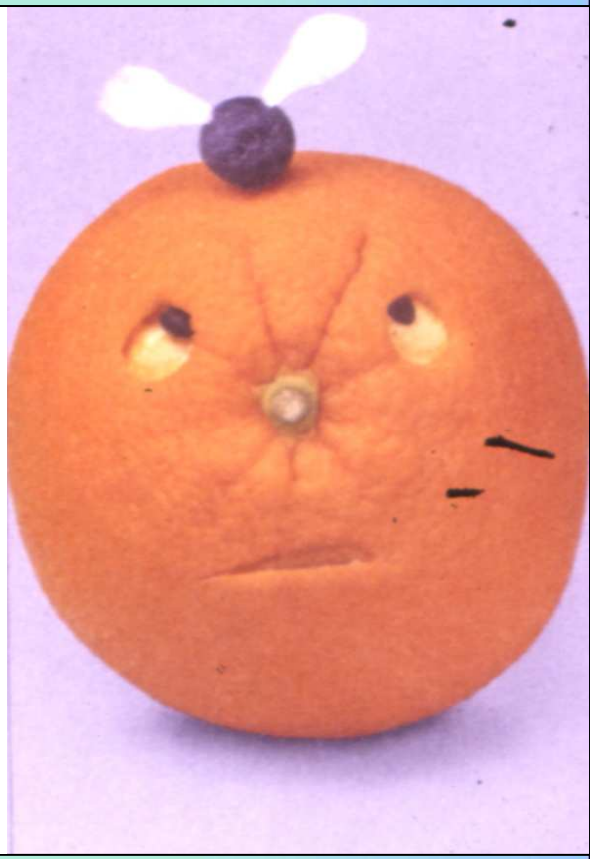
- This recommendation places a high value on avoiding resource consumption and the risk of anaphylactic reactions at home in large proportion of patients who would be incorrectly classified by a skin prick test alone. It places a lower value on anaphylactic reactions in a controlled setting that can be managed by experienced personnel when oral food challenge is performed. This recommendation also places a high value on avoiding any unnecessary treatment in patients who would be incorrectly classified by a skin prick test as allergic to cow's milk.

Remark : An average pre-test probability of CMA (~40%) can be estimated based on the history and presenting symptoms and would represent the majority of situations

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; in press

If SPT positive: unnecessary treatment of
8 in 20 patients misclassified as CMA
(40% false positive results).

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105



Courtesy of Sami Bahna

Quale latte

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Esiste una prima scelta?

implementazione delle linee-guida

Scelta della formula e storia naturale della APLV

Informal Question	Comparators	Outcomes
Should ***extensively hydrolysed cow's milk formulae*** be used in patients with CMA?	soy, rice, amino acid formula, other cow's milk hydrolysed formula	symptoms quality of life of a patient & caregivers failure to thrive iron, calcium, vitamin D deficiency protein, fats and other minerals and vitamins deficiency weight/height excessive weight gain anthropometric values secondary sensitization to that formula allergic reaction (milk hydrolyzed formula) allergic reaction to soy other adverse effects unpleasant taste resource utilization (cost) burden for parents cross-reactivity with cow's milk (soy formula)
Should ***soy-based formulae*** be used in patients with CMA?	other soy-based formula, rice, amino acid, cow's milk hydrolysed formula	
Should ***rice hydrolysate*** be used in patients with CMA?	soy, amino acid, cow's milk hydrolysed formula	
Should ***amino acid formulae*** be used in patients with CMA?	soy, rice, cow's milk hydrolysed formula	

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; in press

	RH	ML	ME	MG	AM	AS	AF	MB	JB	HS	KB	SB	GL	SV	m
severe symptoms of CMA (severe laryngeal edema, severe asthma, anaphylaxis)	9	9	9	9	9	8	9	9	9	9	9	8	9	8	**9**
allergic reaction to protein in the formula	8	4	8	6	9	5	9	9	9	7	7	5	7	5	**7**
moderate symptoms of CMA (mild laryngeal edema, mild asthma)	9	7	9	9	7	5	6	7	7	8	7	5	6	5	**7**
failure to thrive	8	4	5	8	8	6	8	9	8	8	7	6	7	6	**7**
enteropathy, entero/proctocolitis	8	5	6	8	9	6	7	8	7	9	7	6	6	6	**7**
protein and fats deficiency	8	4	7	8	7	6	7	8	8	5	7	6	7	6	**7**
iron, calcium, vitamin D, and other minerals and vitamins deficiency	8	3	9	8	7	6	6	7	7	5	7	6	7	6	**7**
weight/height	8	4	5	8	8	7	7	7	6	5	7	7	7	7	**7**
mild symptoms of CMA (erythema, urticaria, angioedema, pruritus, vomiting, diarrhoea, rhinitis, conjunctivitis)	9	7	9	9	6	4	6	7	5	7	5	7	4	8	**7**

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; in press

	RH	ML	ME	MG	AM	AS	AF	MB	JB	HS	KB	SB	GL	SV	m
quality of life of a patient	6	6	5	9	8	5	7	8	8	3	6	6	6	6	**6**
duration of CMA	6	5	5	9	8	4	3	7	7	3	8	8	6	8	**6**
unpleasant taste (child may refuse to take the formula)	6	4	8	6	8	2	8	9	6	4	4	4	6	4	**6**
quality of life of caregivers	6	6	5	9	6	4	7	5	7	3	6	6	6	6	**6**
anthropometric values	6	4	3	7	8	5	7	8	5	3	7	7	6	7	**6**
resource utilization (cost)	6	4	5	7	8	4	7	9	4	4	4	4	3	4	**5**
cross-reactivity with cow's milk	6	4	2	2	9	4	9	7	6	3	5	5	7	5	**5**
development of secondary sensitization to proteins present in a formula	6	6	4	1	9	5	9	6	7	2	7	7	1	7	**5**
excessive weight gain	6	3	3	7	6	5	6	3	7	4	7	7	5	7	**5**
skin fold thickness	6	3	3	6	6	6	4	5	5	4	7	7	3	7	**5**
burden for parents: need to change from bottles to beakers (milk hydrolysed, rice, and amino acid formulas are high in sugar)	5	2	2	7	7	2	5	9	5	5	3	3	4	3	**5**
sexual maturation (development of secondary and tertiary sexual traits)	1	3	1	1	8	4	6	7	5	2	7	4	5	3	**4**

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; in press

Resource utilisation (costs)

Milk/formula	Cost per liter [US$ (Euro)]	Cost per 6 months [US$ (Euro)]
normal cow's milk	1.2 (0.9)	100 (75)
normal formula	2.5 (2.0)	230 (160)
extensively hydrolysed formula	9 (6)	800 (550)
soy formula	7 (5)	750 (450)
rice formula	9 (6)	800 (550)
amino acid formula	20 (14)	1800 (1250)

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; in press

Guidelines for replacement formula choice

- **Question 7.** Should *cow's milk hydrolysed formulae* be used in patients with CMA?
- **Question 8.** S…ents with CMA?
- **Question 9**. S… with CMA?
- **Question 10**. …tients with CMA?
- **Question 11**. …with CMA?

Records identified through database searching (all study designs)

EMBASE = 724
MEDLINE = 574
CENTRAL = 908

(Total n = 2206)

CMA treatment

PRISMA diagram

Should extensively hydrolysed milk, soy, amino acid or extensively hydrolysed rice formula be used in patients with cow's milk allergy?

Records identified through database searching (all study designs)
EMBASE = 724
MEDLINE = 574
CENTRAL = 908
(Total n = 2206)

Additional records identified through other sources (n = 0)

Records after duplicates removed (n = 1579)

Records screened (n = 1579)

Records excluded (n = 1525)

Full-text articles assessed for eligibility (n = 54)

Full-text articles excluded, with reasons (n = 44)

Studies included in qualitative synthesis (n = 10)

Studies included in quantitative synthesis (meta-analysis) (n = 7)

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

Recommendation 7. 1

- In children with IgE-mediated cow's milk allergy at high risk of anaphylactic reactions (prior history of anaphylaxis and currently not using extensively hydrolysed milk formula), we suggest amino acid formula rather than extensively hydrolysed milk formula (conditional recommendation | very low quality evidence).

Underlying values and preferences

- This recommendation places a relatively high value on avoiding possible anaphylactic reactions and a lower value on avoiding the direct cost of amino acid formula in settings where the cost of amino acid formulas is high.

Remark

- In controlled settings a trial feeding with an extensively hydrolysed milk formula may be appropriate

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

Expensive, but necessary

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

Recommendation 7. 2

In children with IgE-mediated cow's milk allergy at low risk of anaphylactic reactions (no prior history of anaphylaxis or currently on extensively hydrolysed milk formula), we suggest extensively hydrolysed milk formula over amino acid formula (conditional recommendation | very low quality evidence).

Underlying values and preferences

This recommendation places a relatively high value on avoiding the direct cost of amino acid formula in settings where the cost of amino acid formula is high. In settings where the cost of amino acid formula is lower the use of amino acid formula may be equally reasonable.

Remark

Extensively hydrolysed milk formula should be tested in clinical studies before being used. (American Academy of Pediatrics Committee on Nutrition 2000 [19]) If a new formula is introduced, one should carefully monitor if any adverse reactions develop after first administration.

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

-Controlled risk of sensitisation
- less expensive
-low risk of anaphylactic reactions

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

Recommendation 7.3

- In children with IgE-mediated cow's milk allergy, we suggest extensively hydrolysed milk formula rather than soy formula (conditional recommendation | very low quality evidence).

Underlying values and preferences

- This recommendation places a relatively high value on avoiding adverse reactions to soy formula, and a relatively low value on an inferior acceptance of the extensively hydrolysed formula and resource utilization. In settings where relative importance of resource expenditure is lower an alternative choice may be equally reasonable.

Remark

- Soy should not be used in first 6 months of life, because of nutritional risks.

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

- Growth, (length and weight for age z-score) adequate, but trend towards improved growth in extensively hydrolysed formula compared to soy formula
- Fewer children had allergic reaction to extensively hydrolysed formula than to soy formula (relative risk: 0.18; 95% CI: 0.05 to 0.71)
- Fewer children developed secondary sensitization to eHF than to soy formula

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

Recommendation 7. 4

- In children with IgE-mediated cow's milk allergy, extensively hydrolysed milk formula rather than extensively hydrolysed rice formula.

(conditional recommendation | very low quality evidence).

Underlying values and preferences

- This recommendation places a relatively high value on wide availability of extensively hydrolysed milk formulae relative to hydrolysed rice formulae.

Fiocchi A, Schunemann H. WAO Special Committee on Food Allergy. Diagnosis and Rationale for Action against Cow's Milk Allergy. The DRACMA guideline. WAO Journal 2010; S1 (April), 1-105

RICE MILK

Just add water!

- Dairy Free Alternative to Milk
- Soy Free
- Gluten Free
- Lactose Free
- Fortified
- Calcium Enriched

(Makes 4 Litre) 450g

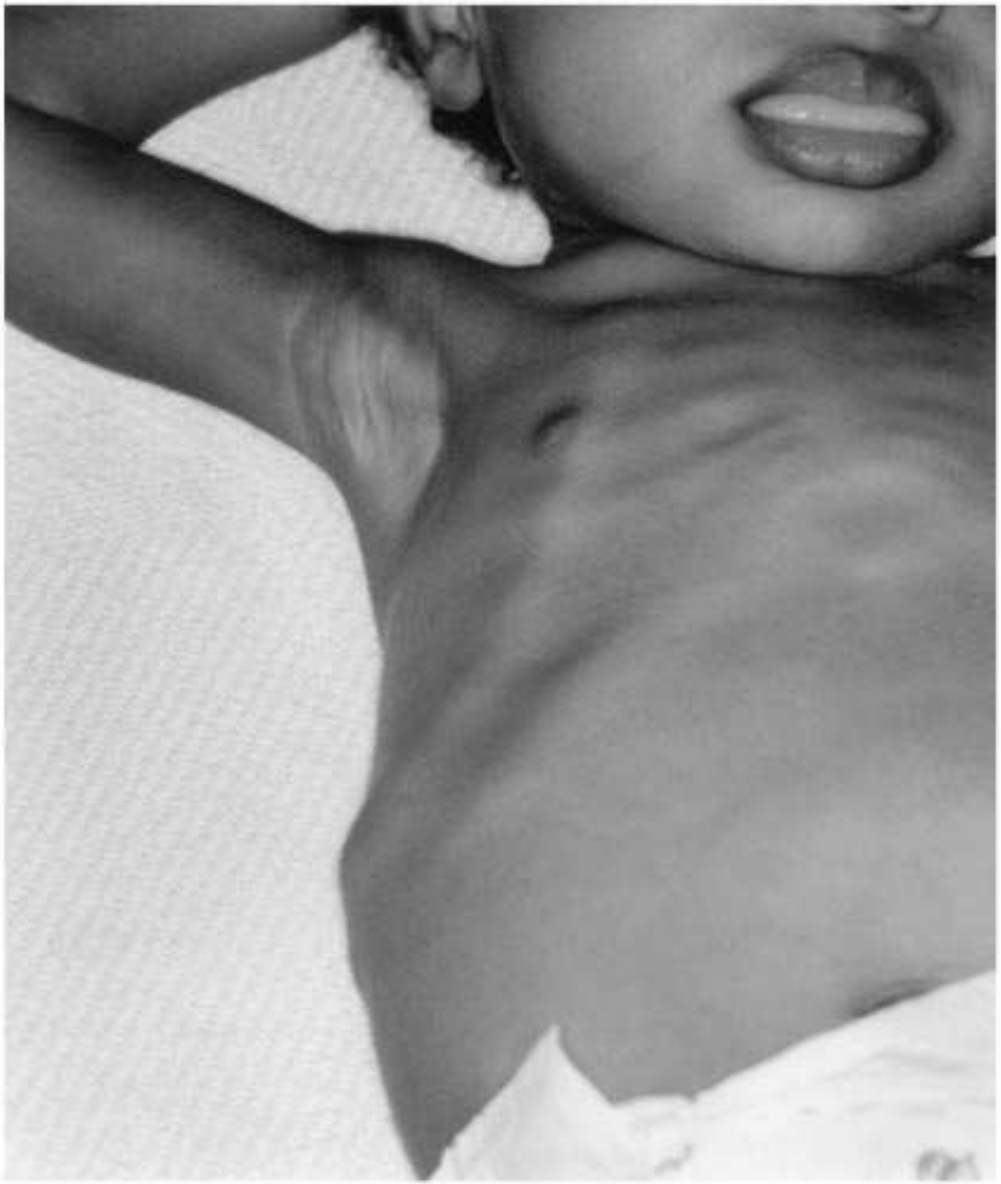
Rice milk is a perfect substitute for people with a lactose, dairy or soy intolerance or allergy. It is lactose free, dairy free, soy free and kosher. Our rice milk powder is made from milling sound broken long grain white rice, and blended with the remaining ingredients to produce the final product. Used as a substitute for milk and milk powder.

Ingredients: Rice Flour, Maltodextrin, Vegetable fat, Fructose, Xanthan Gum, Salt, Vitamin & mineral supplement, Nature Identical flavour .

Generalized edema more evident (A) in the face and (B) in the legs (fovea sign)

Novembre E. Severe hypoproteinemia in infant with AD. Allergy. 2003;58:88-9

Carvalho NF. Severe nutritional deficiencies in toddlers resulting from health food milk alternatives. Pediatrics. 2001;107(4):E46



Carvalho NF. Severe nutritional deficiencies in toddlers resulting from health food milk alternatives. Pediatrics. 2001;107(4):E46

Should we ban all milks because of CMA?

Jarvinen K. Mammalian Milk Allergy: Clinical Suspicion, Cross-Reactivities and Diagnosis Curr Opinion Allergy Clin Immunol 2009; 9:234-7

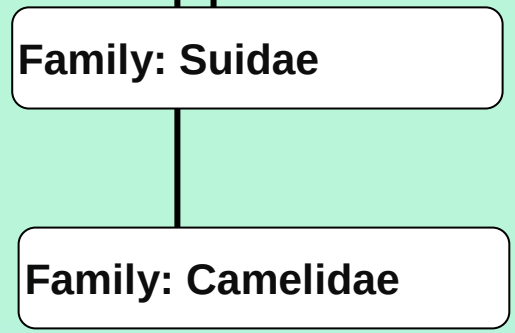


TABLE 17-1. Indications

Clinical Presentation	1st Choice	2nd Choice	3rd Choice
Anaphylaxis	AAF*	eHF§,¶	SF
Immediate gastrointestinal allergy	eHF†,§	AAF‖/SF**	
Food protein-induced enterocolitis syndrome (FPIES)	eHF‡	AAF	
Asthma and rhinitis	eHF†,§	AAF‖/SF**	
Acute urticaria or angioedema	eHF†,§	AAF‖/SF**	
Atopic dermatitis	eHF†,§	AAF‖/SF**	
Gastroesophageal reflux disease (GERD)	eHF†	AAF	
Allergic eosinophilic oesophagitis	AAF		
Cow's milk protein-induced enteropathy	eHF†,§	AAF	
Constipation	eHF†	AAF	Donkey milk§§
Severe irritability (colic)	eHF†	AAF	
CM protein-induced gastroenteritis and proctocolitis	eHF†	AAF	
Milk-induced chronic pulmonary disease (Heiner's syndrome)**	AAF‖	SF	eHF

*Recommendation 7.1.
†Recommendation 7.2.
‡If AAF refusal.
§Subject to local availability, HRF can be considered instead than eHF (7.4).
¶Subject to a negative SPT with the specific formula (panel recommendation).
‖AAF if a relatively high value on avoiding sensitization by SF and/or a low value on resource expenditure are placed.
**SF if a relatively low value on avoiding sensitization by SF and/or a high value on resource expenditure are placed.
††Subject to local availability.
‡‡This suggestion attributes a high value on avoiding exposure to even residual antigenic cow's milk proteins.
§§Based on reports from one case series (section 15).
¶¶Given that more than 50% of such children are allergic to soy, a careful clinical evaluation is necessary (panel recommendation).

WORLD ALLERGY ORGANIZATION

Fiocchi A, Schunemann H. Diagnosis and Rationale for Action against Cow's Milk Allergy. The WAO DRACMA guideline. WAO Journal & Pediatr Allergy Immunol 2010; *S1 (April), 1-105*.

POSITION STATEMENT

Guidelines for the use of infant formulas to treat cows milk protein allergy: an Australian consensus panel opinion

Andrew S Kemp,* David J Hill,* Katrina J Allen, Kym Anderson, Geoffrey P Davidson, Andrew S Day, Ralph G Heine, Jane E Peake, Susan L Prescott, Albert W Shugg and John K Sinn

2 Formula feeding in syndromes associated with cows milk protein allergy*

Syndrome	Onset of reaction	Maternal elimination of CMP if breastfeeding?	Choice of formula: First†	Second (if first not tolerated)	Third (if second not tolerated)
Immediate reaction					
Immediate food allergy	< 1 h	Yes	eHF (< 6 months)	AAF	—
			Soy (> 6 months)	eHF	AAF
Anaphylaxis	< 1 h	Yes	AAF (followed by urgent consultation with paediatric allergist)	—	—
Food protein-induced enterocolitis syndrome	1–3 h	No	eHF	AAF	—

Kemp AS. Med J Aus 2008; 188:109-112

Guidelines for the use of infant formulas to treat cows milk protein allergy: an Australian consensus panel opinion

Andrew S Kemp,* David J Hill,* Katrina J Allen, Kym Anderson, Geoffrey P Davidson, Andrew S Day, Ralph G Heine, Jane E Peake, Susan L Prescott, Albert W Shugg and John K Sinn

Delayed reaction					
Atopic eczema	Hours to days	Yes¶	eHF (< 6 months or > 6 months with FTT)	AAF	—
			Soy (> 6 months, no FTT)	eHF	AAF
Gastrointestinal syndromes, GORD, allergic eosinophilic gastroenteritis, food protein-induced enteropathy, constipation, severe irritability (colic)	Hours to days	Yes¶	eHF (< 6 months or > 6 months with FTT)	AAF	—
			Soy (> 6 months, no FTT)	eHF	AAF
Food protein-induced proctocolitis					
Formula-fed	> 24 h	—	eHF	AAF	—
Breastfed	> 24 h	Yes¶	—	—	—
Eosinophilic oesophagitis in infants	Days to weeks	Yes	AAF	—	—

Kemp AS. Med J Aus 2008; 188:109-112

How to Use These Recommendations

The DRACMA guidelines are not intended to impose a standard of care for individual countries and jurisdictions. They should, as any guideline, provide a basis for rational decisions for clinicians and their patients about the management of cow's milk allergy. Clinicians, patients, third-party payers, institutional review committees, other stakeholders, or the courts should never view these recommendations as dictates. Strong recommendations based on high quality evidence will apply to most patients for whom these recommendations are made, but they may not apply to all patients in all circumstances. No recommendation can take into ac-

WAO WORLD ALLERGY ORGANIZATION

Fiocchi A, Schunemann H. Diagnosis and Rationale for Action against Cow's Milk Allergy. The WAO DRACMA guideline. WAO Journal & Pediatr Allergy Immunol 2010; *S1 (April), 1-105*.

Quale latte

Chi è il bambino allergico al latte di mucca

Come si diagnostica

DRACMA

Esiste una prima scelta?

Implementazione delle linee-guida

Scelta della formula e storia naturale della APLV

Next steps - 1

1. DRACMA publication: WAO Journal, April 2010 – PAI, May 2010
2. Milan Meeting proceedings: JACI 2010
3. GLORIA educational modules
4. World allergy societies endorsement & input sought
5. World sister societies endorsement & input sought
6. DRACMA symposia during allergy and nutrition society meetings
7. Outreach towards patient organisations
8. Creation of an international bureau for dissemination and update

Next steps - 2

The international bureau for dissemination and update:

a. Translation and publication

b. Educational materials

c. Translational updates to link-up with basic & clinical R&D and the industry

d. Communication with government agencies and NGOs

e. Cultural adaptation

Quale latte

Chi è il bambino allergico al latte di mucca

Come si diagnostica

DRACMA

Esiste una prima scelta?

Implementazione delle linee-guida

Scelta della formula e storia naturale della APLV

Recommendations for avoidance or delayed introduction of allergenic foods

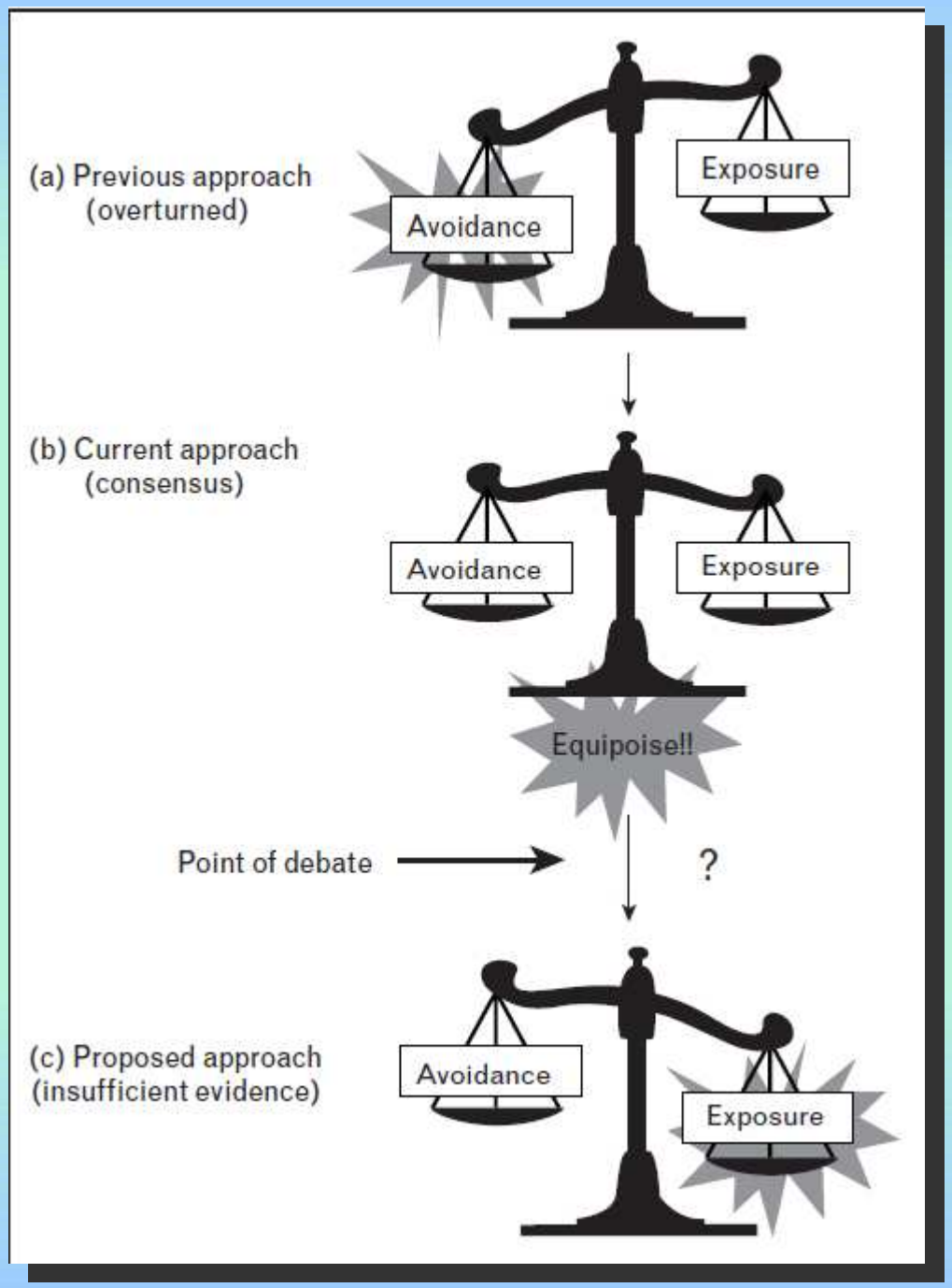
Year (author)	Publication type	Title	Setting
1999 - Host	Joint position statement ESPACI-ESPGHAN	Dietary products used in infants for treatment and prevention of food allergy.	Primary Treatment
2000	Position statement (AAP)	Hypoallergenic Formulas	Primary
2004 - Muraro	Literature review (EAACI)	Dietary prevention of allergic diseases in infants and small children.	Primary
2006 – Adverse Reactions to Foods Committee	Literature review (ACAAI)	Food allergy and the introduction of solid foods to infants: a consensus document	Primary

Allen CW. Food allergy: Is strict avoidance the only answer? Pediatr Allergy Immunol 2009: 20: 415–22.

Recommendations for avoidance or delayed introduction of allergenic foods

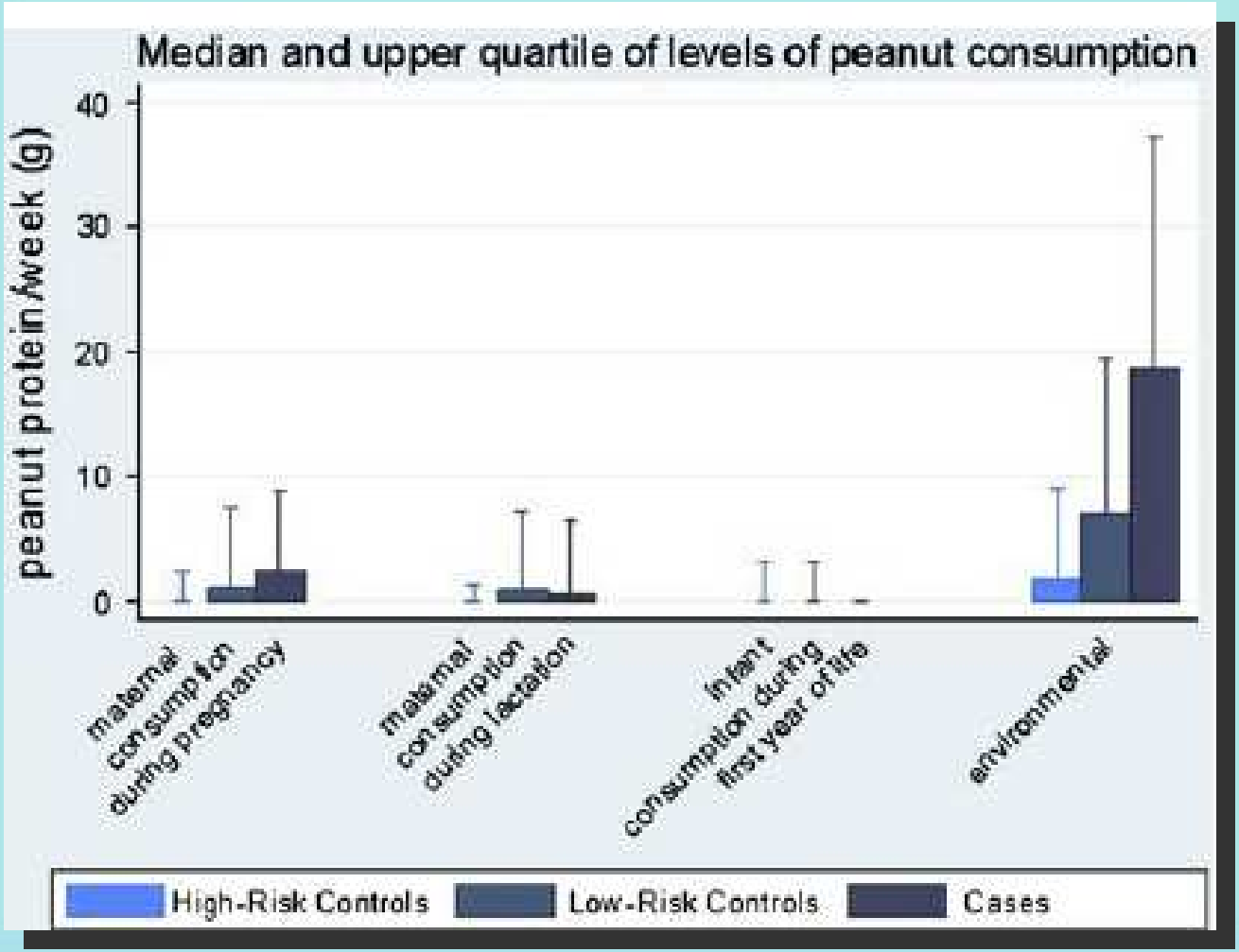
Year (author)	Publication type	Title	Setting
2006 - Osborne	Cochrane systematic review	Formulas containing hydrolysed protein for prevention of allergy and food protein intolerance in infants.	Primary
2006 - Kramer	Cochrane systematic review	Maternal dietary antigen avoidance during pregnancy and/or lactation, or both, for preventing or treating atopic disease in the child.	Primary Treatment
2007 - Prescott	Position statement ASCIA	Primary allergy prevention in children	Primary

Allen CW. Food allergy: Is strict avoidance the only answer? Pediatr Allergy Immunol 2009: 20: 415–22.



Pregcott S, Fiocchi A. Avoidance or exposure to foods in prevention and treatment offood allergy? Corr Opin Allergy Clin Immunol 2010,10:258–66

Exposures associated with peanut allergy



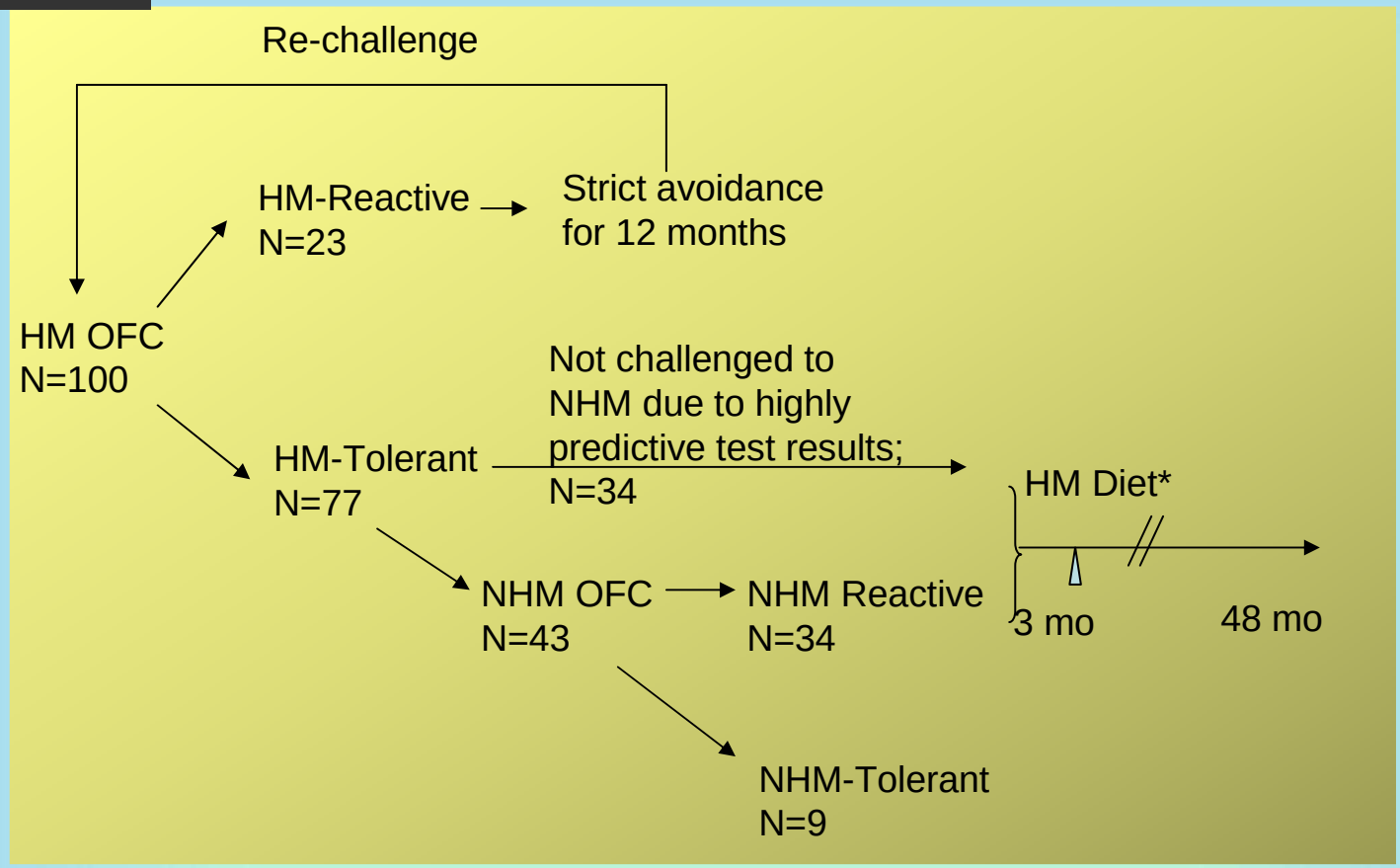
Fox AT. High environmental exposure to peanut in infancy as a risk factor for peanut allergy. J Allergy Clin Immunol 2009;123:417-23

“Baked-Milk” Study

- 100 milk-allergic subjects enrolled
  - mean age: 6.7 yrs; range: 2.6 – 17.3 yrs
  - 62% males
- Challenged with baked muffin, waffle & uncooked milk [~ 3 oz milk protein/baked product]
- Milk challenges:
  - 77 HCM tolerant [baked-milk products only]
  - 23 Allergic [could not tolerate milk in any form]

Nowak-Wegrzyn A. Tolerance to extensively heated milk in children with cow's milk allergy. J Allergy Clin Immunol 2008, 122:342-7

“Baked Milk” Study

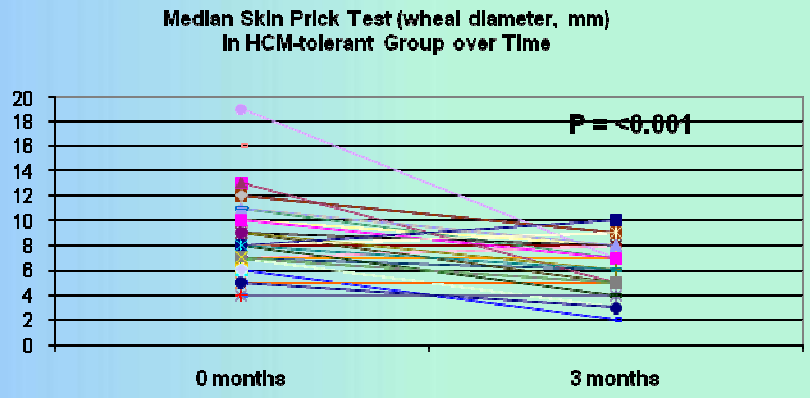


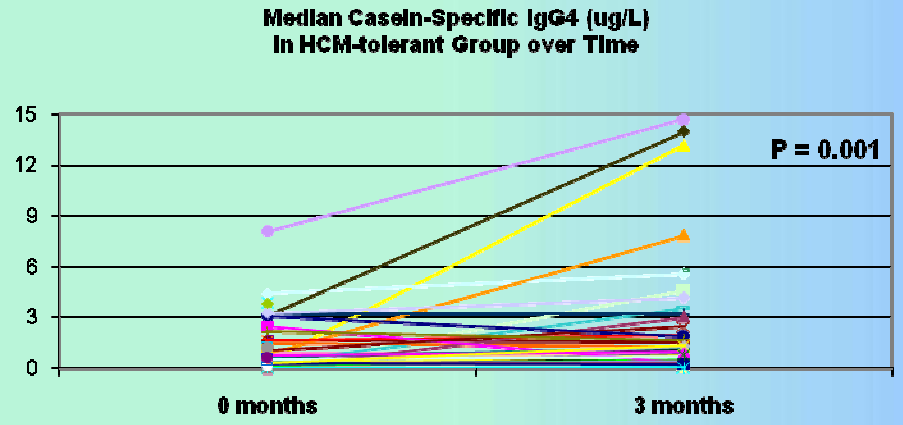
*The subjects in the HM Diet group will be followed every 6 months for up to 48 months or until become cow’s milk-tolerant.

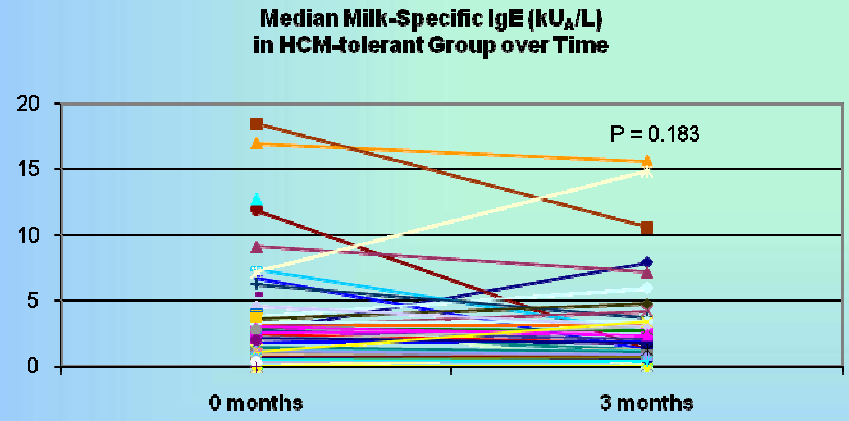
Nowak-Wegrzyn A. Tolerance to extensively heated milk in children with cow's milk allergy. J Allergy Clin Immunol 2008, 122:342-7

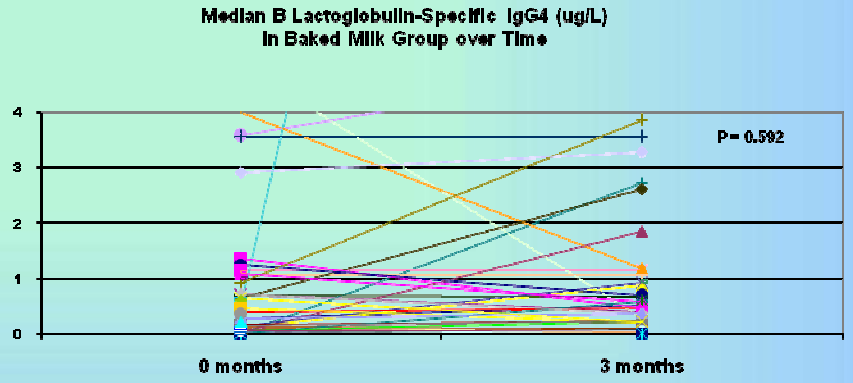
Changes in Milk-specific PST, IgE & IgG_4 in HCM-Tolerant Subjects

Milk PST decreases and casein-specific IgG4 increases









Nowak-Wegrzyn A. Tolerance to extensively heated milk in children with cow's milk allergy. J Allergy Clin Immunol 2008, 122:342-7

Eliciting dose at diagnostic challenge in 112 CMA children

ED	n	%	Epinephrine?
0.1 mL	14	12.5	12.5
0.4 mL	10	8.9	21.4
1.4 mL	20	17.9	39.3
		19.6	60.7%
		17.9	
		10.7	
		12	
		100	

Can I recommend a non absolute avoidance?

Can I avail the use of little doses?

Fiocchi A. Factors associated with cow's milk allergy outcomes in infant referrals: the Milan Cow's Milk Allergy Cohort study. Ann Allergy Asthma Immunol 2008;101:166-73

A vastly altered approach to food allergy management

1. The change from a milk avoidance diet to a milk-limited diet could provide a substantial improvement to the quality of life of milk-allergic individuals.
2. The frequency of prolonged or permanent milk allergy may be reduced if this type of diet can augment the development of tolerance.
3. These children receiving limited, extensively heated essentially reported no acute milk-induced allergic a result of this diet.

Skripak JM. Mammalian milk allergy: avoidance strategies and oral desensitization
Curr Opin Allergy Clin Immunol. 2009;9:259-64.

Modification of allergenicity as a promoter of tolerance?

Protection on CMA with hypoallergenic formula in high risk infants: seen for both partially and extensively hydrolysed formula.

not allergen avoidance

but

allergen modification?

Allen CW. Food allergy: Is strict avoidance the only answer? Pediatr Allergy Immunol 2009: 20: 415–422.

In vivo (skin prick test and/or challenge) studies on residual allergenicity of CM hydrolysates

Hydrolysate	Authors				
	Sampson	Wahn	Ragno	Hill	Giampietro
Nutramigen	P	P	-	C	-
Pregestimil	-	P	-	N	-
Alimentum	P	-	P/C	-	-
Profylac	-	P/C	-	P/C	C
Nutrilon Pepti	-	-	-	P/C	C
Alfarè	-	P/C	-	C	-
Nan HA	-	-	P/C	-	-
P= skin prick-positive; C= challenge positive; N= negative; - = not tested					

Terracciano L. Use of hydrolysates in the treatment of cow's milk allergy
Ann Allergy Asthma Immunol 2002; 89 (Suppl), 86-90

Loss of tolerance after an exclusion diet

The anecdote

At the age of 18 she inadvertently entered a dairy shop and inhaled milk proteins experiencing a fatal reaction (asthma, hurticaria, angioedema).

The literature

MARTIN ESTEBAN M, PASCUAL C, FLANDOR A, OJIEDA JA. A possible consequence of long term elimination diet in IgE mediated subclinical food hypersensitivity. Allerg Immunol (Paris) 1988;**20**:55–56.

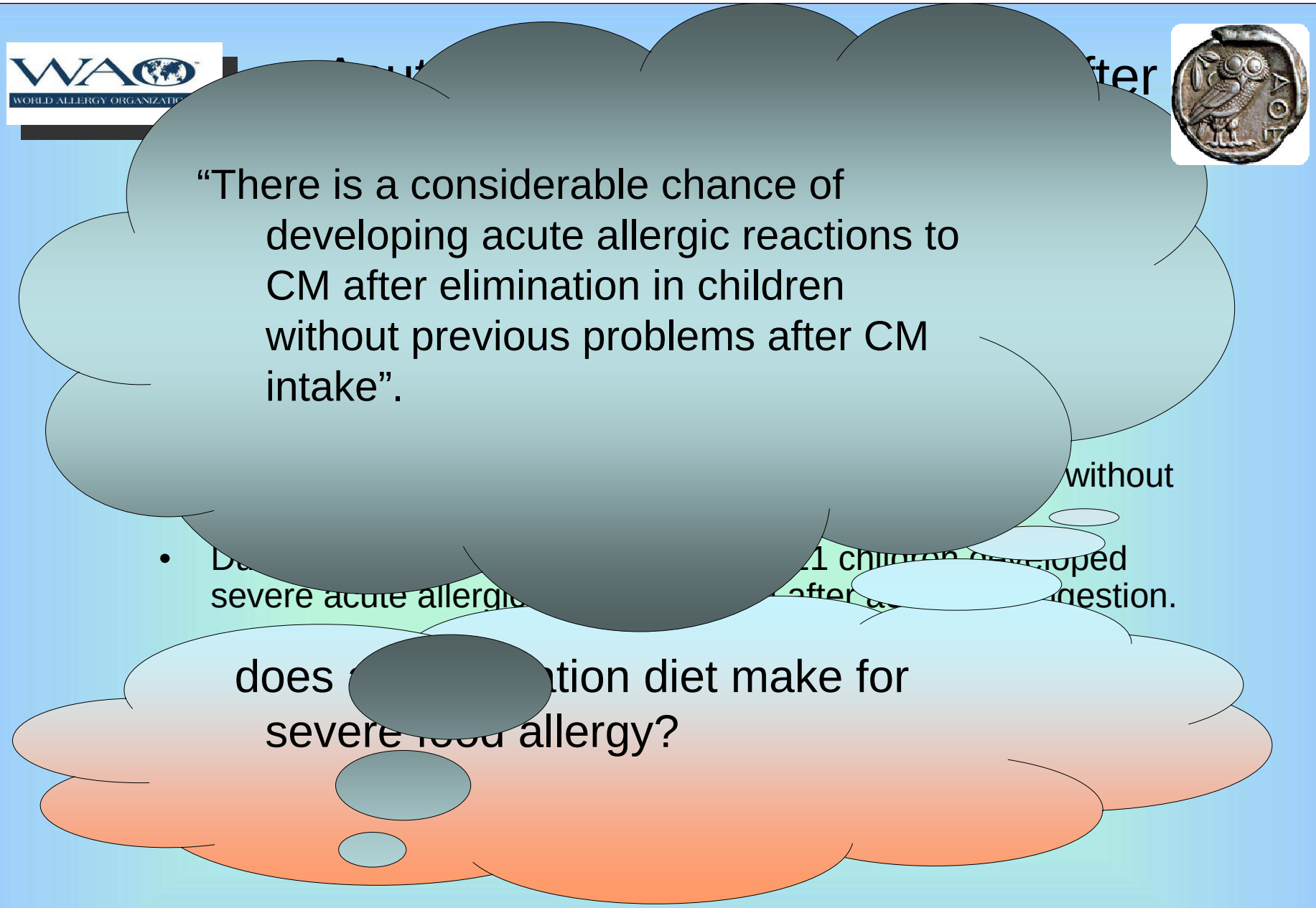
LARRAMENDI CH, MARTIN ESTEBAN M, PASCUAL M, FIANDOR A, DIAZ PENA JM. Possible consequences of elimination diets in asymptomatic immediate hypersensitivity to fish. Allergy 1992;**47**:490–494.

DAVID TJ. Anaphylactic shock during elimination diets for severe atopic eczema. Arch Dis Child 1984;**59**:983–986.

The non sequitur

. In our case the temporal link between the diet and the development of symptoms is suggestive for a causal relationship between the two.

Barbi et al. *Allergy* 2004;**59**:668



Flinterman AE. Acute allergic reactions in children with AEDS after prolonged cow's milk elimination diets. Allergy 2006; 61:370-4

Wrongful conviction: allergens found guilty of allergy epidemic

Prescott S, Fiocchi A. Avoidance or exposure to foods in prevention and treatment of food allergy? Curr Opin Allergy Clin Immunol 2010,10:258–66

There is a considerable chance of developing acute allergic reactions to CM after elimination in children without previous problems after CM intake.

There is a considerable chance of developing tolerance to CM after elimination in children with previous problems after CM intake.

AEDS after prolonged
ination diets. Allergy 2006; 61:370-4
JM. T istory of IgE-mediated cow's milk allergy.
J Allergy Clin Immunol 2007;120:1172-7

Lessons from OIT

At least a subset of children treated wit SOTI acquire definitive tolerance

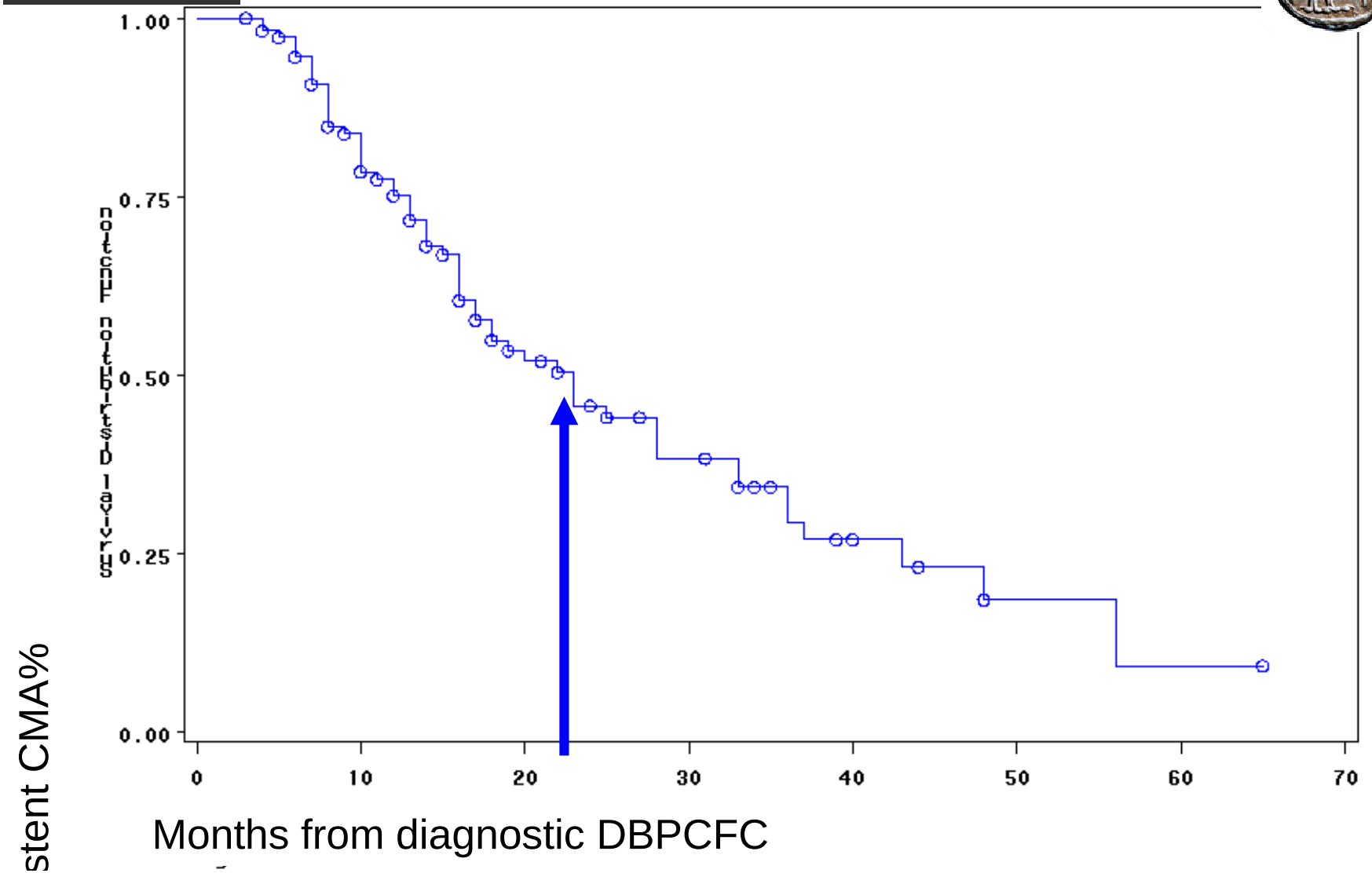
Food -specific IgE levels decrease over 24 months

Such studies have been interpreted as not lending support for the proposition that continued exposure to allergen will increase the IgE level or delay the acquisition of tolerance.

Allen CW. Food allergy: Is strict avoidance the only answer? Pediatr Allergy Immunol 2009: 20: 415–22

Buchanan AD,. Egg oral immunotherapy in nonanaphylactic children with egg allergy. J Allergy Clin Immunol 2007: 119: 199–205.

MiCMAC cohort: survival curve



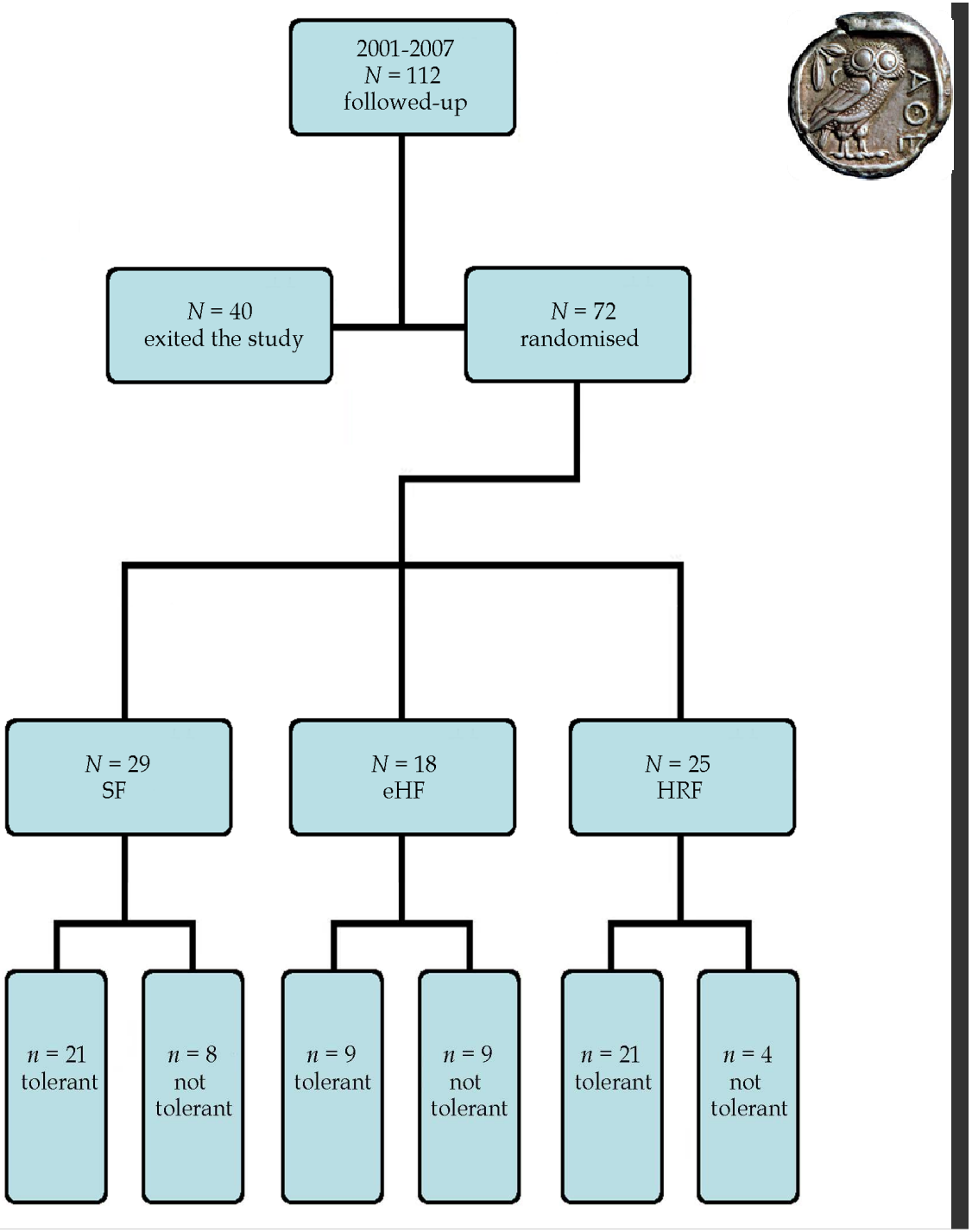
stent CMA%

Fiocchi A. Factors associated with cow's milk allergy outcomes in infant referrals: the Milan Cow's Milk Allergy Cohort study. Ann Allergy Asthma Immunol 2008;101:166-73

Profile of the child with long-term CMA

1. Presenting with asthma
2. CM sensitisation at ImmunoCAP®
3. Co-sensitisation to foods at SPT
4. Co-sensitisation to beef
5. Co-sensitisation to grass and dog dander
6. Co-sensitisation to less prevalent allergens (soy)

Fiocchi A. Factors associated with cow's milk allergy outcomes in infant referrals: the Milan Cow's Milk Allergy Cohort study. Ann Allergy Asthma Immunol 2008;101:166-73



Terracciano L.
Impact of dietary regimen on the duration of cow's milk allergy. Cin Experim Allergy 2010, 40:125-9

Methods: randomisation

Children breastfed, or symptomatic despite e
prescription were switched to a diffe

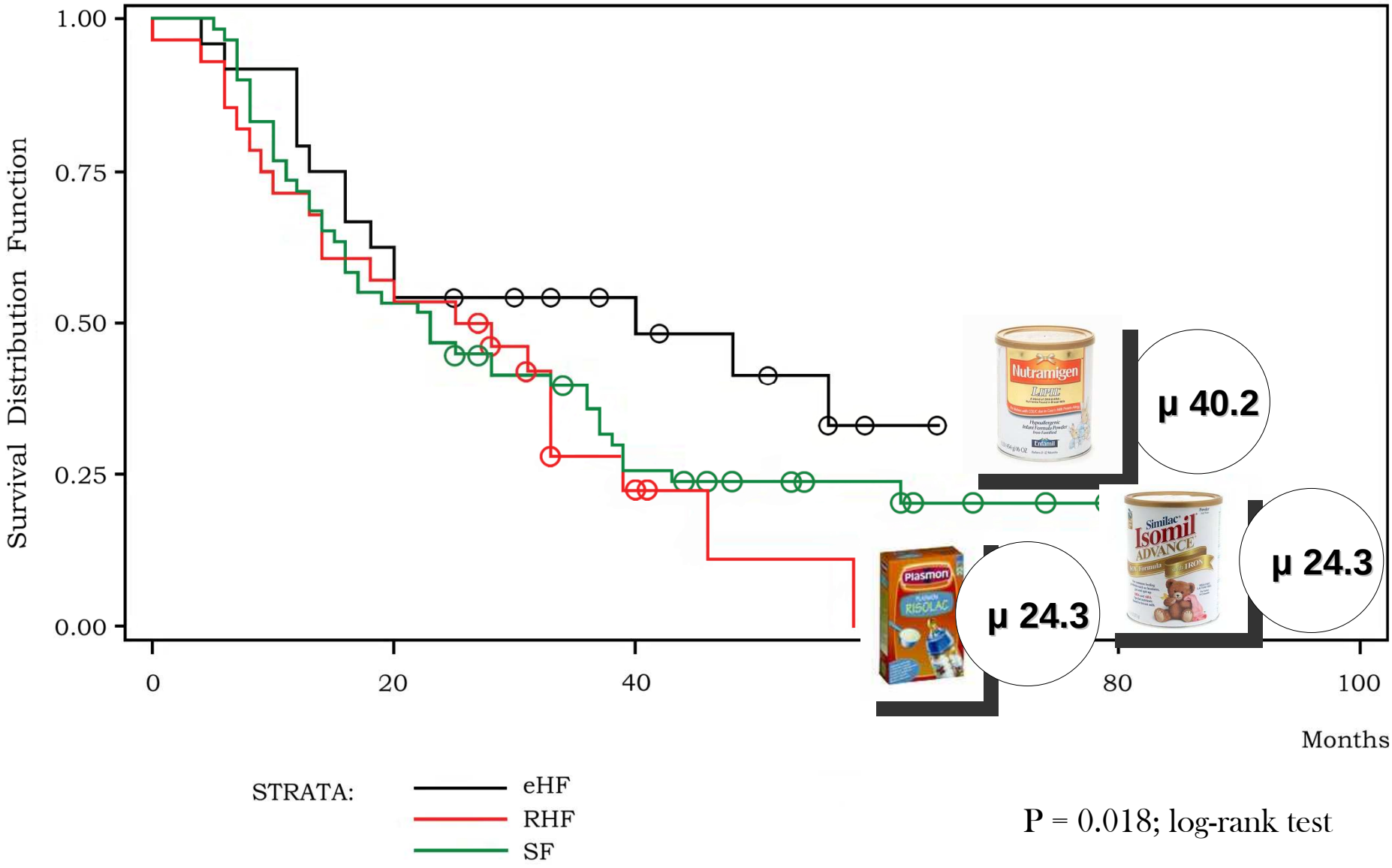
Jan – Apr: SF

May – Aug: eHF

Sept – Dec: SF

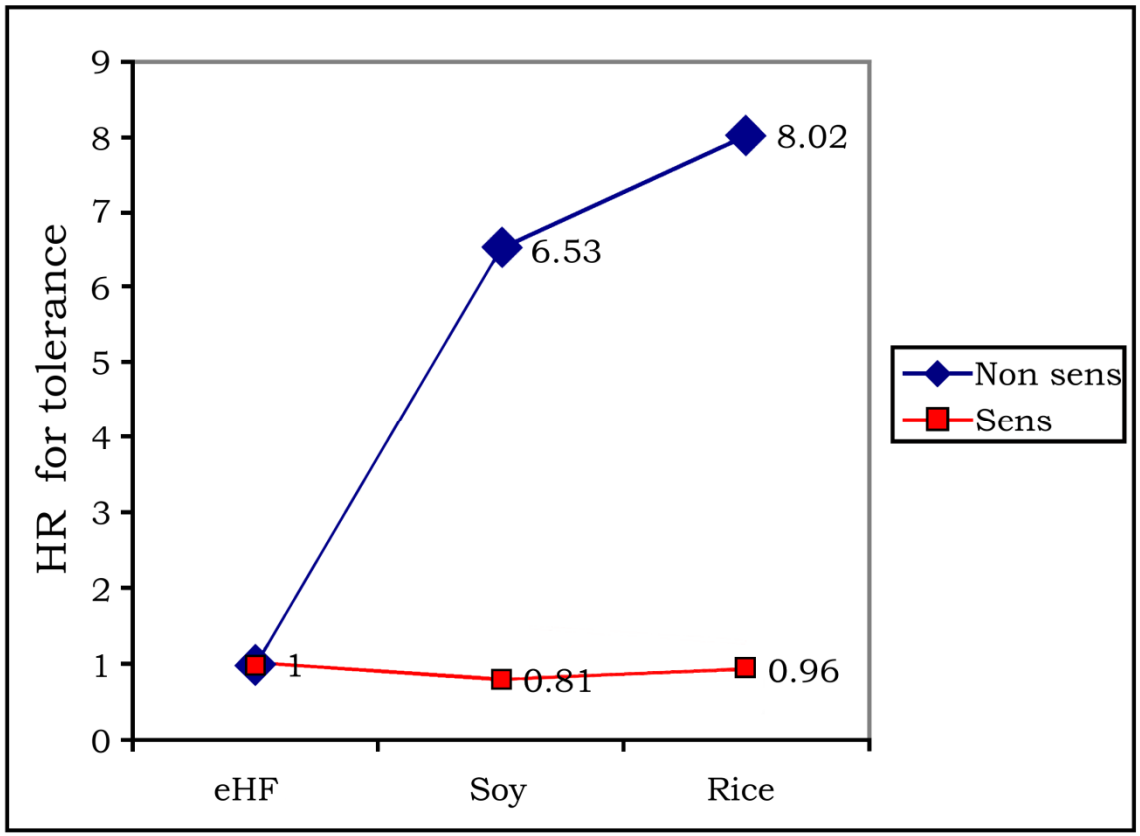
An elemental formula (Neocate ®, SHS, UK) was administered as rescue therapy

Results: mean duration of CMA



P = 0.018; log-rank test

Polysensitised children are insensitive to avoidance



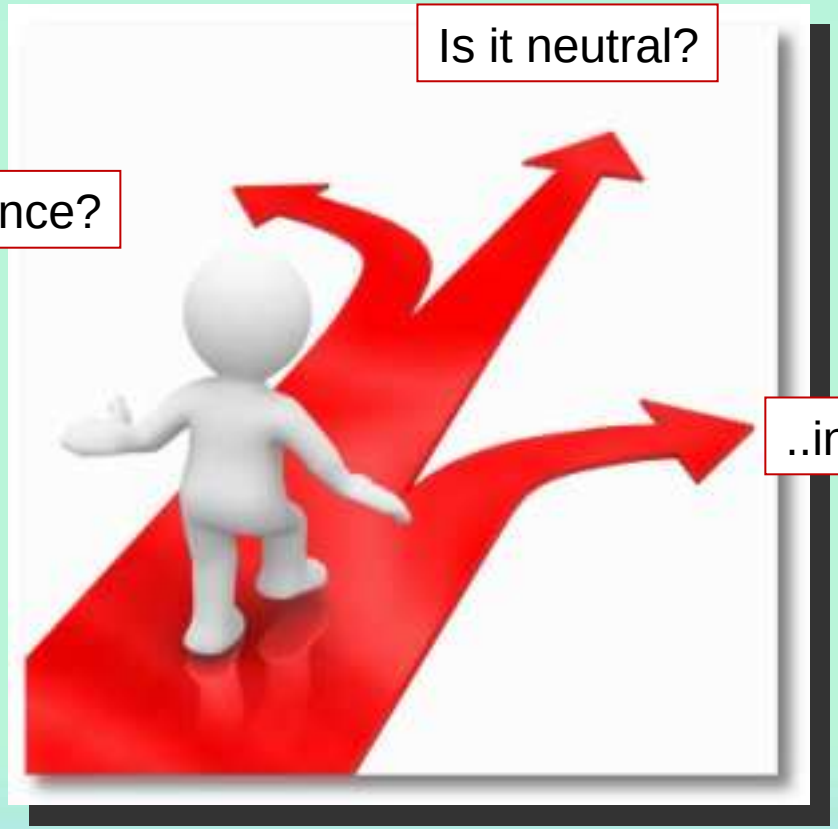
Terracciano L. Impact of dietary regimen on the duration of cow's milk allergy. Clin Exper Allergy 2010; , 40:125-9

Profile of the child with long-term CMA

1. Presenting with asthma
2. CM sensitisation at ImmunoCAP®
3. Co-sensitisation to foods at SPT
4. Co-sensitisation to beef
5. Co-sensitisation to grass and dog dander
6. Exposed to CM proteins
7. Co-sensitisation to less prevalent allergens

Fiocchi A. Factors associated with cow's milk allergy outcomes in infant referrals: the Milan Cow's Milk Allergy Cohort study. Ann Allergy Asthma Immunol 2008;101:166-73

Exposure and natural history

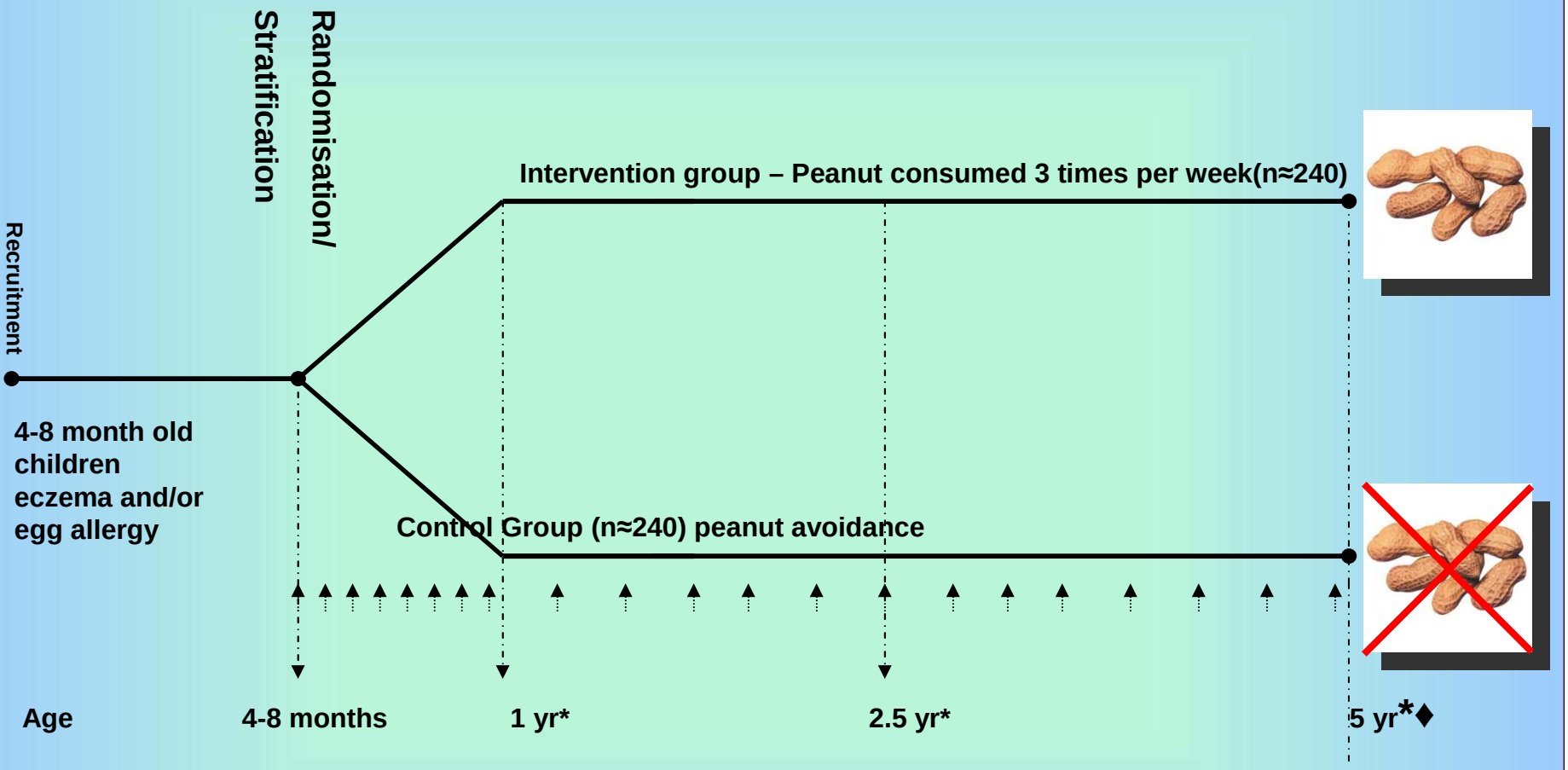


Is it neutral?

… decrease tolerance?

..increase tolerance?

LEAP Study – Immune Tolerance Network



WAO Meeting Bangkok 2007 - Courtesy of Stephen Durham,

Immune Tolerance Network


WAO Meeting Bangkok 2007 - Courtesy of Stephen Durham,

WAO Meeting Bangkok 2007 - Courtesy of Stephen Durham,

WAO Meeting Bangkok 2007 - Courtesy of Stephen Durham,

dilemmas that have not yet been addressed. Based on the currently available evidence, there can only be one verdict beyond any reasonable doubt: to uphold the current approaches until such time that there is sufficient evidence to indicate that these should be changed. Again, the burden of proof lies with those who are proposing change, and so far clear evidence has not been produced.

Prescott S, Fiocchi A. Avoidance or exposure to foods in prevention and treatment of food allergy? Curr Opin Allergy Clin Immunol 2010,10:258–66

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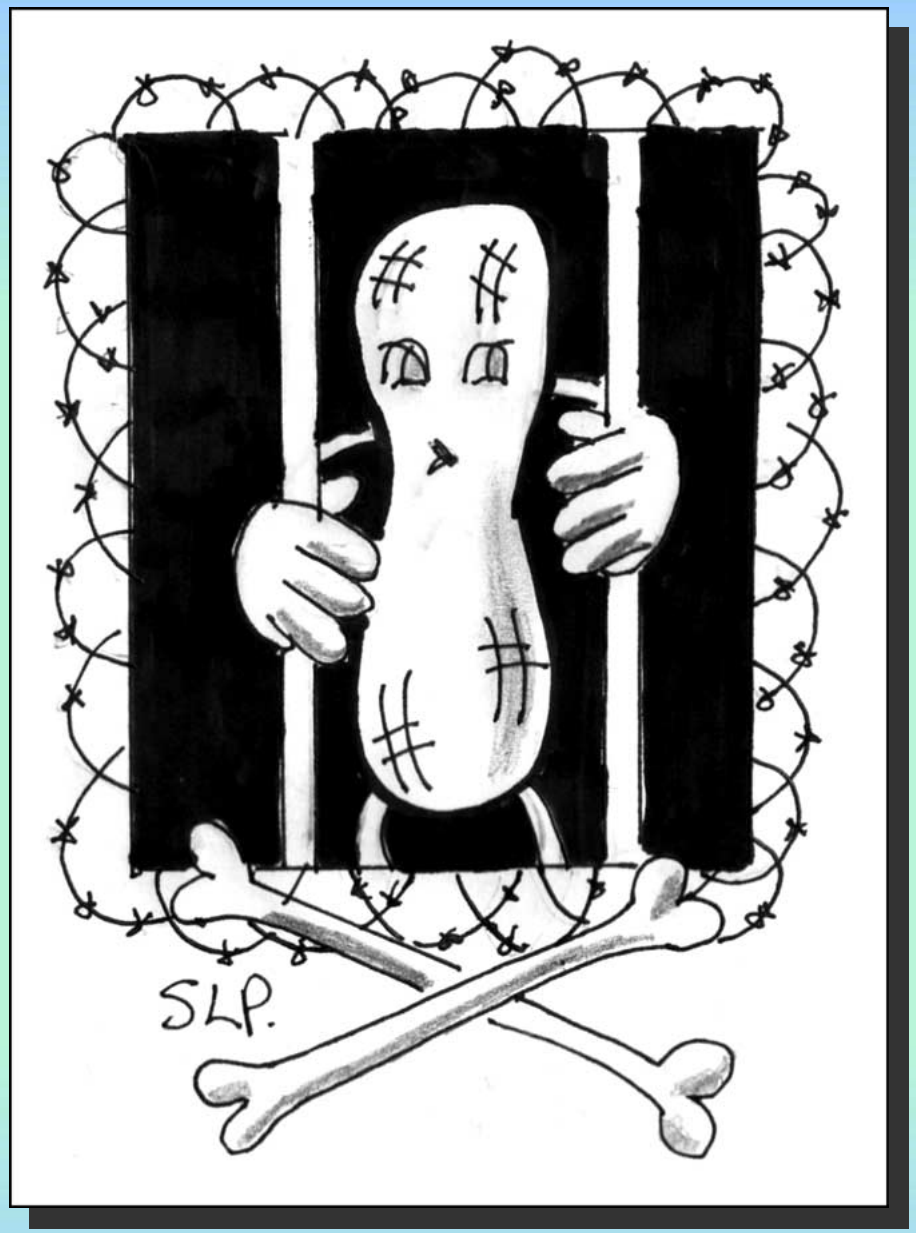

Prescott S, Fiocchi A. Avoidance or exposure to foods in prevention and treatment of food allergy? Curr Opin Allergy Clin Immunol 2010,10:258–66

Between a strict diet and desensitisation

Diet therapy: not for everybody suspicious – not for all the sensitised. Just for the challenge+

Strict avoidance:

a. Prevents severe reaction risk
b. Does not worsen food allergy
c. Helps some to reach tolerance

Some avoidance:

a. Possible in some cases
b. Could expose to severe reactions
c. Could modulate food allergy: tolerance? persistence?

Does OIT modify natural history?

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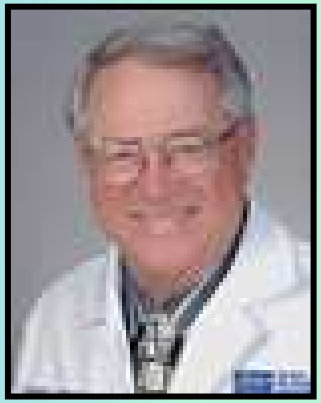

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We look forward to seeing you in Dubai!