ISTITVTO SVPERIORE DI SANITÀ

AiC Associazione Italiana Celiachia

SISTE

Allergie, intolleranze e celiachia: tra verità scientifiche e falsi miti

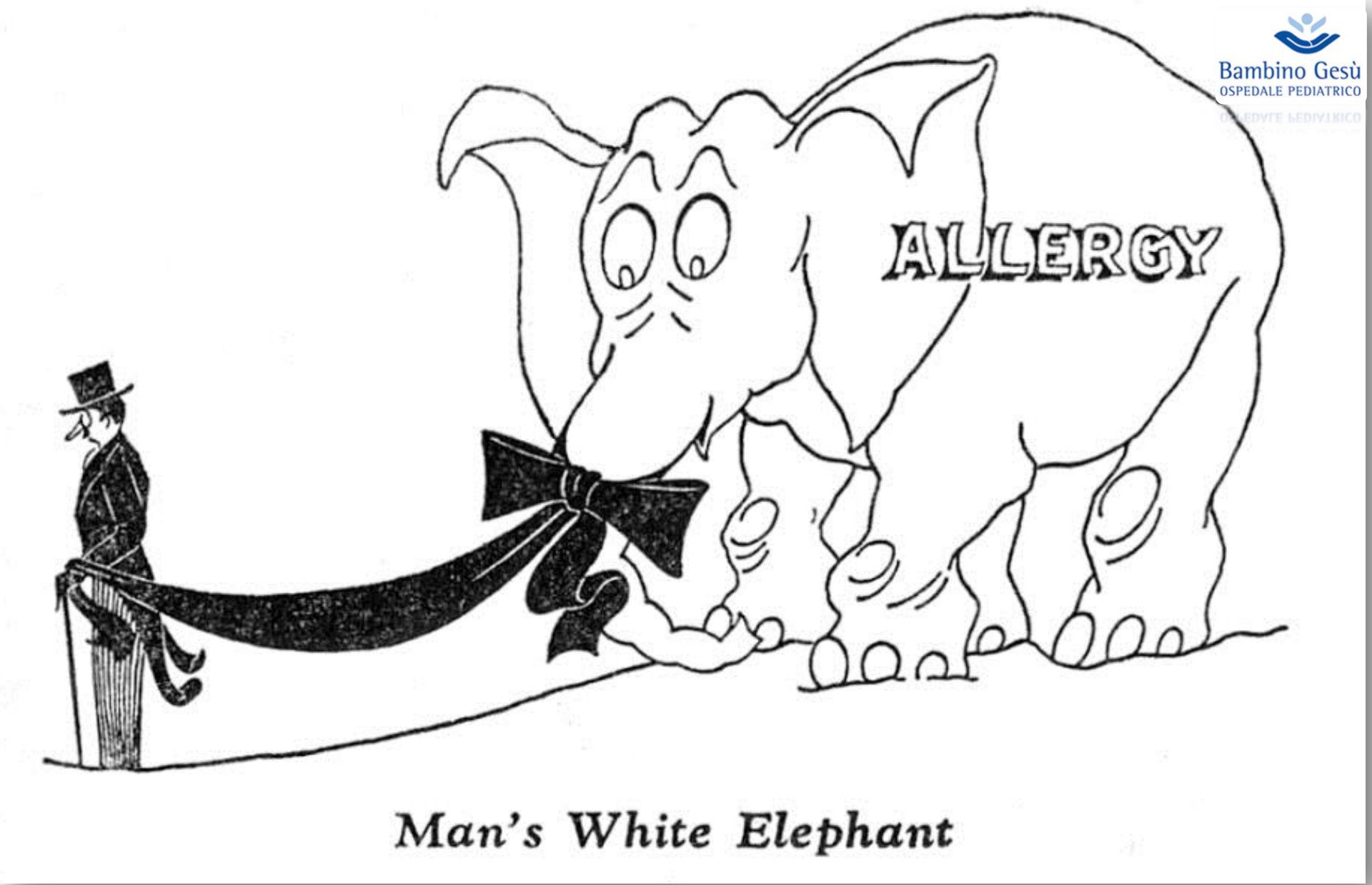
Roma, 20 maggio 2016

Attualità sulle allergie alimentari

Alessandro Fiocchi

UOC Allergologia
OPBG

Roma, 20 maggio 2016



Man's White Elephant

Vaughan VT. Primer of allergy. Mosby, St Louis MO, 1939

Over 10% with challenge-proven food allergy!

Bambino Gesù
OSPEDALE PEDIATRICO

Reactions on challenge:

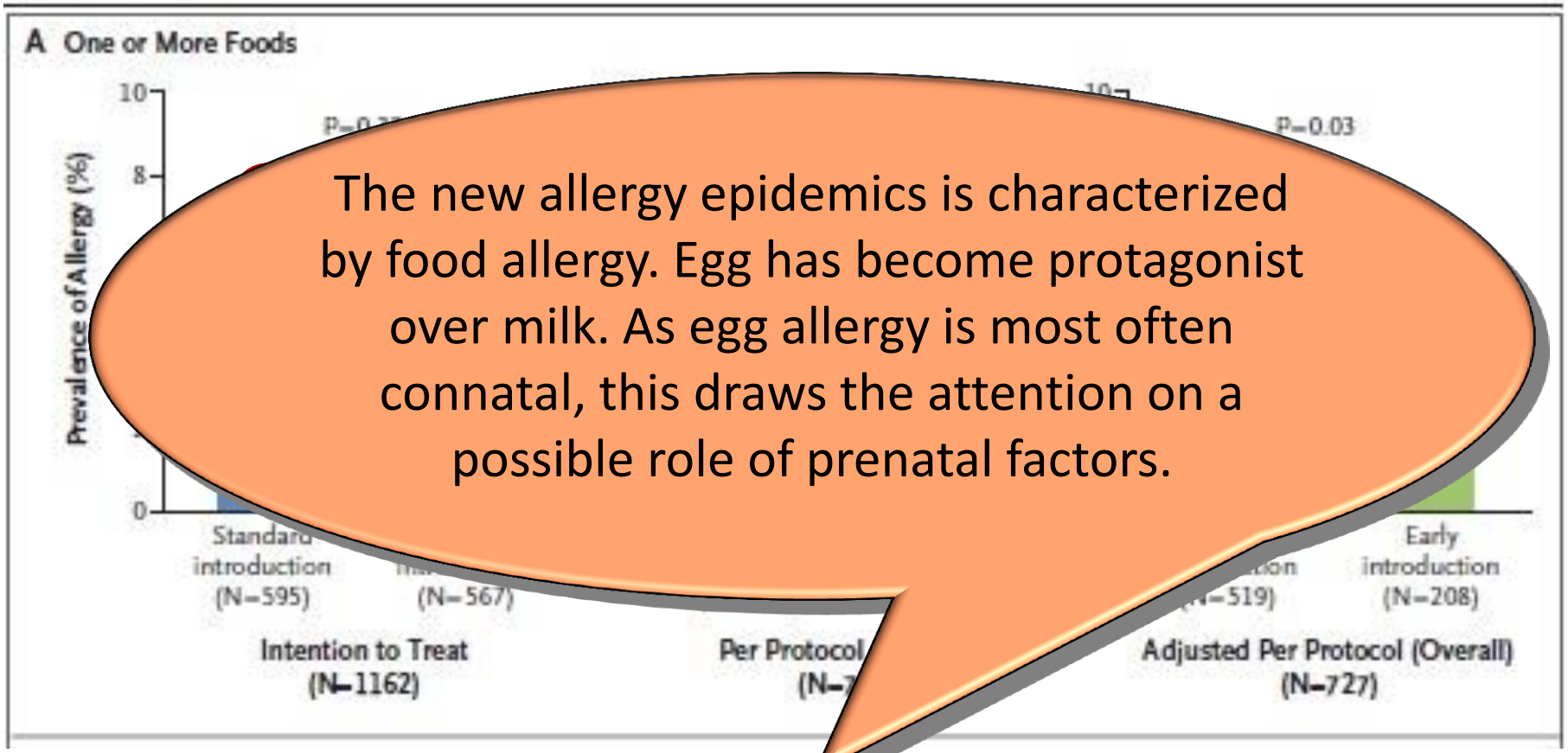
- egg: 9%
- peanut: 3%
- other: 2%

- **TOTAL: >10%**

Osborne NJ. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined chal-lenge criteria in infants. J Allergy Clin Immunol 2011;127:668-76

Does early intro prevent all food allergies?

1303 exclusively breast-fed infants from the general population



The new allergy epidemics is characterized by food allergy. Egg has become protagonist over milk. As egg allergy is most often connatal, this draws the attention on a possible role of prenatal factors.

Perkin MR; EAT Study Team. Randomized trial of introduction of allergenic foods in breast-fed infants. N Engl J Med. 2016 May 5;374:1733-43

Bambino Gesù
OSPEDALE PEDIATRICO

Società Italiana di Pediatria

Club Allergologico:

Il bambino allergico tra ospedale e territorio

10 giugno 2016

ROMA

Sede - Auditorium S. Paolo
Ospedale Pediatrico Bambino Gesù
Viale F. Baldelli, 38 – 00146 Roma
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www.allegriallergia.org
www.biomedia.net

Università di Roma Tor Vergata
Bambino Gesù OSPEDALE PEDIATRICO
SCUOLA DI PEDIATRIA

Roma Pediatria

1. L'intolleranza alimentare
2. La dieta modifica la storia naturale dell'AA?
3. Svezzamento e prevenzione dell'allergia
4. Le diete inutili
5. Conclusioni

Cronache

Barletta La vittima aveva 29 anni. Due donne salvate dall'antidoto

Test anti allergie da eBay Muore nel centro clinico

Medicina forse contaminata, controlli in tutta Europa

DAL NOSTRO INVIATO

BARLETTA — Cinque grammi. Solo cinque. Di una sostanza innocua. Ma acquistata via internet su eBay da una partita probabilmente contaminata da un veleno potentissimo. Che ora si cerca, in tutta Europa, di fermare prima che possa uccidere ancora. Sperando che, come si sospetta, non lo abbia già fatto. Teresa Sunno, ventinovenne di Andria, residente a Trani, è morta così. In dieci minuti. Dopo aver bevuto quella sostanza, somministratale dal suo gastroenterologo privato alla ricerca di intolleranze alimentari. Non ha avuto il tempo nemmeno di arrivare al pronto soccorso, Teresa. Dove invece sono state salvate per un soffio Anna Abrescia di 40 anni e Addolorata Piazzolla, di 62, che avevano ingerito la stessa sostanza e in pochi minuti hanno avuto un collasso. Vive grazie a una fiala blu che Cosimo Sannito, responsabile del Pronto soccorso mostra orgoglioso: «Siamo riusciti tempestivamente a individuare l'antidoto e a somministrarlo». Ora vi siano nitrati fortemente tossici. A Rovigo si indaga su un altro laboratorio che commercializzava la stessa sostanza. Un'operazione capillare seguita passo passo dal ministro della Salute, Renato Balduzzi. Che ieri ha portato ad un primo risultato: ci sono altre situazioni sospette.

Il capo della Procura di Trani, competente delle indagini, Carlo Maria Capristo, raccomanda cautela: «Non dobbiamo spargere il panico. Sono in corso test specialistici sulla tossicità del farmaco. Sono analisi approfondite. Occorre un po' di tempo e un po' di prudenza». Forse ne doveva avere di più il medico ad acquistare il farmaco online. Dove sicuramente si può risparmiare. Ma si trovano, sempre più spesso provenienti dalla Cina. Il test letale, si sospetta che possa essere stato originariamente prodotto lì. Ora il medico, Ruggero Spinazzola, rischia un'accusa di omicidio colposo, lesioni gravi e avvelenamento colposo di sostanze alimentari. Ma si approfondisce anche la posizione del dottor Pappagallo, medico associato in quello studio clinico, cui si era rivolta la ragazza.

«Aveva un po' di acidità di stomaco» racconta Giovanni, l'amico che l'aveva accompagnata agli accertamenti e ora non si dà pace. «Teresa è stata sottoposta prima a una gastroscopia e poi a una colonscopia su consiglio del dottor Pappagallo, che la mandava però allo studio Spinazzola a Barletta». E non era sempre andata bene. Lo racconta il ragazzo: «Dopo alcune analisi, ha ritenuto di farla sottoporre a test per le intolleranze alimentari. Il primo lo ha fatto due settimane fa per verificare l'intolleranza al lattosio: è stata male tutto il giorno dopo averlo fatto. Il secondo era oggi (ieri, *ndr*). Si è sentita male, ma non è stata l'unica. Solo che lei poi è morta». Non consola, ma grazie all'allerta lanciato la morte di Teresa potrebbe non essere stata inutile.

Virginia Piccolillo

Giovane La vittima di ieri a Barletta: Teresa Sunno, 29 anni, originaria di Andria. Salve per un soffio altre due donne

Il commento

QUEI FARMACI IN RETE SENZA CONTROLLI

di ADRIANA BAZZI

La vicenda di Barletta (una donna morta dopo un esame per le intolleranze alimentari e altre due ricoverate in osservazione) è complicata e pone almeno tre tipi di problemi. Primo: l'utilizzo di medicinali comperati su eBay (in questo caso il sorbitolo che, usato per il test, doveva dimostrare l'incapacità dell'intestino di assorbire certi cibi e spiegare certi sintomi del paziente, come il gonfiore intestinale, il sovrappeso, la cefalea e via dicendo). Il commercio di medicine via Internet è senza controllo: al top della classifica ci sono i farmaci Viagra-simile, contro l'impotenza sessuale, che di solito sono acquistati da cittadini comuni, ma, a quanto pare, anche i medici privati (per risparmiare?) comprano prodotti farmaceutici (il sorbitolo) da utilizzare nei loro ambulatori, senza prove di sicurezza. Secondo: i centri privati dovrebbero garantire la qualità delle loro prestazioni (il

Risparmi
Per risparmiare i

La sostanza

Sorbitolo

Il sorbitolo è uno zucchero semplice, contenuto in frutti come mele, pere, susine, ciliegie e in quelli del sorbo (da cui deriva proprio il nome sorbitolo). Secondo alcune approfondite ricerche scientifiche la sostanza può essere responsabile di malassorbimento intestinale, con la comparsa di sintomi diversissimi che vanno dal gonfiore di pancia, ai dolori addominali, alla stanchezza, fino al mal di testa. Il test al sorbitolo viene utilizzato per diagnosticare questi disturbi. Il suo uso è, comunque, sconsigliato nei bambini di età inferiore a un anno di vita

Dalla Gran Bretagna
La sostanza prodotta in Gran Bretagna. Sotto sequestro il centro che cura le intolleranze

Bambino Gesù
OSPEDALE PEDIATRICO

Symptom-based Clinical Score (Cow's Milk Protein Intolerance Score)

Symptom	Score	
Crying*	0	<1 hour/day
	1	1-1.5 hours/day
	2	1.5-2 hours/day
	3	2 to 3 hours/day
	4	3 to 4 hours/day
	5	4 to 5 hours/day
	6	>5 hours/day
Regurgitation†	0	0-2 episodes/day
	1	>3-<5 of small volume
	2	>5 episodes of >1 coffee spoon
	3	>5 episodes of +half of the feedings in <half of the feedings
	4	Continuous regurgitations of small volumes >30 min after each feeding
	5	Regurgitation of half to complete volume of a feeding in at least half of the feedings
	6	Regurgitation of the "complete feeding" after each feeding
Stools	4	Type 1 and 2 (hard stools)
(Bristol scale)†	0	Type 3 and 4 (normal stools)
	2	Type 5 (soft stool)
	4	Type 6 (liquid stool, if unrelated to infection)
	6	Type 7 (watery stools)
Skin symptoms	0 to 6	Atopic eczema
		Head-neck- trunk / Arms-hands-legs-feet
		Absent 0 / 0
		Mild 1 / 1
		Moderate 2 / 2
		Severe 3 / 3
	0 or 6	Urticaria (no 0/yes 6)
Respiratory symptoms	0	No respiratory symptoms
	1	Slight symptoms
	2	Mild symptoms
	3	Severe symptoms

*Crying was only considered if the child was crying for 1 week or more, assessed by the parents, without any other obvious cause.
†Vandenplas Y, Hachimi-Idrissi S, Casteels A, Mahler T, Loeb H. A clinical trial with an "anti-regurgitation" formula. Eur J Pediatr 1994;153:419-23.
†Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997;32:920-4.

Vandenplas Y. Treatment of Cow's Milk Protein Allergy. Pediatr Gastroenterol Hepatol Nutr. 2014;17:1-5

Food intolerance [do not] exist

Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

Vandenplas Y. Debates in allergy medicine: food intolerance does exist. World Allergy Organ J. 2015 Dec 14;8:36

Food allergy does not exist: a rather simple task.

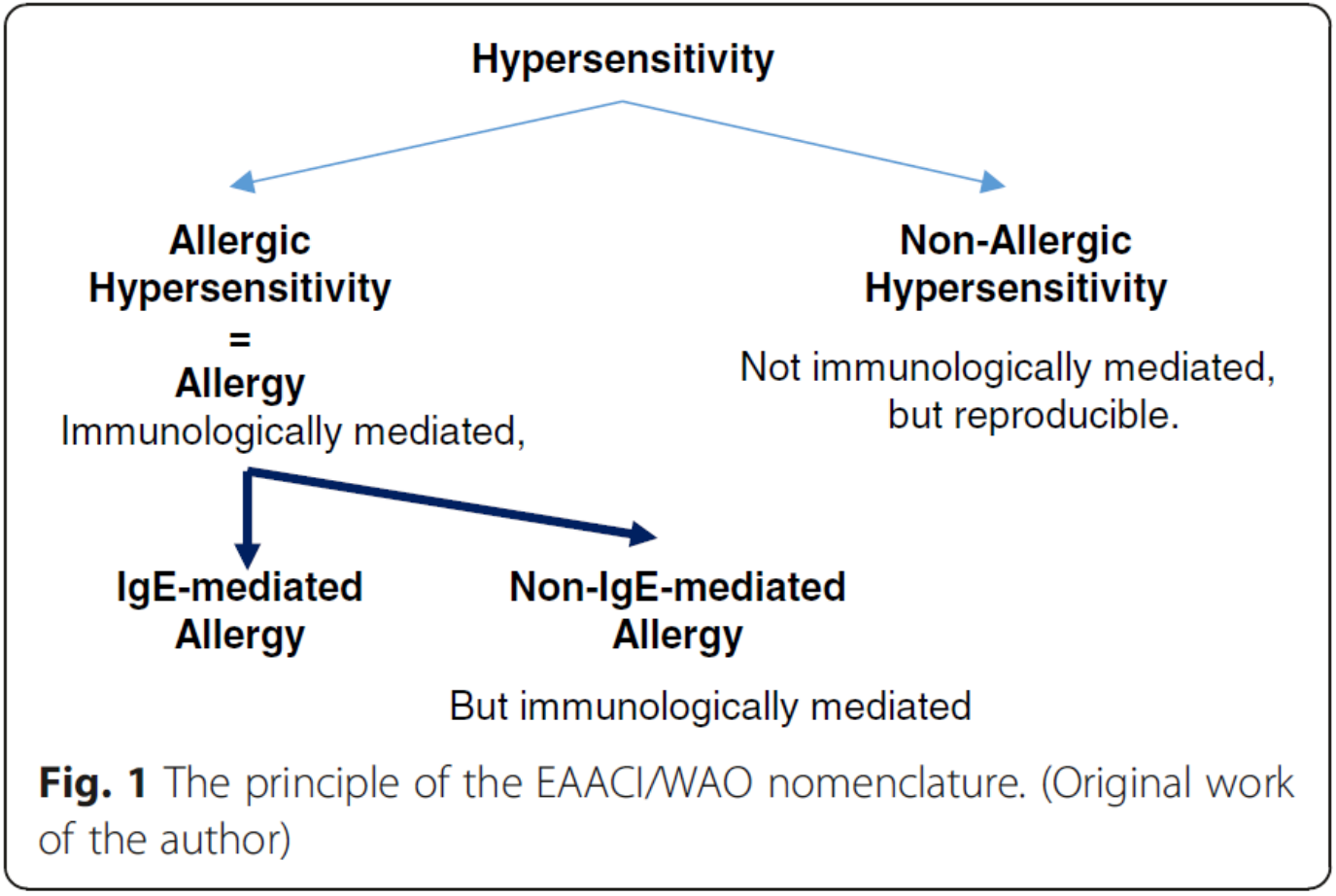

Fig. 1 The principle of the EAACI/WAO nomenclature. (Original work of the author)

Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

The existing intolerances

'In
carb

If restricted to lactose, fructose, sucrose etc., the term "intolerance" can be acceptable – no immunological, i.e. allergic, mechanism involved

Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

Vandenplas Y. Gastrointestinal manifestations of cow's milk protein allergy and gastrointestinal motility. Acta Paediatr. 2012;101:1105–9

CMPA/CMPI?

Overlap bet… …or
intoleran…

The conclusions seem to be:

OFC are difficult to perform in general practice and do not indicate mechanism.
Therefore, these diagnoses are lumped together under CMPA/I.

→ …tipation

…e of the infants with … …tion will have CMPA/I

Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

Vandenplas Y. Debates in allergy medicine: food intolerance does exist. World Allergy Organ J. 2015 Dec 14;8:36

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CMPA/CMPI?

When he rei… …oms
establis…

The diag…

This statement allows for the possibility of unrestricted use of hypoallergenic formulas in infants with common non-specific complaints.
This is not evidence based.

Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

Vandenplas Y. Gastrointestinal manifestations of cow's milk protein allergy and gastrointestinal motility. Acta Paediatr. 2012;101:1105–9

Are GPs able at diagnosing CMA?

A web-based sur among s in Europe

GPs: 47%

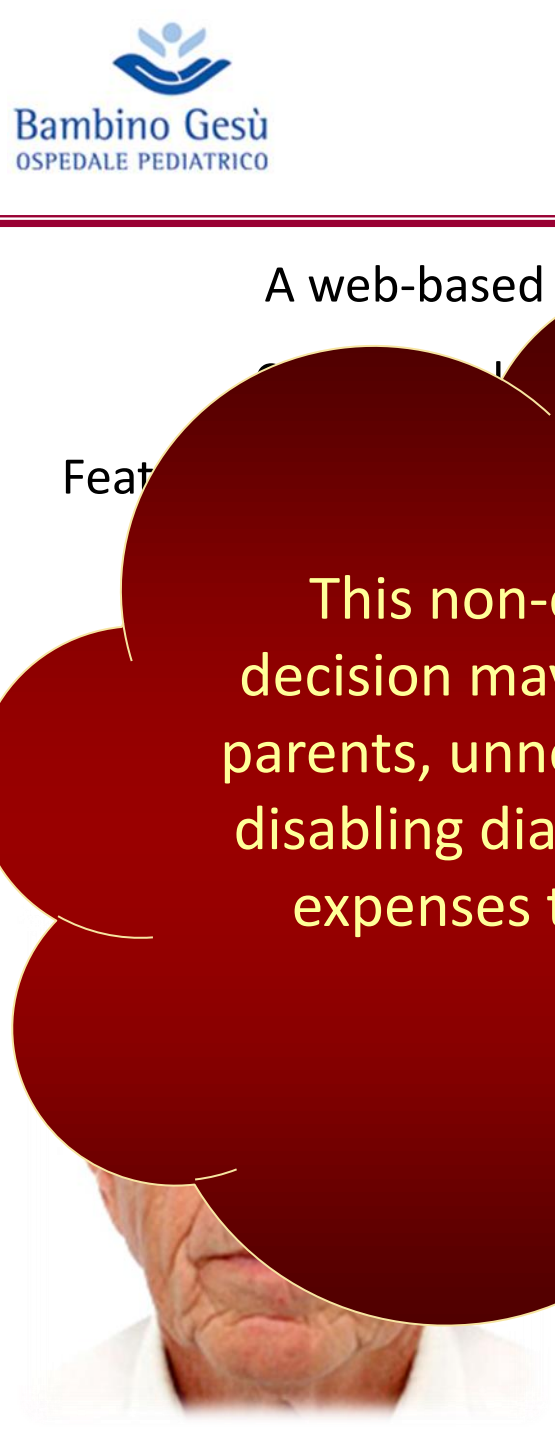
Feat ves, blood in

This non-evidence-based clinical decision may generate anxiety among parents, unnecessary elimination diets, disabling diagnoses, and un-necessary expenses to parents and even the society.

%

61%

sis:



Drebo lergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

ne management of food allergy in infants with special asis on cow's milk allergy. European Paediatric Association Newsletter. EPA; 2012. 1–2

Medical intolerance in Wikipedia

Intolerance, or hypersensitivity, includes but is not limited to allergy

- Cold intolerance
- Drug intolerance
- Exercise intolerance
- Fructose malabsorption
- Heat intolerance
- Hereditary fructose intolerance
- Lactose intolerance
- Lysinuric protein intolerance
- Multiple chemical sensitivity
- Orthostatic intolerance (?)
- Perfume intolerance
- Salicylate intolerance, also known as aspirin intolerance
- Sucrose intolerance
- Food intolerance
- Gluten sensitivity
- Milk soy protein intolerance

[a]Downloaded on June 1 2015

Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

Symptom-based Clinical Score (Cow's Milk Protein Intolerance Score)

Symptom	Score	
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	4	3 to 4 hours/day
	5	
	6	
Regurgitation†	0	
	1	
	2	
	3	
	4	
	5	
	6	
Stools (Bristol scale)†	4	
	0	
	2	
	4	
	6	
Skin symptoms	0 t	
		Severe 3 3
	0 or 6	Urticaria (no 0/yes 6)
Respiratory symptoms	0	No respiratory symptoms
	1	Slight symptoms
	2	Mild symptoms
	3	Severe symptoms

*Crying was only considered if the child was crying for 1 week or more, assessed by the parents, without any other obvious cause.
†Vandenplas Y, Hachimi-Idrissi S, Casteels A, Mahler T, Loeb H. A clinical trial with an "anti-regurgitation" formula. Eur J Pediatr 1994;153:419-23.
†Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997;32:920-4.

10. Vandenplas Y, Steenhout P, Planoudis Y, Grathwohl D; Althera Study Group Treating cow's milk protein allergy: a double-blind randomized trial comparing two extensively hydrolysed formulas with probiotics. Acta Paediatr 2013;102:990-8.
11. Vandenplas Y, Althera Study Group, Steenhout P, Grathwohl D. A pilot study on the application of a symptom-based score for the diagnosis of cow's milk protein allergy. SAGE Open Med 2014;2:2050312114523423.

Vandenplas Y. Treatment of Cow's Milk Protein Allergy. Pediatr Gastroenterol Hepatol Nutr. 2014;17:1-5

Towards a new nomenclature

Intolerance does not exist within the area of allergy

It should not be part of the allergy nomenclature

The mixed term CMPA/I should be actively counteracted in collaboration with related societies.

Intolerance only for lack of enzyme-causing GI symptoms (lactose,..)

The term ‘non-allergic/ non-immunologic hypersensitivity is too awkward to be generally accepted: it should be given a shortened name.

Other terms to better define:

“tolerance”,

“sensitization” vs. “clinical allergy”,

“de-sensitization”.

Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

Bambino Gesù
OSPEDALE PEDIATRICO

I agree that….

The gold standard to diagnose food allergy is the “elimination-challenge”principle

The challenge test is by preference performed double-blind

IgE-mediated CMA must be diagnosed with OFC

Non IgE-mediated CMA may be supported by eosinophilia, eosinophilic infiltration in colonic biopsies, or a APT.

IgG4 anti-β-lactoglobulin levels failed to show a relation with CMA

More sophisticated tests to demonstrate the involvement of the immune system, are not routinely available

It is important to not mix “CMA” with “functional GI CM-related symptoms”

In relation to CM, the term “intolerance” should be restricted to carbohydrate maladsorption

Vandenplas Y. Debates in allergy medicine: food intolerance Do exist. World Allergy Organ J. 2015 Dec 14;8:36

Bambino Gesù
OSPEDALE PEDIATRICO

However….

GI symptoms related to CM intake are estimated to occur in 10 to 15 % of formula- fed infants

When they disappear on CM elimination diet with negative sIgE or SPT, non-IgE mediated allergy is the only explanation

A positive challenge does not prove that there is an immune mechanism involved

Hypersensitivity differs from allergy as the immune system has not been shown to have a causal role.

It is important to not mix “CMA” with “functional GI CM-related symptoms”

“CMA” may be a different entity than “symptoms related to CM”

Vandenplas Y. Debates in allergy medicine: food intolerance Do exist. World Allergy Organ J. 2015 Dec 14;8:36

Bambino Gesù
OSPEDALE PEDIATRICO

The COw's MIlk related Simptom Score (COMISS)

Table 1 Symptom-based clinical score (*)

Symptom	Score	
Crying (°)	0	≤1 h/day
	1	1–1.5 h/day
	2	1.5–2 h/day
	3	2–3 h/day
	4	3–4 h/day
	5	4–5 h/day
	6	≥5 h/day
Regurgitation (23)	0	0–2 episodes/day
	1	≥3 to ≤5 of small volume
	2	>5 episodes of >1 coffee spoon
	3	>5 episodes of ± half of the feed in < half of the feeds
	4	Continuous regurgitations of small volumes >30 min after each feed
	5	Regurgitation of half to complete volume of a feed in at least half of the feeds
	6	Regurgitation of the complete feed after each feeding
Stools (Bristol scale) (25)	4	Type 1 and 2 (hard stools)
	0	Type 3 and 4 (normal stools)
	2	Type 5 (soft stool)
	4	Type 6 (liquid stool, if unrelated to infection)
	6	Type 7 (watery stools)
Skin symptoms	0–6	Atopic eczema — Head neck trunk — Arms hands legs feet
		Absent — 0 — 0
		Mild — 1 — 1
		Moderat — 2 — 2
		Severe — 3 — 3
	0 or 6	Urticaria (no 0/yes 6)
Respiratory symptoms	0	No respiratory symptoms
	1	Slight symptoms
	2	Mild symptoms
	3	Severe symptoms

*Although many infants with cow's milk-related symptoms have no impaired growth or weight gain, faltering of these parameters suggests organic disease, of which CMPA is a possible cause.
(°) Crying was only considered if the child was crying for 1 week or more, assessed by the parents, without any other obvious cause.

Vandenplas Y. Debates in allergy medicine: food intolerance Do exist. World Allergy Organ J. 2015 Dec 14;8:36

1. L’intolleranza alimentare
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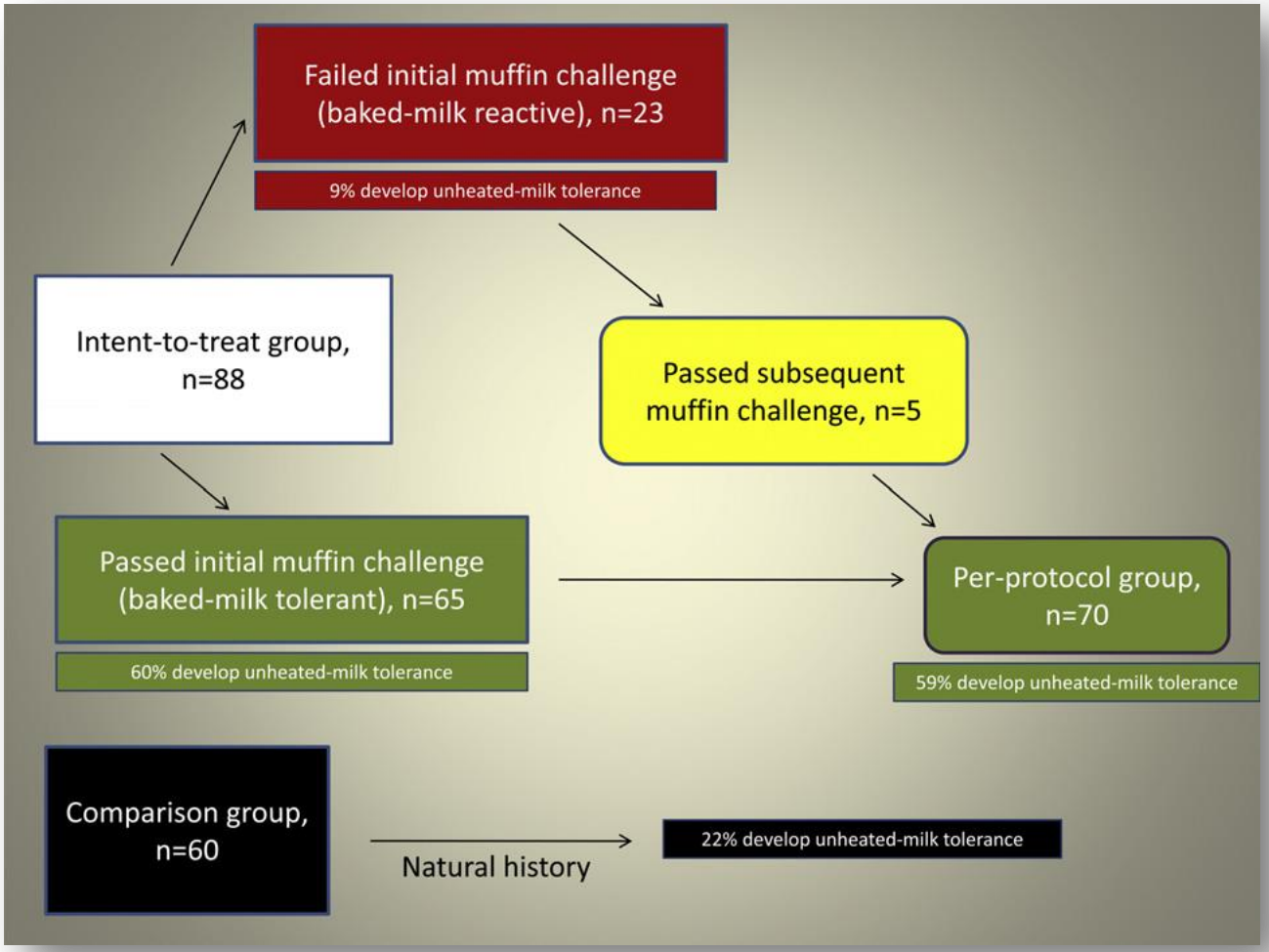
Baked milk & natural history



Kim JS. Dietary baked milk accelerates the resolution of cow's milk allergy in children. J Allergy Clin Immunol. 2011;128:125–31

Bambino Gesù
OSPEDALE PEDIATRICO

"Baked Milk" Study

- 100 children with milk allergy
- 68 tolerated heated milk in waffles/muffins but not regular milk (i.e. plain, yogurt, cheeses)
- Children tolerating HM: smaller SPT, lower sIgE to milk
- Heated milk-tolerant children incorporated baked products into their diets and re-evaluated at 3, 6, 12 months.
- milk SPT ⇓, milk sIgE =, milk sIgG4 ⇧

Lemon-Mule H. Immunologic changes in children with egg allergy ingesting extensively heated egg. J Allergy Clin Immunol 2008; 122:977–83

Bambino Gesù
OSPEDALE PEDIATRICO

"Baked Egg" Study

- 91 children with egg allergy
- 70% tolerated heated egg in waffles/muffins but not regular egg (i.e. scrambled or in French toast)
- Children tolerating HE: smaller SPT, lower sIgE to egg
- Heated egg-tolerant children incorporated heated egg into their diets and re-evaluated at 3, 6, 12 months.
- egg SPT ⇓, egg sIgE =, egg sIgG4 ⇧

Lemon-Mule H. Immunologic changes in children with egg allergy ingesting extensively heated egg. J Allergy Clin Immunol 2008; 122:977–83

Bambino Gesù
OSPEDALE PEDIATRICO

A vastly altered approach to food allergy management

1. Children receiving limited, extensively heated food essentially reported no acute food-induced allergic reactions as a result of this diet

2. The change from a food avoidance diet to a food-limited diet could provide a substantial improvement to the quality of life of food-allergic individuals.

3. The frequency of prolonged or permanent food allergy may be reduced if this type of diet can augment the development of tolerance.

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

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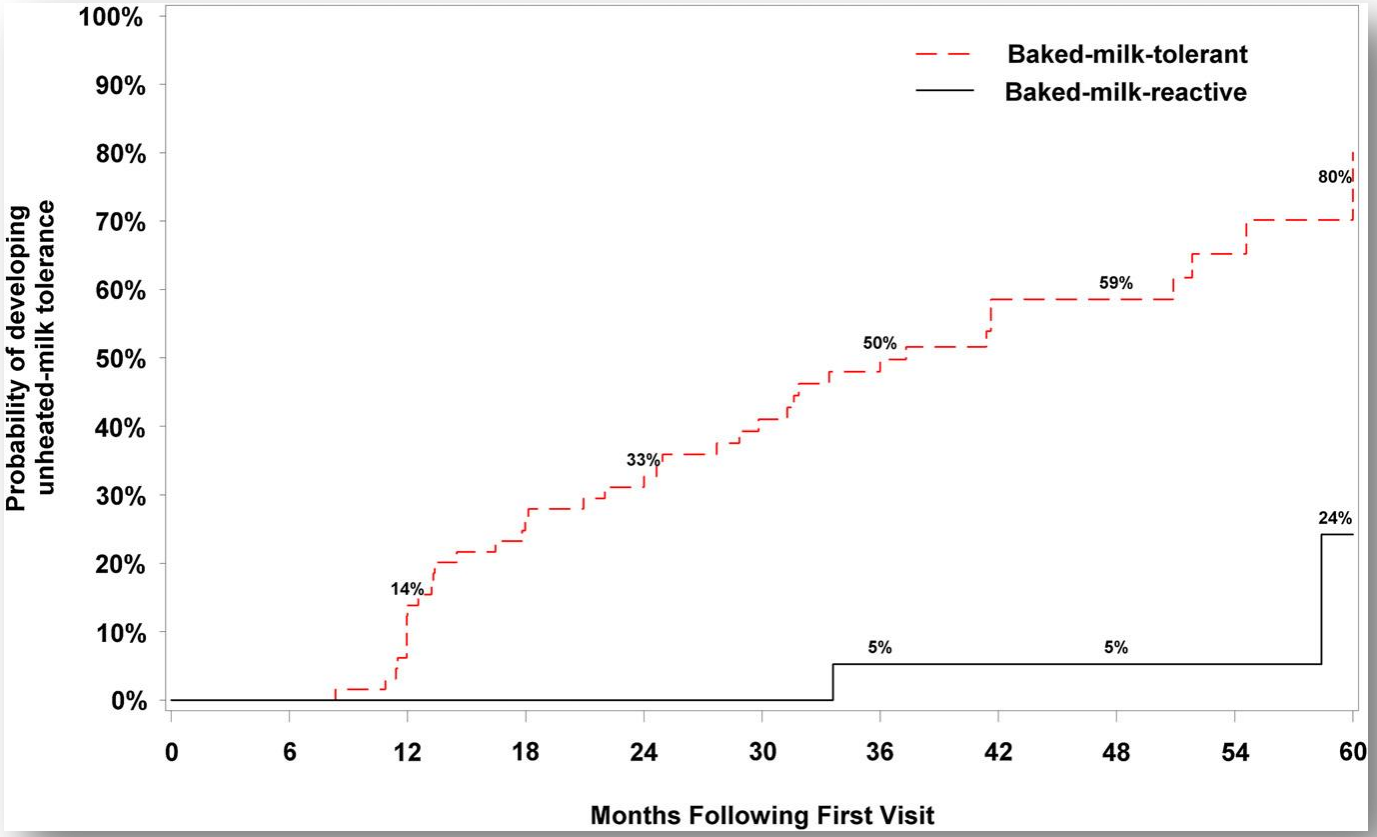
OSPEDALE PEDIATRICO

Baked milk tolerant are 7.6 times more likely to have unheated milk tolerance than initially baked milk reactive

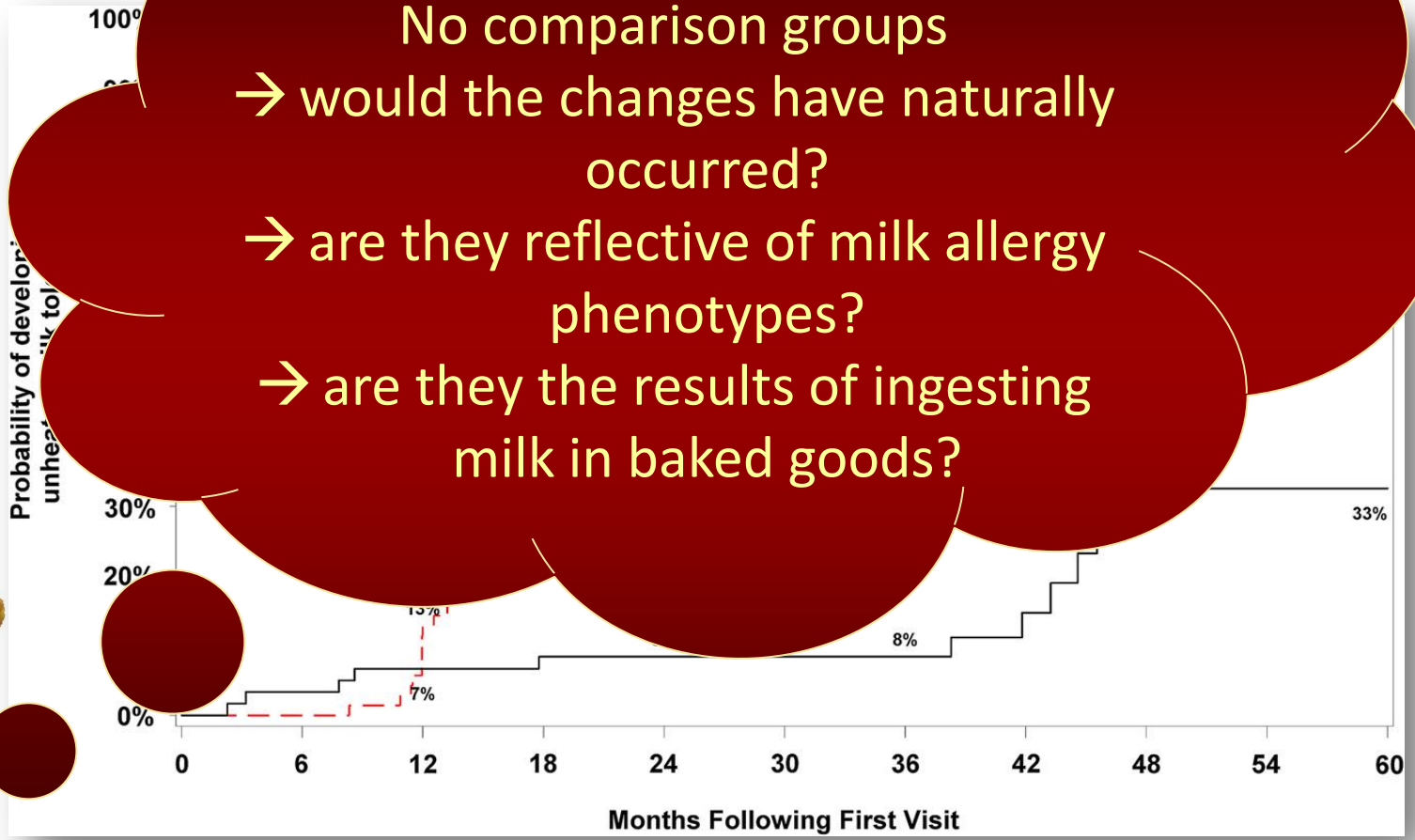


Kim JS. Dietary baked milk accelerates the resolution of cow's milk allergy in children. J Allergy Clin Immunol. 2011;128(1):125–31

Bambino Gesù
OSPEDALE PEDIATRICO

Baked milk tolerant fed BM display a 3.57 higher probabil[illegible] group

No comparison groups
→ would the changes have naturally occurred?
→ are they reflective of milk allergy phenotypes?
→ are they the results of ingesting milk in baked goods?



Dang TD. Debates in allergy medicine: baked milk and egg ingestion do not accelerate resolution of milk and egg allergy. World Allergy Organ J. 2016 Jan 26;9:2

Kim JS. Dietary baked milk accelerates the resolution of cow's milk allergy in children. J Allergy Clin Immunol. 2011;128(1):125–31

Bambino Gesù
OSPEDALE PEDIATRICO

Tolerance of baked milk and resolution of milk allergy

	Type of study	BM tolerant	Resolution of milk allergy
Wood et al. [39] ($n = 155$)	Observational without OFC	21 % by 5 years	Relative hazard after 5 years: 4.1 in those who reported BM tolerance 0.28 in those who reported BM reactivity
Nowak-Wegrzyn et al. [20] ($n = 91$) and Kim et al. [32] ($n = 88$; follow-on study)	Prospective with OFC	75 % initially, 80 % by end of follow-on study	59 % of those ingesting BM (followed for median 37 months) 22 % of control group (followed for median 40 months)
Caubet et al. [21] ($n = 121$)*	Prospective with OFC	69 %	N/A
Bartnikas et al. [22] ($n = 35$)	Retrospective with OFC	83 %	N/A
Mehr et al. [23] ($n = 70$)	Prospective with OFC	73 %	N/A

OFC oral food challenge, *BM* baked milk
*only second cohort; first cohort include subjects from Nowak et al

Leonard SA. Debates in allergy medicine: baked milk and egg ingestion accelerates resolution of milk and egg allergy. World Allergy Organ J. 2016 Jan 26;9:1

Tolerance of baked egg and resolution of egg allergy

	Type of study	BE tolerant	Resolution of egg allergy
Sicherer et al. [40] ($n = 113$)	Observational without OFC	38 % by 6 years	After 6 years:
			71 % in those who reported BE tolerance
			45 % in those not ingesting BE
			57 % in those who reported BE reactivity
Des Roches et al. [30]	Prospective with OFC	73 %	
Lemon-Mule et al. [19] ($n = 91$) and Leonard et al. [31] ($n = 79$; follow-on study)	Prospective with OFC	70 % initially,	53 % of those ingesting BE (followed for median 37.8 months)
		89 % by end of follow-on study	28 % of control group (followed for median 67.3 months)
Clark et al. [24] ($n = 95$)	Longitudinal with OFC	66 %	N/A
Lieberman et al. [25] ($n = 100$)	Retrospective with OFC	66 %	N/A
Cortot et al. [26] ($n = 52$)	Retrospective with OFC	83 %	N/A
Turner et al. [18] ($n = 236$)	Prospective with OFC	64 %	N/A
Tan et al. [27] ($n = 143$)	Prospective with OFC	63 %	N/A
Bartnikas et al. [28] ($n = 169$)	Retrospective with OFC	84 %	N/A
Turner et al. [29] ($n = 186$)	Retrospective with OFC	66 %	N/A
Peters et al. [37] ($n = 158$)	Prospective with OFC or by report	80 % by OFC	By age 2 years of age:
		72 % by report	49 % of those ingesting BE after OFC at 1 year
			74 % of those ingesting BE by report at 1 year
			13 % of those with positive BE OFC at 1 year

OFC oral food challenge, *BE* baked egg

Leonard SA. Debates in allergy medicine: baked milk and egg ingestion accelerates resolution of milk and egg allergy. World Allergy Organ J. 2016 Jan 26;9:1

Resolution of milk and egg allergy

The comparison groups in Leonard et al. and Kim et al. were matched clinic patients collected retrospectively who represented “standard of care”, or how milk and egg allergy was typically managed at that time.

In the baked milk & baked egg studies, specific IgE levels decreased significantly and ovalbumin and ovomucoid-specific IgG4 levels increased significantly from baseline in those ingesting baked egg/milk compared to those strictly avoiding.

This supports the theory that baked milk and egg are immunologically active and can act as a treatment to help children outgrow their milk and egg allergy.

Leonard SA. Debates in allergy medicine: baked milk and egg ingestion accelerates resolution of milk and egg allergy. World Allergy Organ J. 2016 Jan 26;9:1

Does regular ingestion of baked egg delay or hasten the resolution of egg allergy?

117 children and adults with documented "egg allergy": clinical history or sIgElevels

OFC to baked egg → 74% toler

Instructed to consume baked

SPT significantly reduced

ovalbumin and ovomucoid

"ingestion of baked egg may affect the natural gg allergy"

No comparison group
Definition of egg allergy?
Conclusion inappropriate.

Lemon Mulé H. Immunologic changes in children with egg allergy ingesting extensively heated egg. J Allergy Clin Immunol. 2008;122:977–83

Dang TD. Debates in allergy medicine: baked milk and egg ingestion do not accelerate resolution of milk and egg allergy. World Allergy Organ J. 2016 Jan 26;9:2

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OSPEDALE PEDIATRICO

Baked egg & tolerance: limitations of the studies

- Comparison group retrospectively selected
- Comparison of characteristics between the treatment and comparison group (SPT wheal size, eczema, severity of previous reactions or other allergies…) not presented
- The association presented may be biased
- The comparison group was either ‘allergic ‘or ‘never ingested’ to baked egg – not those with known baked egg allergy

It is unclear whether the differential development of tolerance is due to the ingestion of baked egg or different clinical phenotypes of egg allergy.

Dang TD. Debates in allergy medicine: baked milk and egg ingestion do not accelerate resolution of milk and egg allergy. World Allergy Organ J. 2016 Jan 26;9:2

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Baked egg & tolerance: RCTs

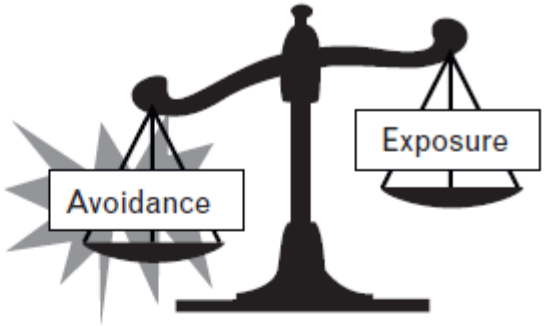
- The CAKE trial (ACTRN12612000173897)
- Egg allergic children able to tolerate baked egg
- 30g baked egg per week for 6 months vs. avoidance
- Rechallenge to raw egg at 7 months

Dang TD. Debates in allergy medicine: baked milk and egg ingestion do not accelerate resolution of milk and egg allergy. World Allergy Organ J. 2016 Jan 26;9:2

1. L’intolleranza alimentare
2. La dieta modifica la storia naturale dell'AA?
3. Svezzamento e prevenzione dell'allergia
4. Le diete inutili
5. Conclusioni

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

(a) Previous approach
(overturned)



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

EAACI food allergy guidelines

Recommendation	Evidence level	Grade
Exclusive breastfeeding is recommended for all infants for the first 4-6 months	II-III	C
No dietary restrictions for all pregnant or the lactating mother for allergy preventive purposes	I-II	B
If breastfeeding is insufficient or not possible:		
- high-risk infants→ hypoallergenic formula with documented preventive effect - other infants → standard formula	I	A-B
Complementary foods after the age of 4 months → normal standard weaning practices	**I**	**A-B**
No withholding or encouraging exposure to "highly allergenic" foods such as cow's milk, hens egg and peanuts irrespective of atopic heredity, once weaning has commenced	II-III	C

Muraro A, EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI Food Allergy and Anaphylaxis Guidelines. Primary prevention of food allergy. Allergy. 2014;69:590-601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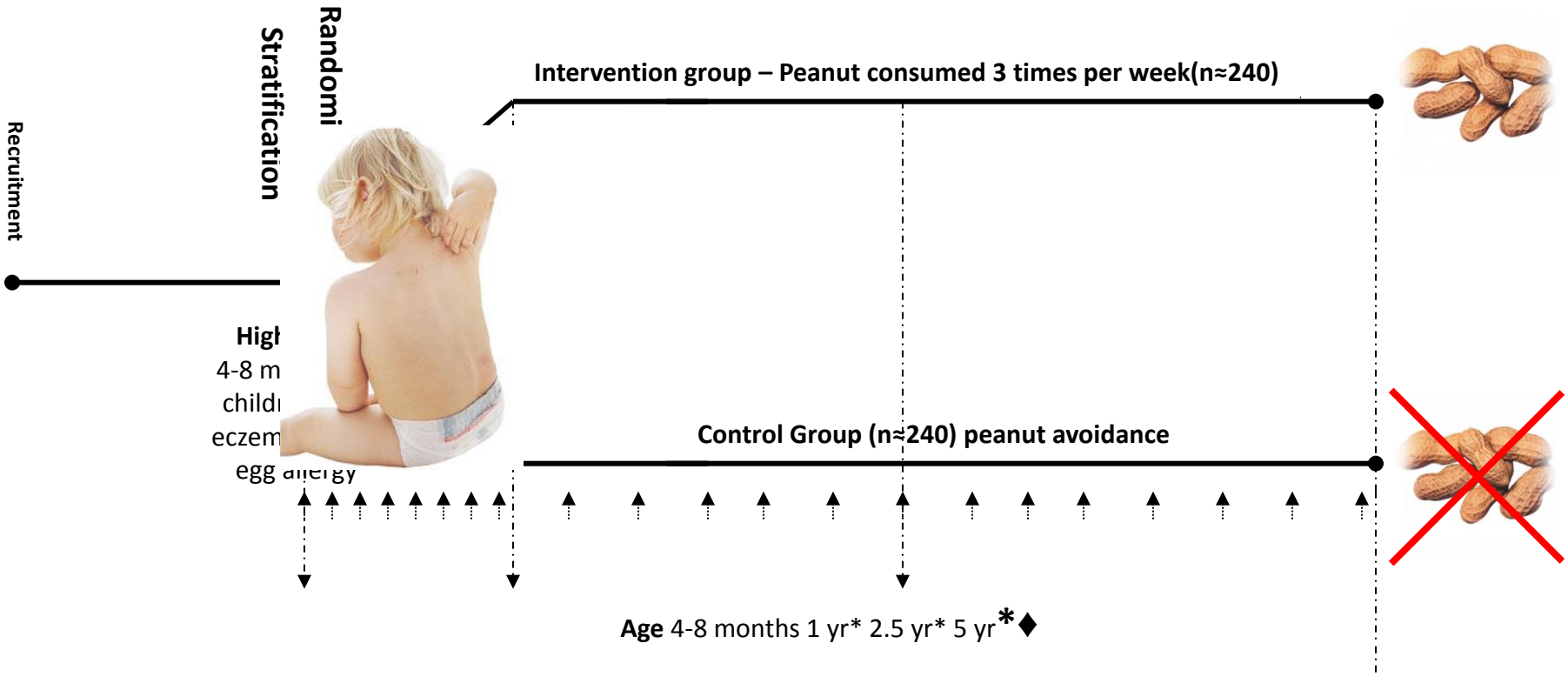
NORMAL
PEANUT
BUTTER

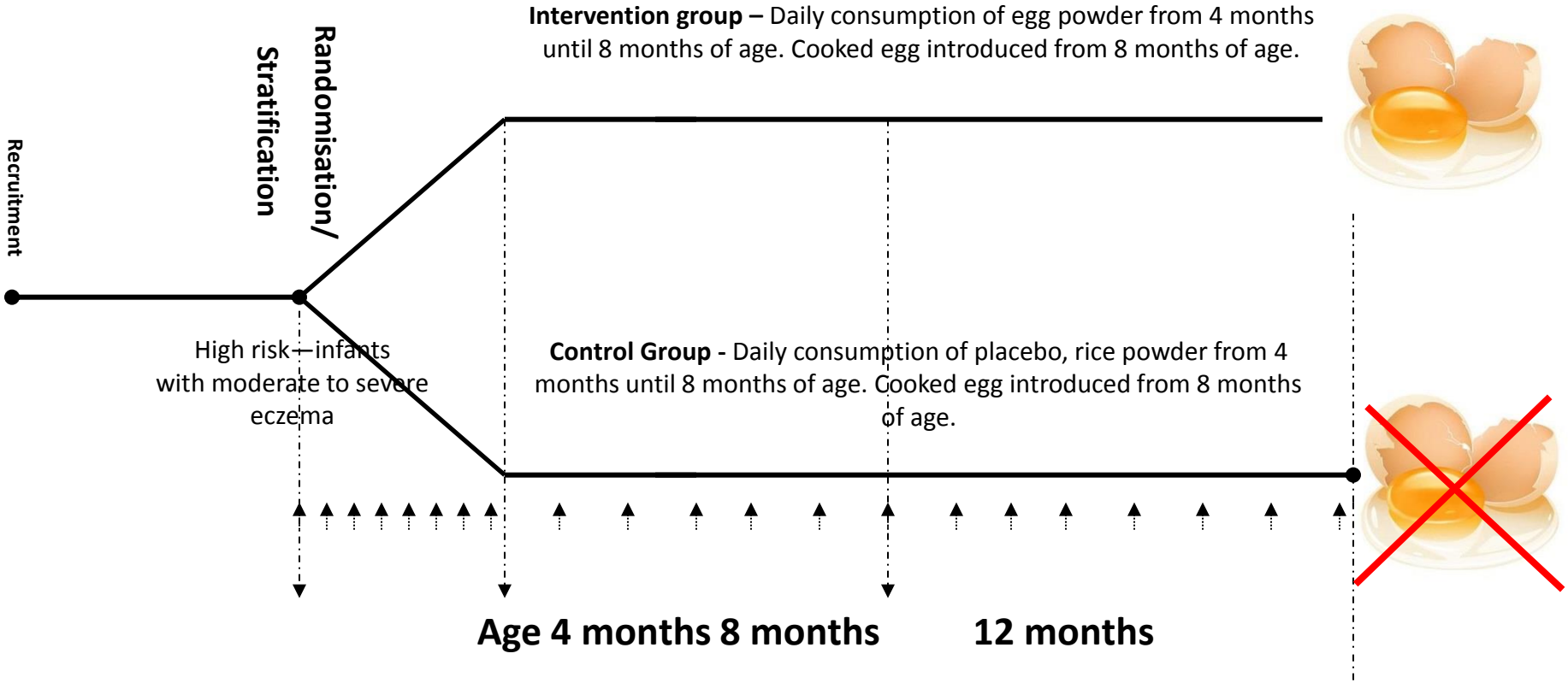
LEAP Study – Immune Tolerance Network – London, UK



Outcome: Prevalence of clinically-defined peanut allergy at 5 years of age.

NCT00329784 - Date of trial registration 23/05/2006 – contact person Gideon Lack

STAR study (Adelaide & Perth, Australia)



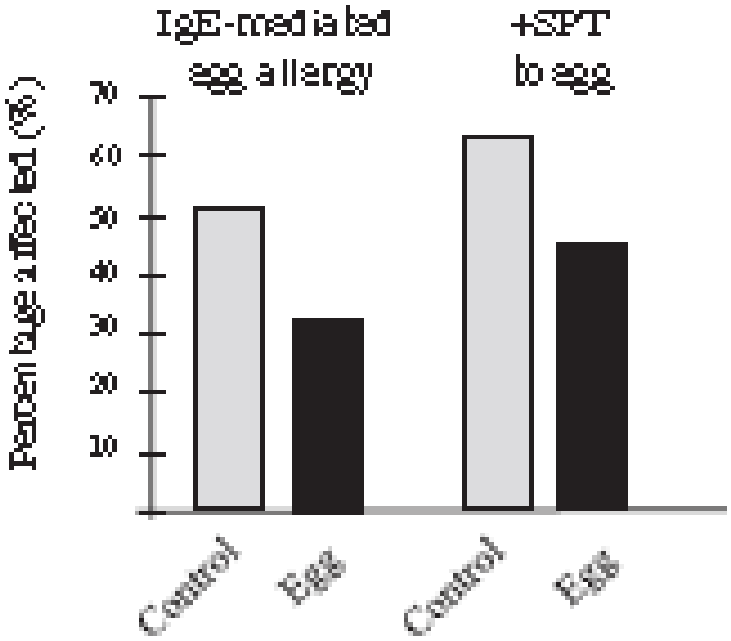
Outcome: IgE mediated egg allergy at 12 months of age based on positive SPT and egg challenge

ACTRN 12609000415202 - Date of trial registration 5/06/2009 – contact person Debbie Palmer

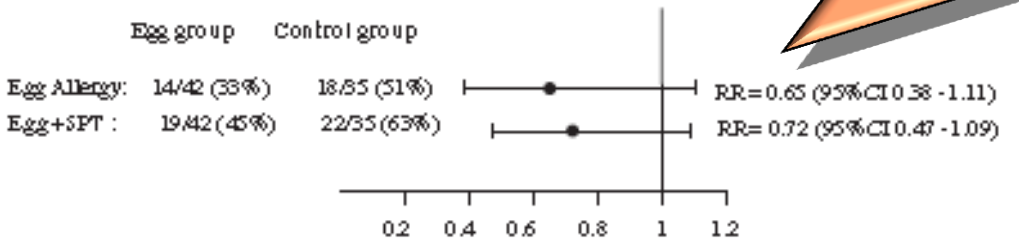
Egg allergy at 12 months

Egg group: 33%

Rice group: 51%



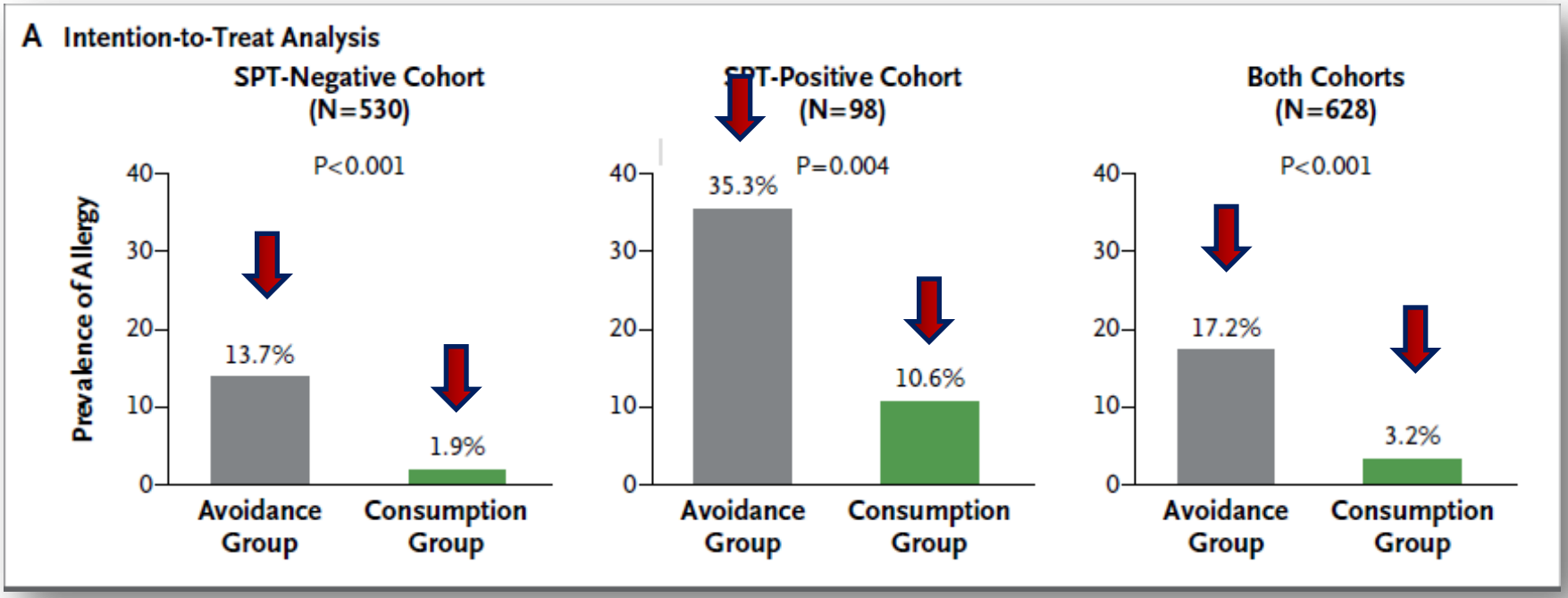
RR 0.65, p = 0.11



Palmer DJ. Early regular egg exposure in infants with eczema: A randomized controlled trial. J Allergy Clin Immunol. 2013;132:387-92


SAMSUNG
RESERVED

LEAP study: primary outcome



Du Toit G; LEAP Study Team. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med. 2015;372:803-13


Mito o realtà
EBM PREVENTION AND MANAGEMENT
OF PEDIATRIC ALLERGY
H. SAMPSON

LEAP study: open questions

1. Should the guidelines be changed?
2. Should we recommend introducing peanuts to all infants before they reach 11 months of age?
3. Do infants need to ingest 2 g of peanut protein (approximately eight peanuts) three times a week on a regular basis for 5 years, or will it suffice to consume lesser amounts on a more intermittent basis for a shorter period of time?
4. If regular peanut consumption is discontinued for a prolonged period, will tolerance persist?
5. Can the findings of the LEAP study be applied to other foods, such as milk, eggs, and tree nuts?

Gruchalla RS, Sampson HA. Preventing peanut allergy through early consumption--ready for prime time? N Engl J Med. 2015;372:875-7

Consensus communication

A landmark collaborative action, 10 medical professional organizations:

1. American Academy of Allergy, Asthma & Immunology (AAAAI)
2. American Academy of Pediatrics (AAP)
3. American College of Allergy, Asthma & Immunology (ACAAI)
4. Australasian Society of Clinical Immunology and Allergy (ASCIA)
5. Canadian Society of Allergy and Clinical Immunology (CSACI)
6. European Academy of Allergy and Clinical Immunology (EAACI)
7. Israel Association of Allergy and Clinical Immunology (IAACI)
8. Japanese Society for Allergology (JSA)
9. Society for Pediatric Dermatology (SPD)
10. World Allergy Organization (WAO)

→a "Consensus communication" suggesting that the approaches taken in the LEAP trial should be actualized for clinical care "in more diverse settings throughout the world."

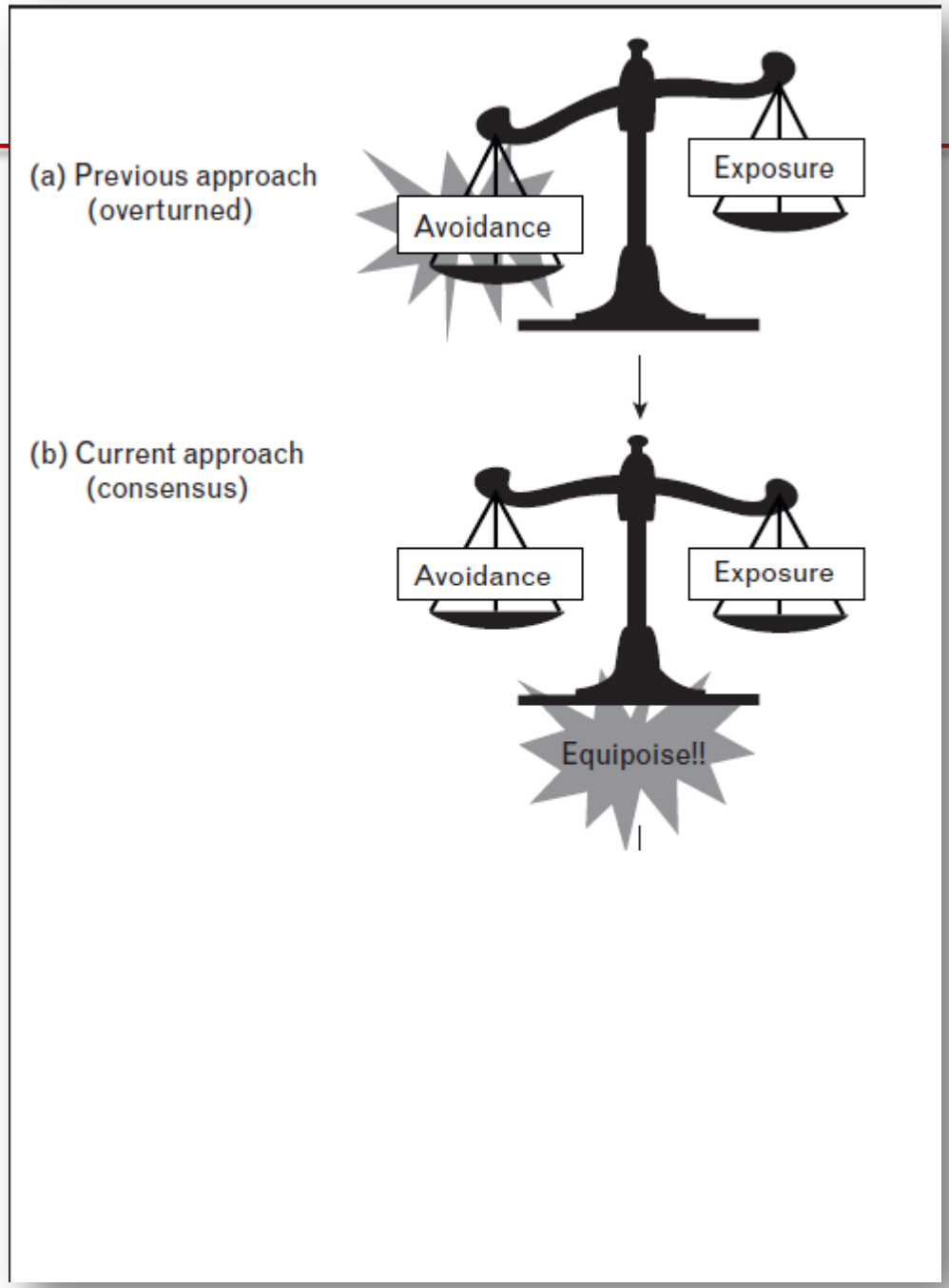
Sicherer SH, Bock SA, Zeiger RS. Implications of the "Consensus Communication on Early Peanut Introduction in the Prevention of Peanut Allergy in High-Risk Infants" for Allergists, Primary Care Physicians, Patients, and Society. J Allergy Clin Immunol Pract. 2015;3:649-51

Consensus communication

- Pediatricians and allergists should recommend introducing peanut-containing products into the diets of “high-risk” infants early in life (between 4 and 11 months of age) in countries where peanut allergy is prevalent

- Infants with early-onset atopic disease might benefit from evaluation by an allergist or trained physician to diagnose any food allergy and assist in implementing these suggestions

Fleischer DM. Consensus communication on early peanut introduction and the prevention of peanut allergy in high-risk infants. World Allergy Organ J. 2015 Aug 3;8(1):27



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

Limitations and constraints

- no data about alternative dosing regimens
- no data about minimal length of time needed for “treatment”
- it has focused on “high risk” infants and peanut allergy and has not attempted to generalize the results to other foods or lower risk populations.
- feeding peanut early to high-risk infants will require engagement of the medical community to change the culture of early feeding practices.
- “a National Institute of Allergy and Infectious Diseases Working Group and European Academy of Allergy, Asthma and Clinical Immunology Guidelines Group are addressing a best-practices approach with more extensive guidelines”.

Fleischer DM. Consensus communication on early peanut introduction and the prevention of peanut allergy in high-risk infants. World Allergy Organ J. 2015 Aug 3;8(1):27

National Institute of Allergy and Infectious Diseases
Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.

NIH guidelines for the diagnosis and management of food allergy

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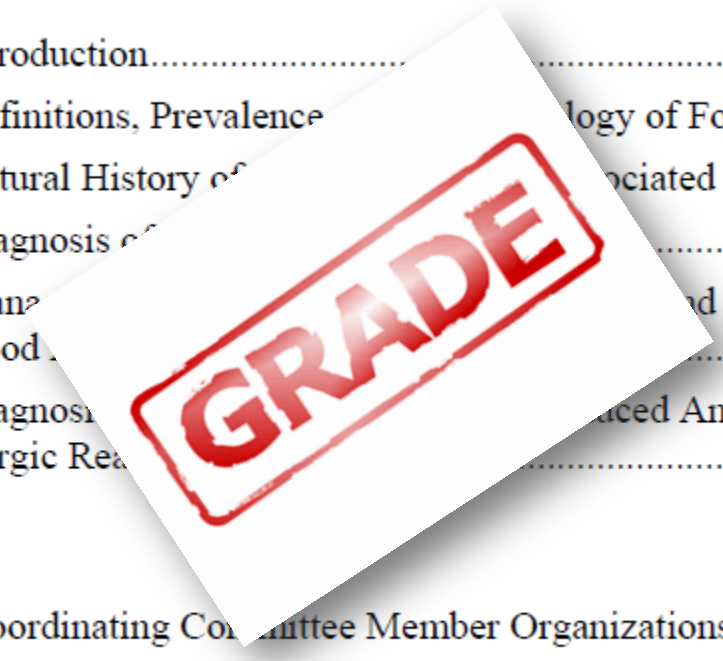

http://www.niaid.nih.gov/topics/foodAllergy/clinical/Documents/guidelines.pdf

NIH guidelines for the prevention of food allergy

Guideline 37: [….] all infants be exclusively breast-fed until 4 to 6 months of age, unless breastfeeding is contraindicated for medical reasons.

Guideline 40: [….] the introduction of solid foods should not be delayed beyond 4 to 6 months of age. Potentially allergenic foods may be introduced at this time as well.

NIAID-Sponsored Expert Panel. Guidelines for the diagnosis and management of food allergy in the United States. J Allergy Clin Immunol. 2010;126(6 Suppl):S1-58

The NIAID guidelines modification

NIH was asked to urgently include the evidence from LEAP study in their food allergy guidelines.

An urgent meeting in June – an expert panel named by NIH

Not able to bring the matter to a consensus →

→ another meeting scheduled for November, addendum produced.

→ The new recommendations are intended to supplement Guidelines 36-40 in 90 Section 5.3.4 of the 2010 Guidelines: "Prevention of Food Allergy."

Matters that are very contentious are the following:

1) Use the LEAP data as published, i.e. skin test all infants with eczema and introduce peanuts at 4 months of age? If so, discussion re. size of the skin tests.
2) Who would do the skin tests and where will the peanuts be introduced, home or office. If office, whose office? Peds or allergist?
3) Extrapolate the data to all children without eczema and tell all of America that they should introduce peanuts in the diet at 4 months of age or not?

NIH guidelines for the prevention of peanut allergy

Addendum Guideline 1: The EP recommends that infants with **severe eczema**, **egg allergy** or both **have** introduction of age-appropriate peanut-containing food as early as 4-6 months of age to reduce the risk of peanut allergy.
Peanut should not be the initial solid food introduced into an infant's diet. Other solid food should be tried first to show the infant is developmentally ready.
The EP recommends that evaluation with peanut-specific IgE or skin prick testing be strongly considered before introduction of peanut to determine il peanut should be introduced and, if so, the preferred method of introduction

NIAID-Sponsored Expert Panel. Guidelines for the diagnosis and management of food allergy in the United States. Currently unavailable

NIH guidelines for the prevention of peanut allergy

Addendum Guideline 2: The EP suggests that infants with **mild to moderate eczema should have** introduction of age-appropriate peanut-containing food as early as 4-6 months of age, in accordance with family preferences and cultural practices, to reduce the risk of peanut allergy. Peanut should not be the initial solid food introduced into an infant's diet. Other solid food should be tried first to show the infant is developmentally ready.

Infants in this category may have dietary peanut introduced at home without an in-office evaluation. However, the EP recognizes that some caregivers and health care providers may desire an in-office evaluation, in which case the decision points shown in Figure 1 should apply.

NIAID-Sponsored Expert Panel. Guidelines for the diagnosis and management of food allergy in the United States. Currently unavailable

NIH guidelines for the prevention of peanut allergy

Addendum Guideline 3: The EP recommends that infants without eczema or any food allergy have age-appropriate peanut-containing foods freely introduced in the diet, together with other solid foods, and in accordance with family preferences and cultural practices.

Look before you LEAP: Risk of anaphylaxis in high-risk infants with early introduction of peanut

NIAID-Sponsored Expert Panel. Guidelines for the diagnosis and management of food allergy in the United States. Currently unavailable

Timing of gluten introduction & CD: 2006

- observational study
- first degree relatives of patients with Dyabetes type 1
- or HLA-DR3/4 positive infants

→ introduce gluten containing food between 4 and 6 months

→ Avoid earlier and later introduction.

Norris JM. Risk of celiac disease autoimmunity and timing of gluten introduction in the diet of infants at increased risk of disease. JAMA. 2005;239:2343–51

- a review and meta-analysis considered
- six observational case–control studies
- an association between duration of breastfeeding and reduced risk of developing CD

Akobeng AK. Effect of breast feeding on risk of celiac disease: a systematic review and meta-analysis of observational studies. Arch Dis Child. 2006;91:39–43,

Timing of gluten introduction & CD: 2008

Recent observational studies suggest that the introduction of small amounts of gluten while the infant is still breast-fed may reduce the risk of CD

More recently, both early (<3 months) and late (>7 months) introduction of gluten-containing cereals were associated with an increased risk of CD.

→ On the basis of current data, the Committee considers it prudent to avoid both early (<4 months) and late (>7 months) introduction of gluten

→ to introduce small amounts of gluten gradually while the infant is still breast-fed.

Agostoni C. Complementary feeding: a commentary by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2008;46:99-110

Timing of gluten introduction & CD: after 2008

"Prevent CD":

- dietary-intervention trial
- 944 children HLA-DQ2 or -DQ8 positive, with at least one first-degree relative with CD.
- placebo or 100 mg of gluten from 16 to 24 weeks of age
- No differences among gluten group and placebo group (5,9 % and 4,5 % respectively).
- Breastfeeding did not influence CD development.

➢ The introduction of small amounts of gluten during breastfeeding in the window between 16 and 24 weeks of age do not protect genetically predisposed infants from CD.

Vriezinga SL. Randomized feeding intervention in infants at high risk for celiac disease. N Engl J Med. 2014;371:1304–15

The Risk of CD and Age at Gluten Introduction (CELIPREV):

- Interventional trial
- 832 newborns with a first-degree relative with CD
- gluten introduction at 6 months (group A) or 12 months (group B)
- CD higher in group A at 2 years – no differences at 5 years

➢ The timing of gluten introduction do not significantly impact the risk of CD.

Lionetti E. Introduction of gluten, HLA status, and the risk of celiac disease in children. N Engl J Med. 2014;371:1295–303

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CMA in infants

Extensively Hydrolysed CM formulae

Nutrilon Pepti

Aptamil Pepti o Polilat

Aptamil Pregomin SP

Alfaré

Althéra

Nutribén Hidrolizada

Blemil Plus Idrolizzato

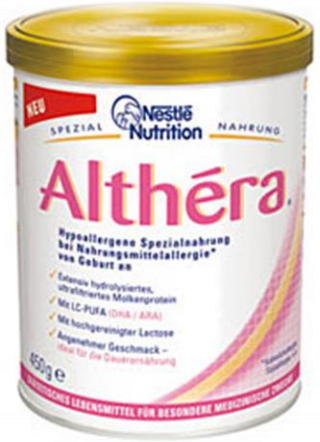
Nutramigen

Pregestimil

Allernova AR

Hypolac

……



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Extensively Hydrolysed Rice formulae

Risolac

Blemil Riso

Bambino Gesù
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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 .

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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

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MALADIE DE LA PEAU, DES ONGLES
ET DU CUIR CHEVELU
ALLERGOLOGIE ESTHÉTIQUE MÉDICALE

SUR RENDEZ-VOUS

9, AVENUE GERY
3ème ETAGE
13600 LA CIOTAT
TÉL : 04 42 83 41 19

LA CIOTAT, LE

REGIME SANS COBALT

SUPPRIMER LES ALIMENTS SUIVANT

haricots, betteraves, choux,

abricots, noix,

foie,

pain complet,

clous de girofle,

café, thé, cacao, chocolats,

bière,

Dieta senza latte vaccino, uovo e loro derivati

EVITARE:

Latte, Yogurt, Burro, Formaggi,

Uovo, Pasta all'uovo,

Prosciutto cotto,Insaccati (salame, salsiccia, wurstel, mortadella…) se contengono latte,

Carne vaccina (vitello, vitellone e manzo), pollo, tacchino,

Omogeneizzati di carne vaccina (vitello, vitellone e manzo), di pollo e tacchino,

Dolci e prodotti commerciali con latte e uovo, mela

PUO' ASSUMERE:

Latte di riso, Latte di soia, Thè, Camomilla, Orzo

Biscotti senza latte e senza uovo, Fette Biscottate senza latte e senza uovo

Cereali: pasta di grano duro, riso, polenta, pane di grano duro, crackers, altri cereali

Prosciutto crudo, Cotto al vapore, Lonza, Bresaola di cavallo

Carne di agnello, coniglio, cavallo, maiale, struzzo

Pesce a piacere (eccetto crostacei e molluschi)

Verdura: carote, patate, finocchi, lattuga, bieta, spinaci, pomodoro

Legumi: fagioli, ceci, piselli, lenticchie

Frutta: a piacere (eccetto mela)

Dolci non contenenti latte e uovo.

CMA in children with beef allergy, BA in children with CMA

	Beef/milk	Milk/beef
DBPCFC	100%	12 – 20%

Werfel SJ. Clinical reactivity to beef in children allergic to cow's milk. J Allergy Clin Immunol 1997;99:293-300

Martelli A. Allergy to cow's milk in beef-allergic children. Ann Allergy Asthma Immunol. 2002; 89S, 25-33

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Conclusions

Words are stones: avoid the term ‘food intolerance’

Bambino Gesù OSPEDALE PEDIATRICO

Food intolerance [do not] exist

Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015 Dec 14;8:37

Vandenplas Y. Debates in allergy medicine: food intolerance does exist. World Allergy Organ J. 2015 Dec 14;8:36

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Tolerance of baked milk and resolution of milk allergy

	Type of study	BM tolerant	Resolution of milk allergy
Wood et al. [39] (n = 155)	Observational without OFC	21 % by 5 years	Relative hazard after 5 years:
			4.1 in those who reported BM tolerance
			0.28 in those who reported BM reactivity
Nowak-Wegrzyn et al. [20] (n = 91) and Kim et al. [32] (n = 88; follow-on study)	Prospective with OFC	75 % initially, 80 % by end of follow-on study	59 % of those ingesting BM (followed for median 37 months)
			22 % of control group (followed for median 40 months)
Caubet et al. [21] (n = 121)*	Prospective with OFC	69 %	N/A
Bartnikas et al. [22] (n = 35)	Retrospective with OFC	83 %	N/A
Mehr et al. [23] (n = 70)	Prospective with OFC	73 %	N/A

OFC oral food challenge, BM baked milk
*only second cohort; first cohort include subjects from Nowak et al

Leonard SA. Debates in allergy medicine: baked milk and egg ingestion accelerates resolution of milk and egg allergy. World Allergy Organ J. 2016 Jan 26;9:1

No excessive illusions in the therapeutic effect of food exposure

The outstanding results of LEAP trial need to be declined against the local needs, values & preferences

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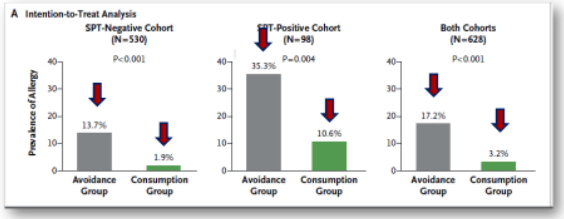
LEAP study: primary outcome



Du Toit G; LEAP Study Team. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med. 2015;372:803-13

WAO Symposium

ROME/VATICAN CITY

27-29 April, 2017 - Rome, Italy/Vatican City