



GEMINI 2008

**GIORNATE MULTIDISCIPLINARI
INTERATTIVE ITALIANE
DI PEDIATRIA**

DEDICATO AL PROF. MAURIZIO MIRAGLIA DEL GIUDICE

**15 - 17 GIUGNO 2008
CENTRO CONGRESSI SIMERI (CZ)**

LA GESTIONE del BAMBINO con GRAVE ALLERGIA AL LATTE



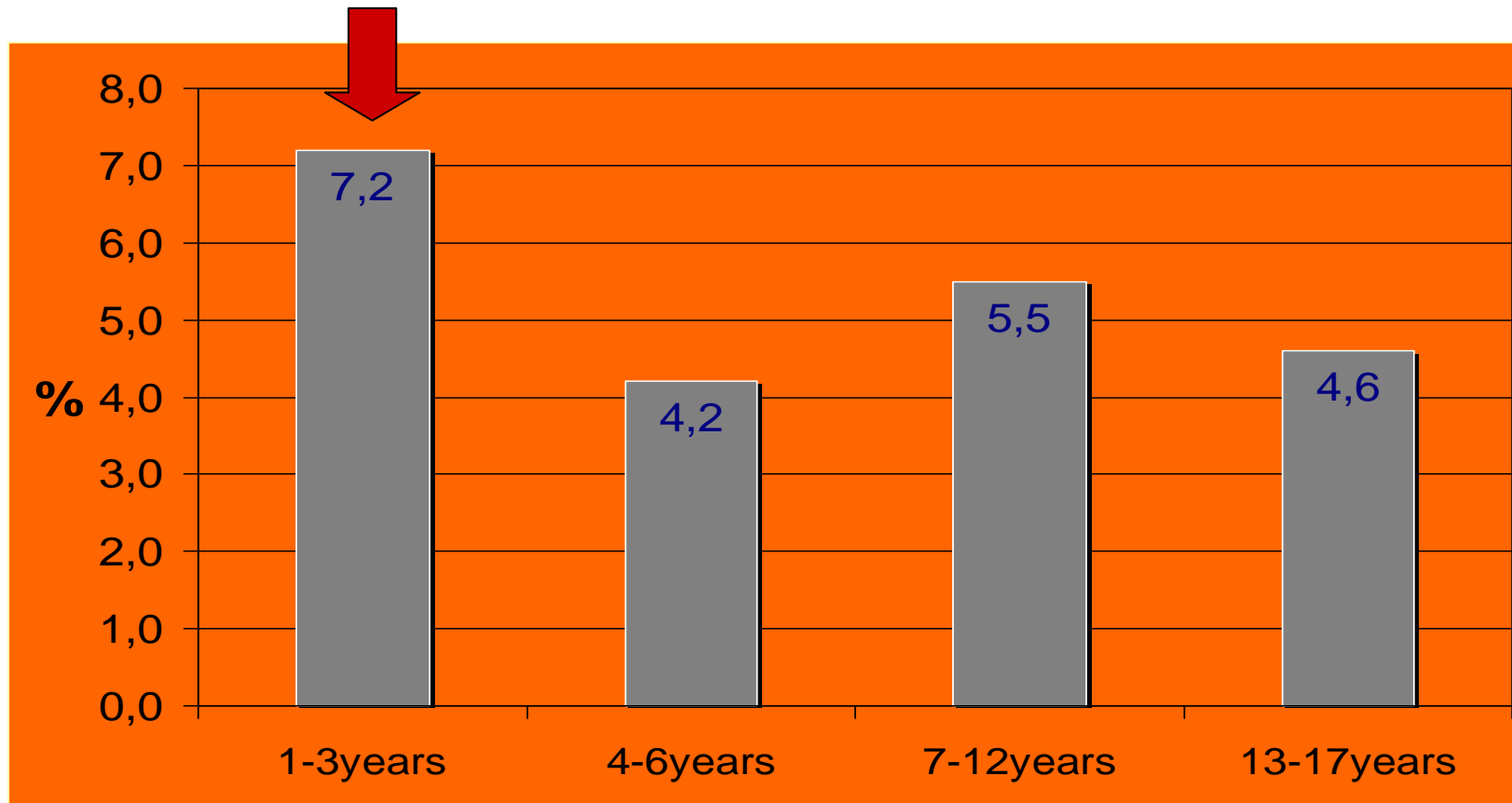
Michele Miraglia del Giudice
Servizio Asma e Fisiopatologia Respiratoria Infantile
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Dipartimento di Pediatria
Seconda Università di Napoli

la dimensione del problema



Food allergy in children and potential allergy medicine users in Europe. A randomised telephone survey of children in 10 European nations.

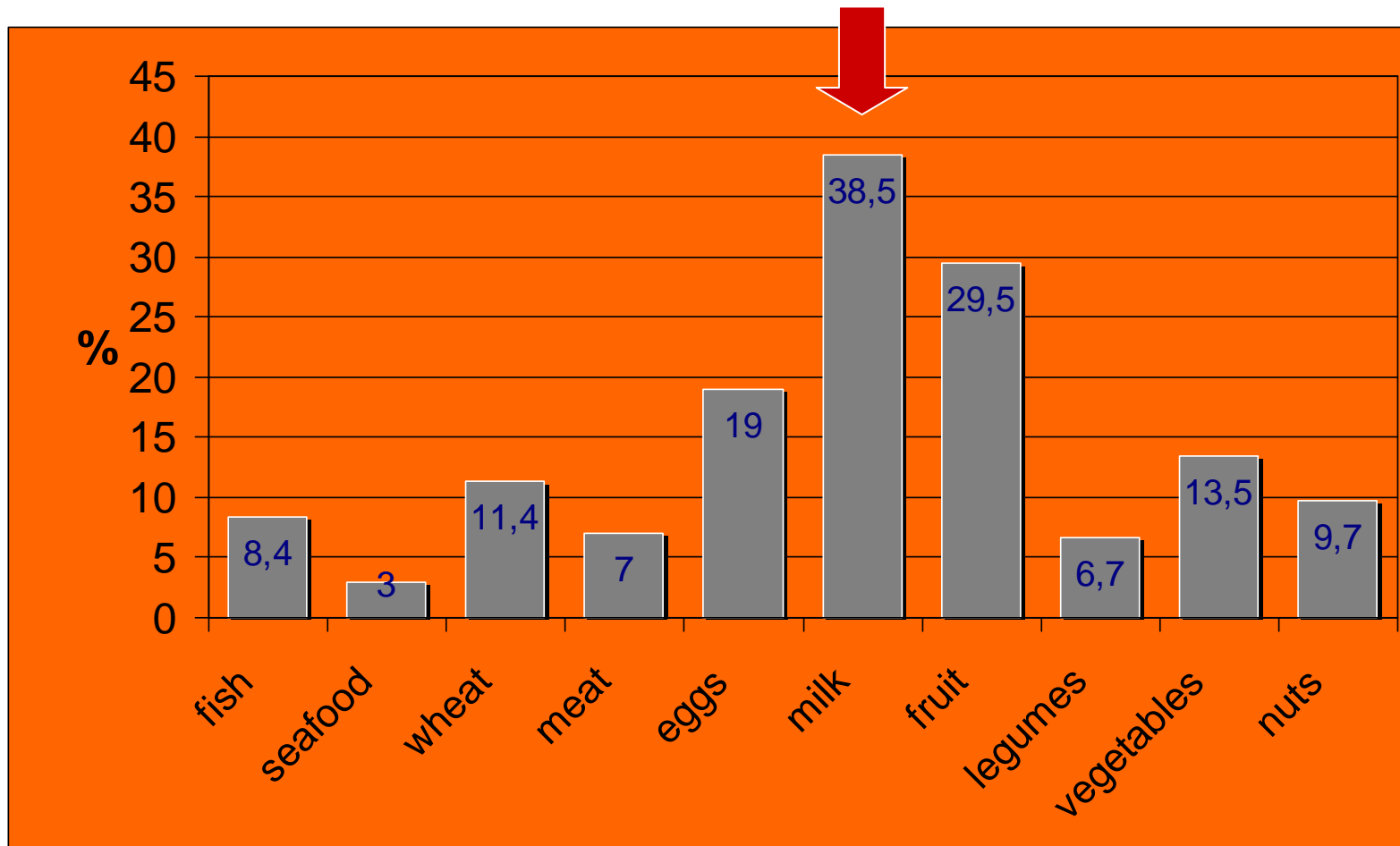
Steinke M. et al. Int Arch Allergy Immunol 2007;143:290-295



prevalenza dell'allergia ad alimenti ed età; dati ottenuti da questionario telefonico

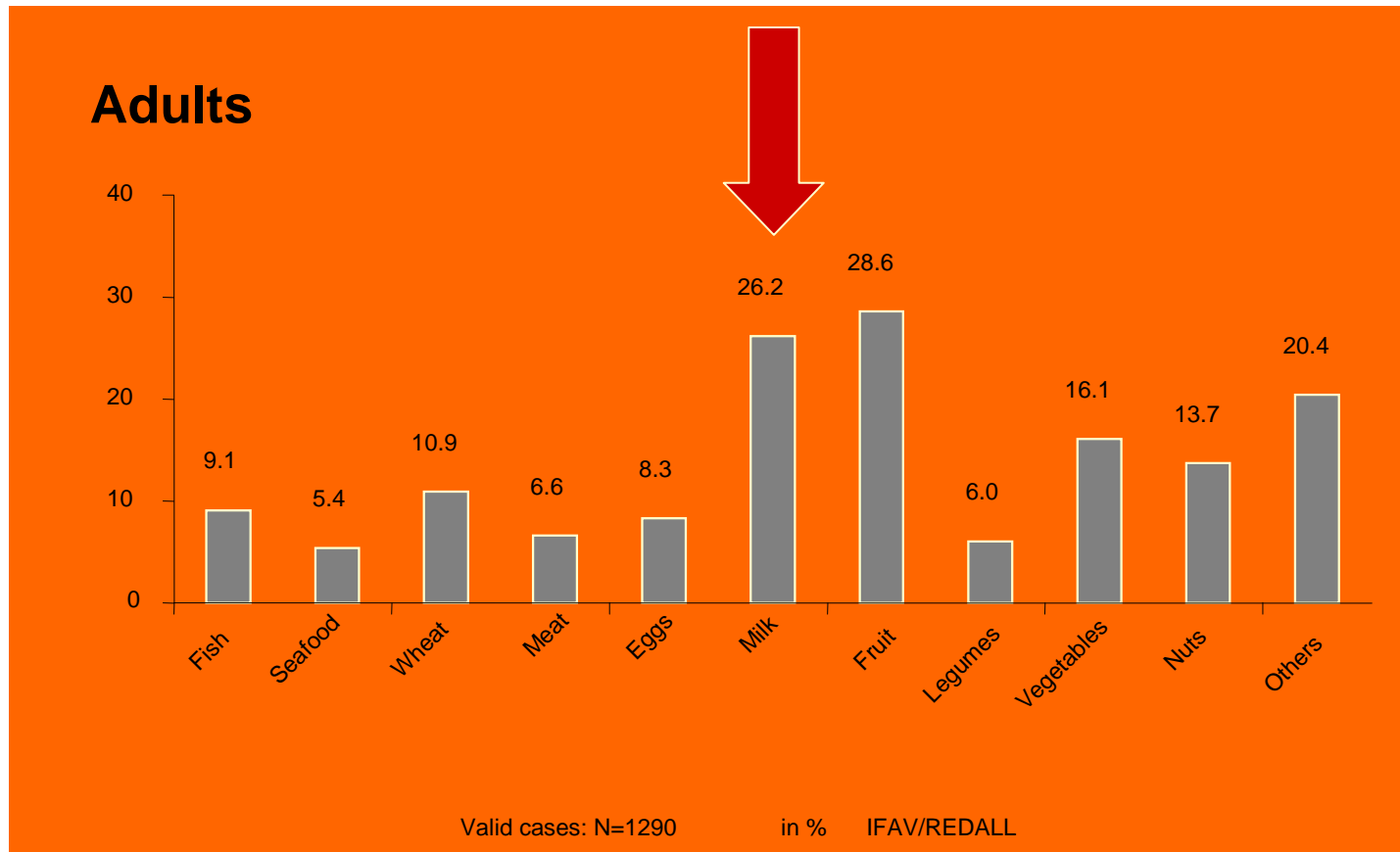
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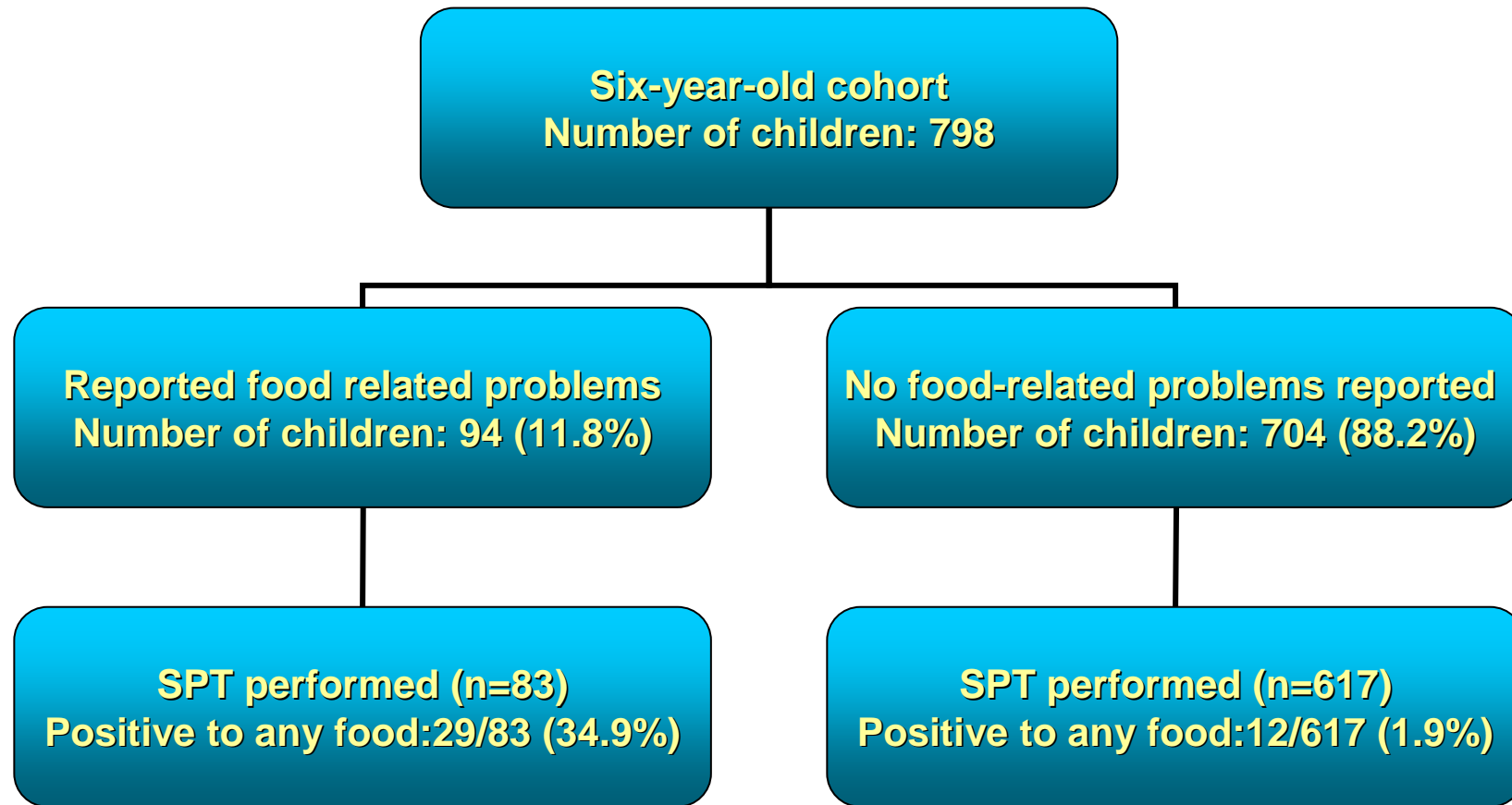
Food allergy in children and potential allergy medicine users in Europe. A randomised telephone survey of children in 10 European nations.

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Prevalence of sensitization reported and objectively assessed food hypersensitivity amongst six-year-old children: a population-based study

Venter C. Pediatr Allergy Immunol. 2006;17:356-63



Not all children reported with CMA are SPT+ve

Prevalence of sensitization reported and objectively assessed food hypersensitivity amongst six-year-old children: a population-based study
Venter C. Pediatr Allergy Immunol. 2006;17:356-63

Not all children reported have CMA

Children aged 6 years	798
Self-report	11.8 %
SPT	3.6 %
Open challenge + history + SPT	2.5 %
DBPCFC + history + SPT	1.6 %

**L'epidemiologia
dovrebbe utilizzare
il DBPCFC!**

INCIDENCE OF CMA IN INFANT BIRTH COHORTS



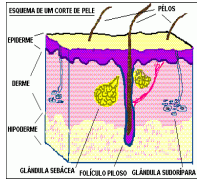
1-year birth cohort - 1,749 newborns \Rightarrow 39 CMA (2.22%)

Høst A. Pediatric Allergy and Immunology 2003; 13 (s15), 23-8

15 months birth cohort – 6209 newborns \Rightarrow 118 CMA (1.9%)

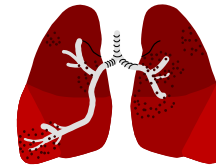
Saarinen KM. J Allergy Clin Immunol 1999;104:457-61.

MANIFESTAZIONI CLINICHE DI ALLERGIA AL LATTE



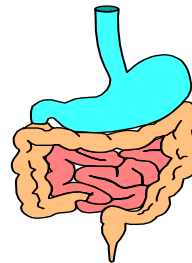
CUTE

- Orticaria-Angioedema acuto
- Orticaria cronica (molto rara)
- Dermatite atopica (EADS)
- Dermatite da contatto da alimenti



APP. RESPIRATORIO

- Rinite (rarissimamente isolata)
- Asma (rarissimamente isolata)



APP. GASTROINTESTINALE

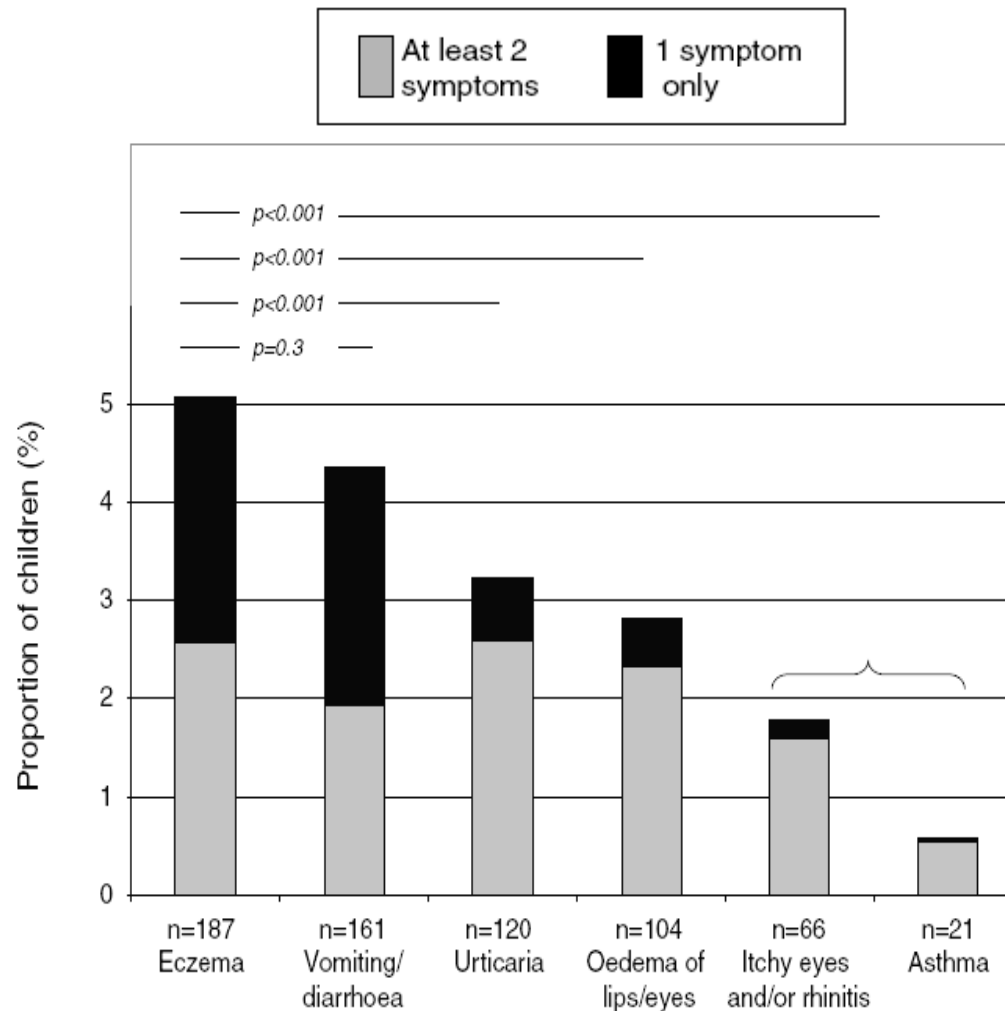
SISTEMICA

- Anafilassi
- Anafilassi da sforzo
alimento-dipendente

- GER
- Ipersensibilità GI immediata ("Anafilassi GI")
- Patologie allergiche GI ad eosinofili
- FPIES
- Proctocolite da proteine alimentari
- Enteropatia da proteine alimentari
- Stipsi cronica (?)
- Coliche del lattante (?)

Reported symptoms of food hypersensitivity and sensitization to common foods in 4-year-old children

Eva Östblom (eva.ostblom@ki.se)^{1,2,3}, Magnus Wickman^{1,3,4}, Marianne van Hage^{3,5}, Gunnar Lilja^{1,2,3} *Acta Paediatrica* 2008 **97**, pp. 85–90



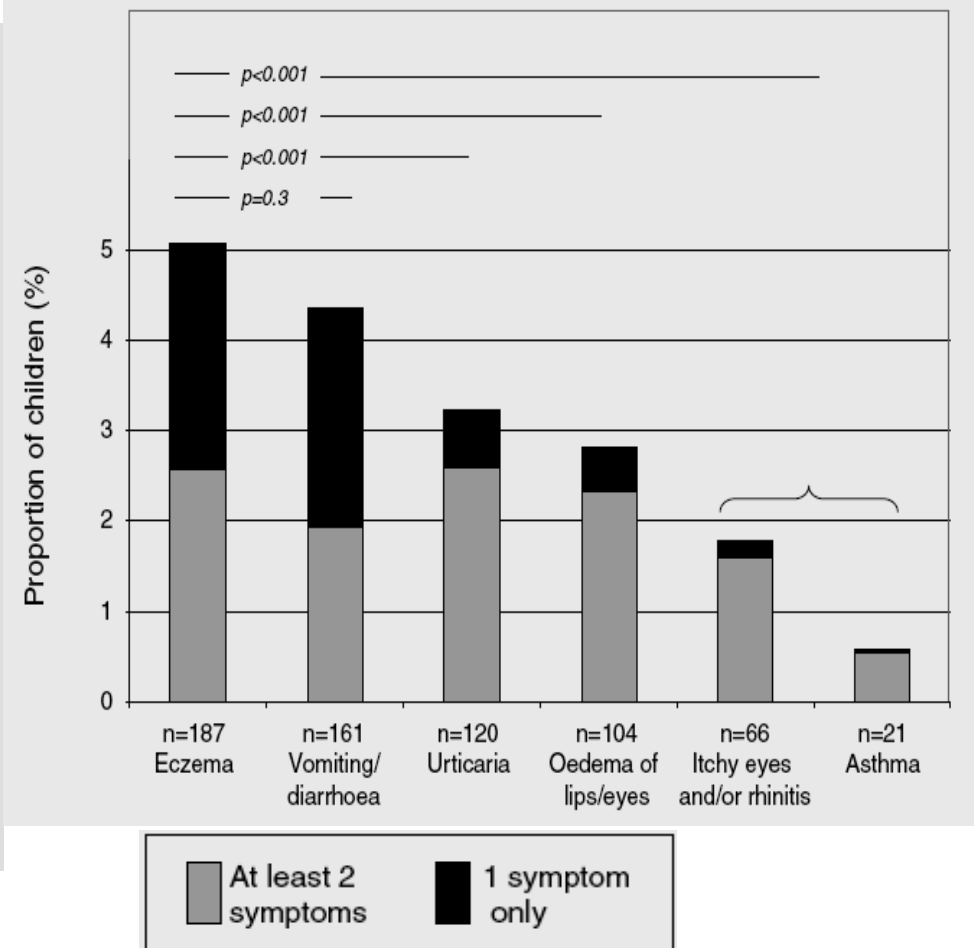
Reported symptoms of food hypersensitivity and sensitization to common foods in 4-year-old children

Eva Östblom (eva.ostblom@ki.se)^{1,2,3}, Magnus Wickman^{1,3,4}, Marianne van Hage^{3,5}, Gunnar Lilja^{1,2,3} *Acta Paediatrica* 2008 **97**, pp. 85–90

FHS was reported in 11% of the children (n=397)


Table 1 Foods reported to cause symptoms of FHS in a birth cohort of 2563 children at 4 years of age

Specific foods reported to cause FHS	Children with FHS at 4 years of age, n = 397		
	(n)	(%)	CI 95%
Cow's milk	129	32	(28–37)
Citrus	127	32	(27–37)
Peanut	102	27	(21–30)
Tree nuts/almond	98	25	(20–29)
Egg	94	24	(19–28)
Stone fruit	86	22	(18–26)
Chocolate	67	17	(13–21)
Fish	42	11	(8–14)
Pea	32	8	(5–11)
Soy bean	30	8	(5–10)
Wheat	19	5	(3–7)
Banana	7	2	(0–3)



Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Vandenplas Y et al. Arch Dis Child 2007;000:1–9.*

Table 1 Alarm symptoms and findings (can be found alone or in combination with items listed in table 2), indicating severe CMPA as the possible cause



Organ involvement	Symptoms and findings
Gastrointestinal tract	Failure to thrive due to chronic diarrhoea and/or refusal to feed and/or vomiting Iron deficiency anaemia due to occult or macroscopic blood loss Hypoalbuminaemia Endoscopic/histologically confirmed enteropathy or severe colitis
Skin	Exudative or severe atopic dermatitis with hypoalbuminaemia or failure to thrive or iron deficiency anaemia
Respiratory tract (unrelated to infection)	Acute laryngoedema or bronchial obstruction with difficulty breathing
General	Anaphylaxis

How dangerous is food allergy in childhood? The incidence of severe and fatal allergic reactions across the UK and Ireland

Macdougall C F Arch Dis Child 2002;86:236–239

✓ A retrospective search for fatalities in children 0–15 years from 1990 to February 1998.

✓ The UK under 16 population is 13 million. Over the past 10 years, eight children died (incidence of 0.006 deaths per 100 000 children 0–15 years per year).

Milk caused four of the deaths



Allergen	Reported reaction	
	Severe	Near fatal
♀ Food	3	
Mixed food	9	2
Cows' milk—includes ice cream, yoghurt, formula milk	5	1
Egg	3	1
Peanut	10	
Yeast extract (Marmite)	2	
Soya	1	
Sesame seed	1	
Potato	1	
Wheat	1	
Lentil		1
Mixed nuts	2	
Walnut	1	1
Brazil nut	2	
Cashew nut	7	
Macadamia nut	1	

che fare?



POSITION STATEMENT

MJA 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

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

Arch Dis Child 2007;000:1–9. doi: 10.1136/adc.2006.110999

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

Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Vandenplas Y et al. Arch Dis Child 2007;000:1–9.*



✓ **Breast feeding** is the gold standard for milk feeding in infant nutrition and is recommended exclusively for the first 4 months of life at least.



✓ **The incidence of CMPA** is lower in exclusively breast-fed infants compared to formula-fed or mixed-fed infants.

✓ Only about 0.5% of exclusively breast-fed infants show clinical reactions to CMP and most of these are mild to moderate.

✓ **Severe forms** of CMPA are very rare in exclusively breast-fed infants. The occasional cases that occur are usually severe atopic dermatitis with protein losses and failure to thrive and anaemia due to colitis with rectal bleeding and protein-losing enteropathy. In these infants, diagnoses other than CMPA are much more likely, and identifying the correct diagnosis should not be delayed

ALGORITHM FOR THE DIAGNOSIS AND MANAGEMENT OF COW'S MILK PROTEIN ALLERGY (CMPA) **IN BREAST-FEED INFANTS**



icon 1



icon 1

Suspicion of cows' milk protein allergy (CMPA)

Clinical assessment

- Clinical findings
- Family history (risk factor)

Suspicion of severe CMPA

One or more of the following symptoms:

- Gastrointestinal: failure to thrive because of diarrhoea or regurgitation/ vomiting; refusal to feed, moderate to large amounts of blood in stool with decreased haemoglobin; protein-losing enteropathy
- Dermatological: failure to thrive and severe atopic dermatitis

Referral to paediatric specialist for diagnosis and treatment, and in the mean time:
elimination diet in mother (no CMP) plus
Ca supplement

Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Vandenplas Y et al. Arch Dis Child 2007;000:1–9.*



In cases of breast-fed with recurrence of symptoms after reintroduction of dairy products in the mother's diet, the algorithm recommends eHF if the mother wants to start weaning the infant and if the child is younger than 9–12 months.

However, one could speculate that since the infant reacted to the (very) small amounts of proteins present in its mother's milk, it might be preferable to recommend AAF.

Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Vandenplas Y et al. Arch Dis Child 2007;000:1–9.*

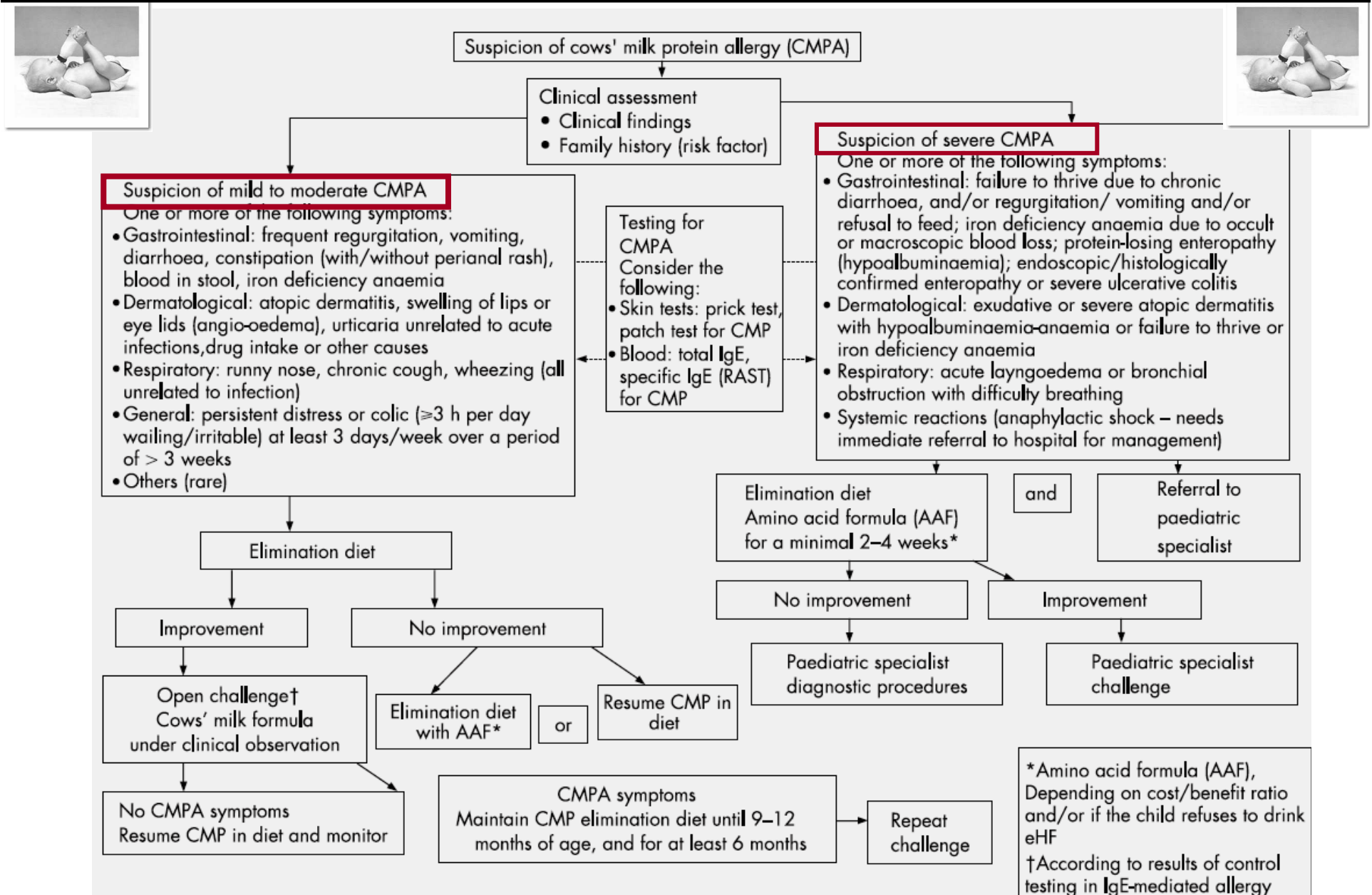


IN FORMULA-FED INFANTS



Patients with life-threatening, particularly respiratory symptoms or anaphylaxis, conditions need to be referred immediately to an emergency department experienced in the treatment of this condition. **In all the other situations**, the initial step in the diagnostic work-up for CMPA is clinical assessment accompanied by history taking, including establishing whether there is a family history of atopic disease

ALGORITHM FOR THE DIAGNOSIS AND MANAGEMENT OF COW'S MILK PROTEIN ALLERGY (CMPA) IN FORMULA-FED INFANTS



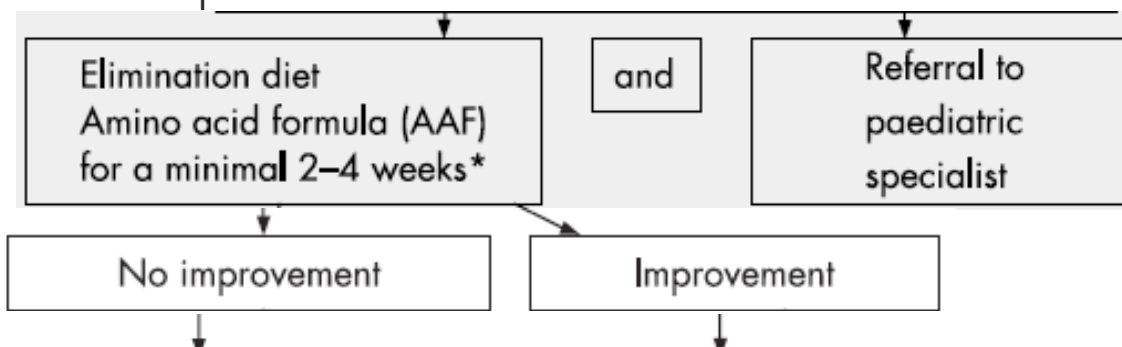
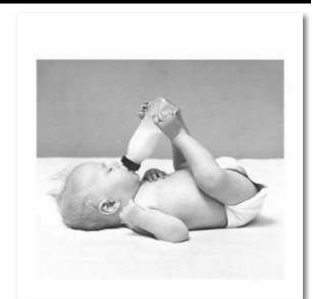
ALGORITHM FOR THE DIAGNOSIS AND MANAGEMENT OF COW'S MILK PROTEIN ALLERGY (CMPA) IN FORMULA-FED INFANTS



Suspicion of severe CMPA

One or more of the following symptoms:

- Gastrointestinal: failure to thrive due to chronic diarrhoea, and/or regurgitation/ vomiting and/or refusal to feed; iron deficiency anaemia due to occult or macroscopic blood loss; protein-losing enteropathy (hypoalbuminaemia); endoscopic/histologically confirmed enteropathy or severe ulcerative colitis
- Dermatological: exudative or severe atopic dermatitis with hypoalbuminaemia-anaemia or failure to thrive or iron deficiency anaemia
- Respiratory: acute laryngoedema or bronchial obstruction with difficulty breathing
- Systemic reactions (anaphylactic shock – needs immediate referral to hospital for management)



The decision concerning allergen challenge in cases with severe CMPA should always be made by a specialist and performed in a hospital setting. **In cases with a history of a lifethreatening reaction, a food challenge may be contraindicated.**

Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Vandenplas Y et al. Arch Dis Child 2007;000:1–9.*



Quando utilizzare gli AAF?

Mild to Moderate CMPA

- ✓ Children may react to residual allergens in eHF, which may be one reason for the failure. The residual allergens in eHFs seem to be more likely to produce gastrointestinal and other non-IgE-associated manifestations compared to AAFs.
- ✓ the infant may be initially switched to an AAF, especially if they experience **multiple food allergies**, **specific gastrointestinal manifestations** or both.
- ✓ If symptoms do not disappear on the AAF, another diagnosis should be considered.

ALGORITHM FOR THE DIAGNOSIS AND MANAGEMENT OF COW'S MILK PROTEIN ALLERGY (CMPA) **IN FORMULA-FED INFANTS**



Quando utilizzare gli AAF?

Infants with Severe Manifestations

AAF is recommended because infants in this group fail to thrive, suffer from macronutrient deficiencies or have pain. In these cases, **AAF minimises the risk of failure** on an eHF **and** further **weight loss**. Many of these children may need further diagnostic work-up to rule out other diagnoses.

Determination of allergenicity to three cow's milk hydrolysates and an amino acid-derived formula in children with cow's milk allergy

C. Caffarelli Clin Exp All 2002; 32:74–79

Table 2. Early (< 12 h) and delayed (> 12 h) symptoms provoked by positive challenge tests to Wp (partially hydrolysed whey formula), Ce (extensively hydrolysed casein formula), We (extensively hydrolysed whey formula), AA (amino acid-based formula) and results of skin prick tests (SPT) and specific IgE antibodies

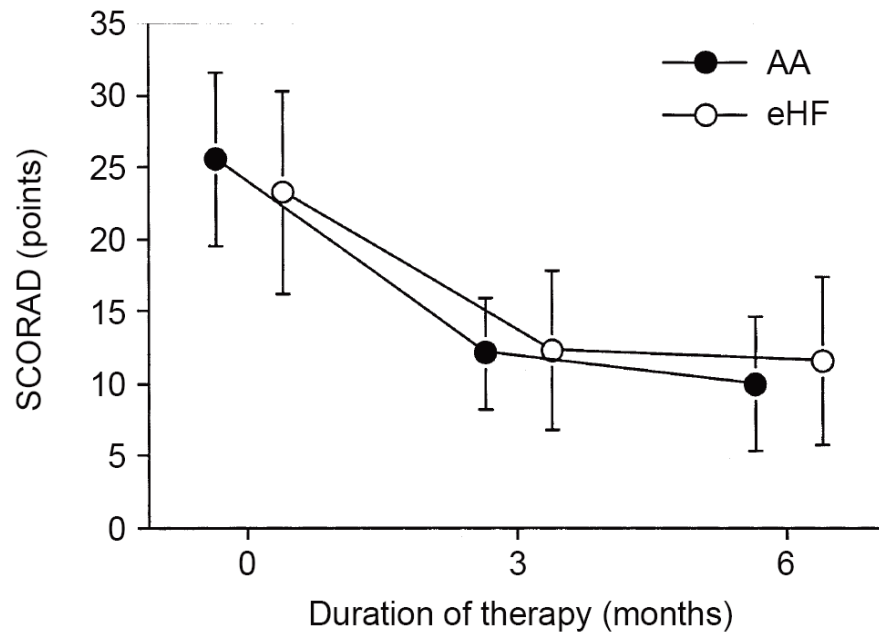
Case	Formula	Symptoms		SPT	IgE
		Early	Delayed		
5	We	Vomiting	Diarrhoea	–	NEG
7	Ce	Diarrhoea	–	+	POS
8	Wp	Urticaria-angioedema, dyspnoea, hypotension	Eczema	++	NEG
9	Wp	Urticaria-angioedema, dyspnoea, hypotension	Eczema	++	NEG
15	We	Urticaria	–	–	NEG
16	Wp	–	Eczema	–	NEG
17	AA	–	Eczema	–	NEG
19	Wp	Urticaria	–	++	NEG
20	We	–	Eczema	–	NEG
20	Wp	–	Eczema	–	NEG
20	AA	–	Eczema	–	NEG

Our results suggest that in children with IgE-mediated cow's milk allergy, the first ingestions of extensively hydrolysed cow's milk protein formulas require strict medical supervision because of immediate reactions. This is not the case for amino acid-derived formula.

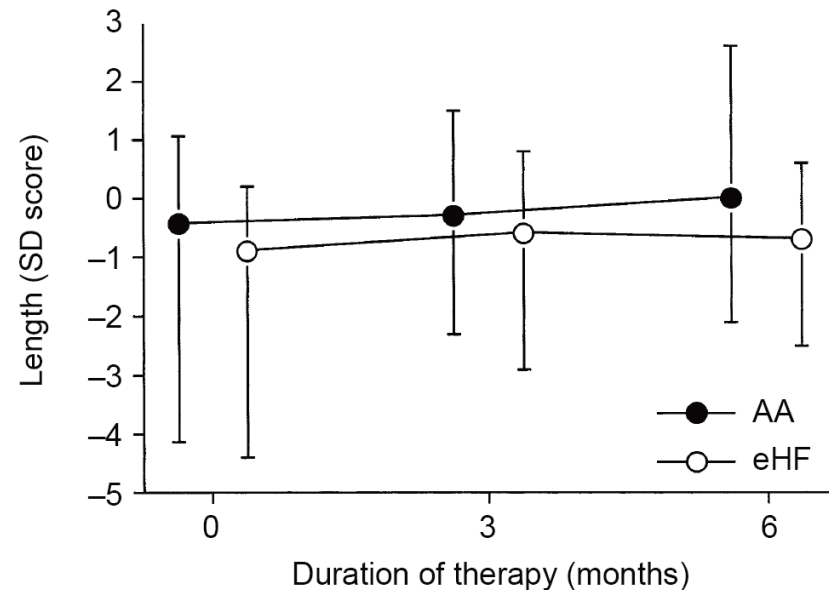
Prospective, controlled, multi-center study on the effect of an amino acid-based formula in infants with cow's milk allergy/intolerance and atopic dermatitis.

Niggemann B. Pediatr Allergy Immunol 2001; 12: 78–82

Efficacy of AA in comparison with eHF for 6 months, on the growth and clinical symptoms of 73 infants with cow's milk allergy/intolerance and atopic dermatitis.



Severity of eczema during treatment. AA, amino-acid-based formula group; eHF, extensively hydrolyzed formula group. significant improvement over time ($P < 0.0001$) in AA group.



Length during treatment expressed as standard deviation scores (median, range). Using the Friedman test, the results were statistically significant for the AA group ($p < 0.04$), with no differences in the eHF group.

The efficacy of amino acid-based formulas in relieving the symptoms of cow's milk allergy: a systematic review

Hill, Clin Exp Allergy 2007;37:808

Table 3. Results of randomized controlled cross-over challenge trials comparing amino acid-based formula (AAF) vs. cow's milk/cow's milk-based formula (CM/CMF) vs. hydrolysed formula (HF) vs. soy-based formula (SF) in patients with confirmed or suspected cow's milk allergy (CMA)

Outcome measures	Sampson et al. [10]			Hill et al. [8]				Caffarelli et al. [35]				
	AAF	eHF	CMF	AAF	eHF	SF	CMF	AAF	pHF (whey)	eHF (casein)	eHF (whey)	SF
Time to resolution of symptoms	-	-	-	< 2 weeks	-	-	-	-	-	-	-	-
Patients with improvement of symptoms	-	-	-	18/18	-	-	-	-	-	-	-	-
Patients with vomiting	0/28	1/28	-	0/18	4/10	2/7	1/1	0/16	0/17	0/16	1/16	0/16
Patients with diarrhoea	-	-	-	0/18	5/10	1/7	0/1	0/10	0/17	1/16	0/16	0/20
Patients with GI symptoms	0/28	-	8/22	-	-	-	-	-	-	-	-	-
Patients with eczema	-	-	-	0/18	1/10	4/7	0/1	2/10	4/17	0/16	1/16	0/20
Patients with rash/'skin symptoms'	0/28	1/28	17/22	-	-	-	-	0/10	3/17	1/16	1/16	0/20
Patients with 'respiratory symptoms'	0/28	1/28	16/22	-	-	-	-	0/10	2/17	0/16	0/16	0/20
Patients with irritability	-	-	-	0/18	6/10	4/7	1/1	-	-	-	-	-
Patients with hypotension	-	-	-	-	-	-	-	0/10	2/17	0/16	0/16	0/20
Patients with 'growth failure'	-	-	-	0/18 post-AAF treatment	2/10 before AAF treatment	2/7 before AAF treatment	0/1 before AAF treatment	-	-	-	-	-

eHF, extensively hydrolysed formula; pHF, partially hydrolysed formula; GI, gastro-intestinal; -, data not reported.

Metanalisi di 20 studi di confronto tra AAF, eHF, soja



Maggiori benefici con AAF in specifici sottogruppi:

- Sintomi durante allattamento materno esclusivo
- Allergia Gastrointestinale
- Allergia non IgE-mediata con ritardo di crescita
- DA atopica severa
- Allergia grave

“[...] Only pure amino acid mixtures
are considered to be
non-allergenic ...”



*Joint Statement ESPACI-ESPGHAN
Arch Dis Child 1999;81:80-4*



dalla teoria...

alla pratica...



...

il caso clinico

O.C. giunge alla nostra osservazione all'età di 5 mesi per la presenza , dai primi mesi di vita , di dermatite atopica associata ad episodi ricorrenti di broncospasmo (2-3/mese)



il caso clinico

Anamnesi familiare Non contributiva per patologie allergiche .

Anamnesi fisiologica Terzogenito , nato alla 26° settimana di gestazione con parto cesareo
Apgar 1':5 5':6 10':7 . Asfissia neonatale e necessità di intubazione alla nascita .
Allattamento misto (M+F) . Accrescimento s.p. 3° percentile.

il caso clinico

Anamnesi patologica remota Ricovero presso reparto di T.I.N. ed assistenza respiratoria prolungata (2 mesi).

Anamnesi patologica prossima La madre riferisce reazioni di orticaria diffusa e wheezing all'ingestione di latte di formula, ha utilizzato idrolizzati estensivi.

il caso clinico

ITER DIAGNOSTICO

- Conferma del sospetto diagnostico di D.A.
criteri di Hanifin e Rajka (1980)
- Valutazione della gravità del quadro clinico

- a) Estensione
- b) Intensità
- c) Sintomi soggettivi

$$a/5+7b/2+c = \text{scorad}$$

The image shows a portion of the SCORAD index form. It includes a body diagram with numbered regions (1-20) for assessing the extent of lesions. Below the diagram are fields for 'A) Numero' (Number) and 'B) Intensità' (Intensity) for each region. To the right, there is a table for 'C) Sintomi soggettivi' (Subjective symptoms) with columns for 'Prurito' (Pruritus), 'Erytema' (Erythema), 'Seccchezza' (Xerosis), and 'Crustole' (Crusts). The table has rows for 'Prurito', 'Erytema', 'Seccchezza', and 'Crustole'.

Scorad index EASI

il caso clinico

ITER DIAGNOSTICO

- Skin Prick Test

Istamina : 3mm. latte vaccino : 4mm. caseina : 3mm.
b.uovo : 3 mm . r.uovo : 3 mm .

- Prick by Prick

Istamina : 3 mm Latte Alfarè : 3mm. Latte Hypolac :
4 mm. Latte Nutramigen : 4mm. Latte Pregomin : 5mm
latte Neocate NEGATIVO .

il caso clinico

ITER DIAGNOSTICO

- RAST

Latte : 8,5 UI/ml Caseina : 4,8 UI/ml B. uovo : 5,2 UI/ml

Si prescrive "latte" a base di miscela di AA (Neocate).



il caso clinico

ITER DIAGNOSTICO

Osservazione clinica (4 settimane)



- NETTO MIGLIORAMENTO DELLA D.A.
- NETTO MIGLIORAMENTO DELLA CRESCITA

il caso clinico

ITER DIAGNOSTICO:

CHALLENGE IN APERTO



COMPARSA DI ORTICARIA



CONTINUA NEOCATE



Grazie



A protocol for oral desensitization in children with IgE-mediated cow's milk allergy Meglio P. Allergy 2004; 59: 980–987

Table 1. Symptoms after double blind placebo-controlled food challenge (DBPCFC) with cow's milk (CM), after accidental ingestion of CM, and during CM desensitization

Patient	Age at the start of CM desensitization (Years, months)	Time between DBPCFC (or accidental ingestion of CM) and onset of symptoms (min)	Symptoms after DBPCFC with CM	Symptoms after accidental ingestion of CM (DBPCFC not done for 'convincing history')	Outcome of CM desensitization	Symptoms during CM desensitization (see text for more details)	Dose of CM when symptom(s) intervened	
1	ChF	7, 3/12	120	Perioral angioedema, urticaria, asthma	—	*	—	
2	DAA	6, 1/12	20	Urticaria, angioedema	—	*	—	
3	DGP	6, 5/12	10	Erythema, urticaria	—	*	—	
4	GF	8, 1/12	20	Pruritus, edema, urticaria, conjunctivitis, abdominal pain	—	*	—	
5	IA	8, 6/12	160	Urticaria, abdominal pain	—	*	—	
6	LPD	10, 4/12	15	Vomiting, abdominal pain	—	*	—	
7	PerM	7, 10/12	90	Pruritus, erythema, perioral urticaria, vomiting	—	*	—	
8	PetM	5, 6/12	1	Pruritus, urticaria, edema	—	*	—	
9	CF	5, 3/12	30	—	Urticaria, perioral angioedema, severe asthma	†	Temporary nasal obstruction	From 7 to 12 ml of undiluted CM
10	CS	5, 6/12	60	—	Acute diarrhea, vomiting, profuse sweating, soles pruritus	†	Rhinitis, abdominal pain	From 45 to 55 ml of undiluted CM
11	ML	10, 2/12	15–20	Pruritus, urticaria, angioedema, cough	—	†	Abdominal pain	From 1 to 5 ml of undiluted CM
12	PI	7, 3/12	15	Urticaria	—	†	Temporary throat pruritus	From 10 drops of CM diluted 1 : 25 to two drops of undiluted CM
13	MR	10	50	Severe asthma	—	†	Temporary throat pruritus	From two drops to 2 ml of undiluted CM
14	RR	8, 7/12	25	Pruritus of tongue, edema	—	†	Temporary erythema (hands and popliteal and elbow folds)	From 9 to 15 ml of undiluted CM
15	TS	6	1	Erythema, urticaria	—	†	Temporary soles pruritus	From 80 to 85 ml of undiluted CM
16	DOA	6, 7/12	120	Erythema, edema, rhinitis, vomiting, rhinitis (1)	—	‡	Moderate asthma	47 ml of undiluted CM
17	PM	7, 6/12	70	Erythema, cough (2)	—	‡	Angioedema	45 ml of undiluted CM
18	VS	8, 3/12	1	Tickly throat, cough, asthma (3)	—	‡	Asthma, whole body erythema	90 ml of undiluted CM
19	DV	5, 10/12	10	Rhinitis, pharyngeal pruritus	—	§	Urticaria, throat pruritus	10 drops of undiluted CM
20	GS	6, 11/12	1	Vomiting	—	§	Throat pruritus, epigastric pain, vomiting	2 drops of diluted CM
21	PD	6, 1/12	70	—	Severe asthma	§	Moderate asthma	18 drops of undiluted CM

Outcome of CM desensitization:

* Tolerates 200 ml of whole CM per day.

† Tolerates 200 ml of whole CM per day (presented some symptoms which occurred in a short time after ingestion of CM and persisted for <2 h).

‡ Tolerates between 40 and 80 ml of whole CM per day. During the DBPCFC they had symptoms: (1) with 60 ml of verum (= 30 ml of CM); (2) with 5 ml of verum (= 2.5 ml of CM); (3) with 30 ml of verum (= 15 ml of CM).

§ Oral CM desensitisation failed (immediate onset of allergic symptoms after a few doses).

Results: Overall, 15 of 21 children (71.4%) achieved the daily intake of 200 ml during a 6-month period; three of 21 children (14.3%) tolerated 40–80 ml/day of undiluted CM; three of 21 children (14.3%) failed the desensitization because they presented allergic symptoms after ingesting minimal amounts of diluted CM.

Oral desensitization in children with immunoglobulin E-mediated cow's milk allergy – follow-up at 4 yr and 8 months

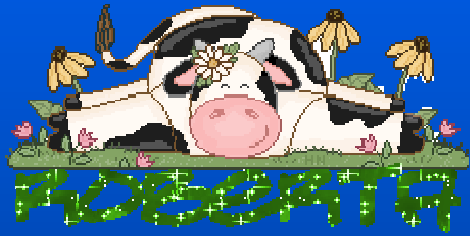
Meglio P *Pediatr Allergy Immunol* 2008

Clinical tolerance induced by oral CM desensitization persists in time. Negativization of SPT and reduction of specific CM IgE could be considered prognostic indicators of CM tolerance. Oral CM desensitization seems to be a promising method to treat CM food allergy.



CHALLENGE

- After a physical examination of the undressed infant, with inspection of the skin, a drop of the formula is put on the lips.
- If no reaction occurs after 15 min, the formula is given orally and the dose is increased stepwise (0.5, 1.0, 3.0, 10, 30, 50 to 100 ml) every 30 min.
- Thereafter, the infant is observed for 2 h and examined for cutaneous and respiratory reactions before going home. If no reaction occurs, the child should receive at least 250 ml of cow's milk-based formula each day for the next week and the parents told to observe the child for late reactions.



Evaluation of the residual antigenicity and allergenicity of cow's milk substitutes by in vitro tests. *Docena G. Allergy 2002: 57: 83–91*

Aim: investigate the presence of residual allergenic cow's milk proteins (CMP) milk substitutes for the treatment of cow's milk allergy (CMA) by ELISA, EAST and immunoblotting methods.

IPOALLERGENICITA' "IN VIVO" DEGLI IDROLISATI

FORMULA	Sampson J Pediatr 1991	Wahn J Pediatr 1992	Ragno Eur J Pediatr 1993	Halken PAI 1993	Martin- Esteban JPGN 1998	Gianpietro PAI 2001	Caffarelli CEA 2002	Klemola J Pediat 2002
Nutramigen	100	100	-	100	-	-	94	-
Pregestimil	-	100	-	-	-	-	-	-
Alimentum	100	-	90	-	-	-	-	-
Prophylac	-	-	87	100	-	94	-	-
Pregomin	-	87	-	-	-	-	-	-
Nutrilon Pepti	-	-	-	-	-	97	-	-
Alfarè	-	75	-	-	-	-	-	-
Hypolac	-	-	-	-	-	-	82	-
Damira					94			
Peptiditutteli	-	-	-	-	-	-	-	98
Nidina HA	-	-	55	-	-	-	-	-
Humana HA	-	-	-	-	-	-	71	-

Terracciano, AAI 2002;89(suppl):86 (modif)

Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Vandenplas Y et al. Arch Dis Child 2007;000:1–9.*

An AAF is indicated: if the child refuses to drink the eHF, but accepts the AAF (eHF has a more bitter taste than AAF), if the symptoms do not improve on the eHF after 2–4 weeks, or if the cost–benefit ratio favours the AAF over the eHF. The cost–benefit ratio of AAF versus eHF is difficult to elaborate in this global overview since health care cost differs substantially from country to country, as does the cost of the eHF and the AAF, which in some countries is (partially) reimbursed by national or private health insurance. The risk of failure of eHF is up to 10% of children with CMPA.

Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Vandenplas Y et al. Arch Dis Child 2007;000:1–9.*

Infants with mild-to-moderate symptoms should receive eHFs, or AAF if the infant refuses to drink eHF or if the cost–benefit ratio favours AAF, for at least 2–4 weeks.

Children who show a substantial improvement or disappearance of symptoms should undergo a challenge under medical supervision. If symptoms of CMPA emerge upon food challenge, the child should be maintained on eHF or AAF for at least 6 months or until 9–12 months of age. If symptoms do not improve on eHF, primary care physicians and general paediatricians should consider an elimination diet with AAF, other differential diagnoses or both for the symptoms and/or refer the patient to a paediatric specialist.

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

MJA 2008; 188: 109–112

Syndrome	Onset of reaction	Maternal elimination of CMP if breastfeeding?	Choice of formula			NHMRC level of evidence [‡]	Consensus panel agreement [§]
			First [†]	Second (if first not tolerated)	Third (if second not tolerated)		
Immediate reaction							
Immediate food allergy	< 1 h	Yes	eHF (< 6 months) Soy (> 6 months)	AAF eHF	— AAF	II	11/11
Anaphylaxis	< 1 h	Yes	AAF (followed by urgent consultation with paediatric allergist)	—	—	IV	11/11
Food protein-induced enterocolitis syndrome	1–3 h	No	eHF	AAF	—	IV	10/11
Delayed reaction							
Atopic eczema	Hours to days	Yes [¶]	eHF (< 6 months or > 6 months with FTT) Soy (> 6 months, no FTT)	AAF eHF	— AAF	IV	11/11
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) Soy (> 6 months, no FTT)	AAF eHF	— AAF	I (severe irritability), III (GORD), IV (others)	11/11
Food protein-induced proctocolitis							11/11
Formula-fed	> 24 h	—	eHF	AAF	—	IV	
Breastfed	> 24 h	Yes [¶]	—	—	—		
Eosinophilic oesophagitis in infants	Days to weeks	Yes	AAF	—	—	IV	11/11

Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Vandenplas Y et al. Arch Dis Child 2007;000:1–9.*

If the clinician suspects severe CMPA in a formula-fed infant, the patient should receive AAF and be referred to a paediatric specialist experienced in managing infant allergies. Food challenges in infants with severe symptoms should be performed only in a setting with personnel experienced in treating anaphylaxis.

The use of unmodified mammalian milk protein, including unmodified cow's, sheep, buffalo, horse or goats' milk, or unmodified soy or rice milk, is not recommended for infants. These milks are not adequately nutritious to provide the sole food source for infants. Furthermore, the risk of possible allergenic cross-reactivity means that these milks or formulas based on other mammalian milk protein are not recommended for infants with suspected or proven CMPA.

Soy protein, for example, is not hypo-allergenic. The incidence of soy allergy in soy formula-fed infants is comparable to that of CMPA in cow's milk formula-fed babies. In particular, infants with multiple food allergies and eosinophilic enterocolitis syndrome react to formulas which include soy protein.

Although soy formulations are significantly cheaper and have a better acceptance than eHF and AAF, the risk that the child will develop soy allergy in addition to CMPA, particularly in infants below 6 months of age, was considered by the authors to be too high for it to be recommended as the first choice. Soy may be considered in infants refusing to drink eHF and/or AAF, especially beyond the age of 6 months

Formule ipoallergeniche: *Definizione AAP*



[...] To be labeled hypoallergenic, these formulas, after appropriate preclinical testing, must demonstrate in clinical studies that they do not provoke reactions in 90% of infants or children with confirmed cow's milk allergy with 95% confidence when given in prospective randomized, double-blind, placebo-controlled trials [...]



*AAP. Committee on Nutrition.
Pediatrics 2000;106:346-9*

Potenziali sostituti del LV nella terapia dell'allergia alimentare



- Idrolisati di proteine del LV con parziale grado di idrolisi (pHF)
- Idrolisati di proteine del LV con elevato grado di idrolisi (eHF)

- Formule a base di soia
- Idrolisati di soia e collagene suino

- Idrolisati di riso

- Miscele di AA

- Latti di mammiferi alternativi alla specie bovina

Le Linee Guida...



American Academy
of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™
Committed to the attainment of optimal physical, mental,
and social health and well-being for all infants,
children, adolescents, and young adults

*AAP. Committee on Nutrition.
Pediatrics 2000;106:346-9*



*Joint Statement ESPACI-ESPGHAN
Arch Dis Child 1999;81:80-4*

A chi

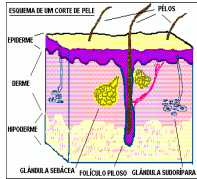
TERAPIA
CON I LATTI
FORMULA

Quali

Per quanto
tempo

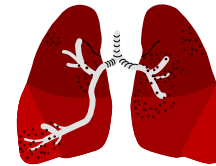


MANIFESTAZIONI CLINICHE DELL' ALLERGIA ALIMENTARE



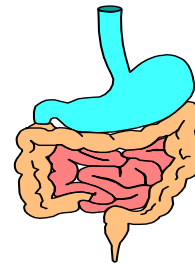
CUTE

- Orticaria-Angioedema acuto
- Orticaria cronica (molto rara)
- Dermatite atopica (EADS)
- Dermatite da contatto da alimenti
- Dermatite erpetiforme [glutine]



APP. RESPIRATORIO

- Rinite (rarissimamente isolata)
- Asma (rarissimamente isolata)
- S. di Heiner



APP. GASTROINTESTINALE

SISTEMICA

- Anafilassi
- Anafilassi da sforzo alimento-dipendente

- Sindrome Orale Allergica ("Pollen-Food Allergy S.")
- Ipersensibilità GI immediata ("Anafilassi GI")
- Patologie allergiche GI ad eosinofili
- FPIES
- Proctocolite da proteine alimentari
- Enteropatia da proteine alimentari
- Stipsi cronica (?)
- Coliche del lattante (?)

PATOLOGIE IMPROBABILMENTE CAUSATE DA UN'ALLERGIA ALIMENTARE

- DAR isolati
- Ritardo di accrescimento isolato
- Otiti ricorrenti
- Cefalea
- Purito sine materia
- ADHD
- Disturbi del comportamento
- Insonnia
- Aftosi ricorrenti (eccetto celiachia)
- IRR
- Laringospasmo ricorrente



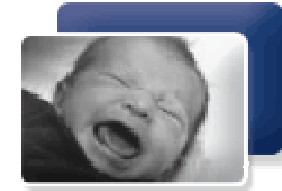
Sampson HA, JACI 2001; 107; 891-6

[...] However, many physicians find DBPCFC impractical in the busy practice setting and continue to rely on patient history, result of **skin tests** results of **RAST's**, and elimination diets to make the diagnosis, a practice that may lead to misdiagnosis in as many as one half the cases.

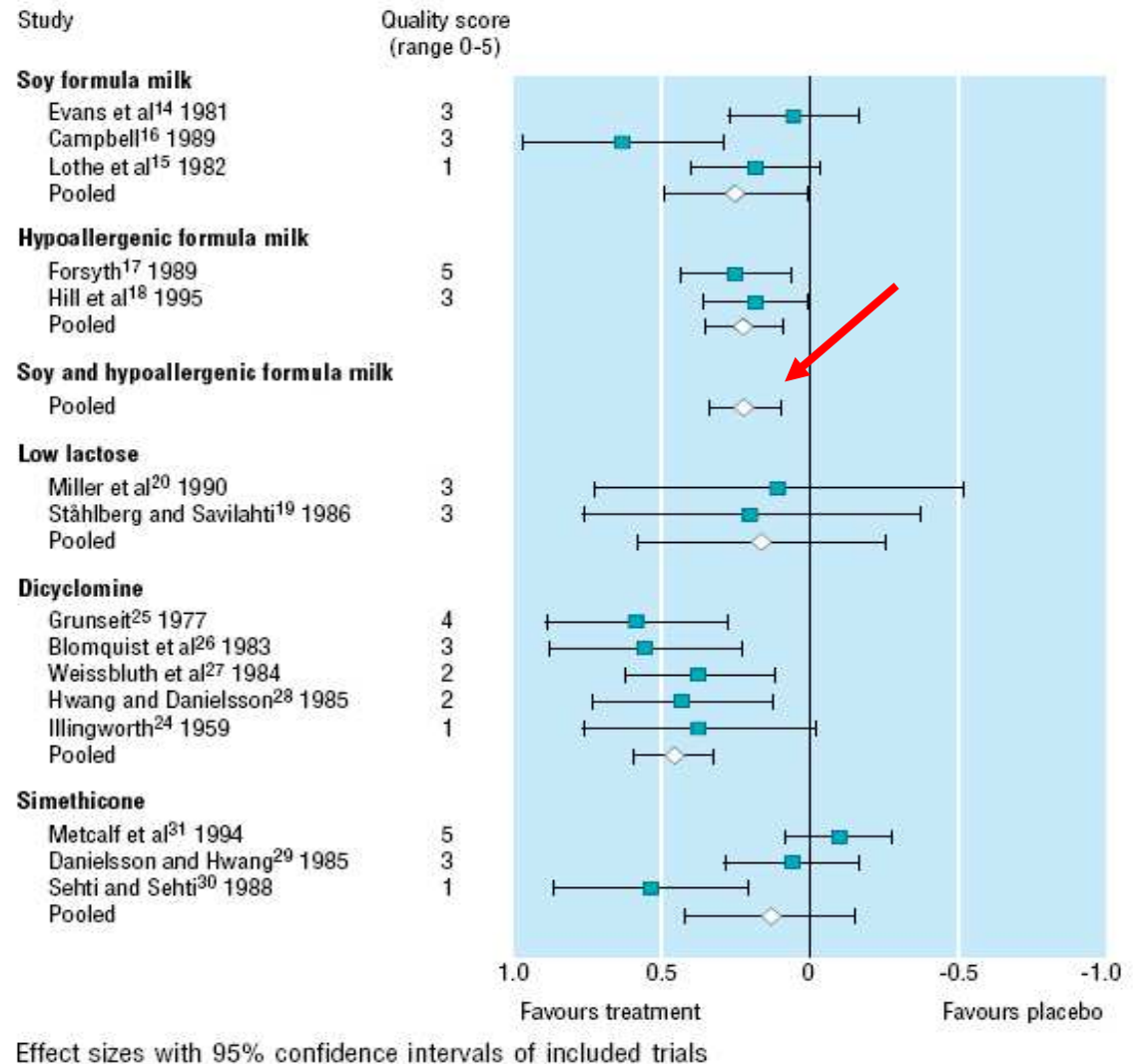


Effectiveness of Treatments for Infantile Colic: Systematic Review

Lucassen, BMJ 1998;316:1563

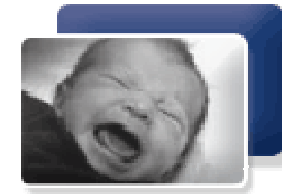


Metanalisi di 5 studi valutanti l'effetto di formule ipoallergeniche sulle coliche del lattante



Infantile Colic: Crying Time Reduction With a Whey Hydrolysate: A Double-Blind, Randomized, Placebo-Controlled Trial

Lucassen, Pediatrics 2000;106:1349



43 lattanti <6 mesi con coliche recidivanti (pianto ≥ 3 h/die per almeno 3 gg/sett) randomizzati per eHF-W o formula standard per 1 settimana



riduzione dei minuti di pianto maggiore ($\downarrow 77'$ /die) nei bb alimentati con eHF-W

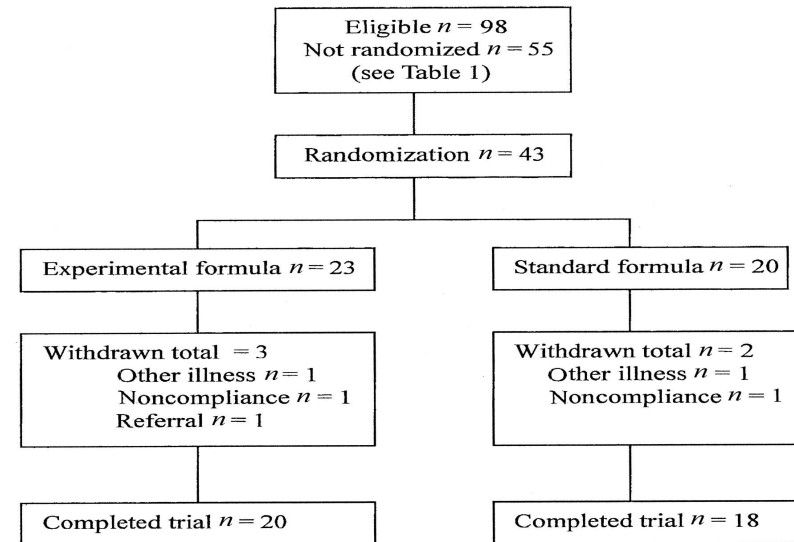


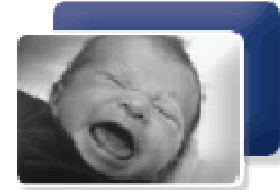
TABLE 3. Results

Primary Outcome: The Reduction of Crying Between the Baseline Week and Intervention in Minutes per Day (95% Confidence Interval)				
	Whey Hydrolysate	Standard Cow's Milk	Difference	P
Intention to treat (n = 43)				
Unadjusted	104 (55-155)	3 (-63-67)	101 (25-179)	.02
Adjusted†			63 (1-127)	.05
Patients completing trial (n = 38)				
Unadjusted	111 (62-160)	34 (-1-69)	77 (17-136)	.01
Adjusted*			47 (3-91)	.04
Secondary Outcome: Proportion of Infants Not Fulfilling the Inclusion Criteria Any More After the Intervention Week				
	Whey Hydrolysate	Standard Cow's Milk	χ^2	P
	8/20 (40%)	5/18 (28%)	0.20	.65

* Adjusted for gender and level of crying in the baseline week.

Effect of a Low-Allergen Maternal Diet on Colic Among Breastfed Infants: A Randomized, Controlled Trial

Hill, Pediatrics 2005;116:e709



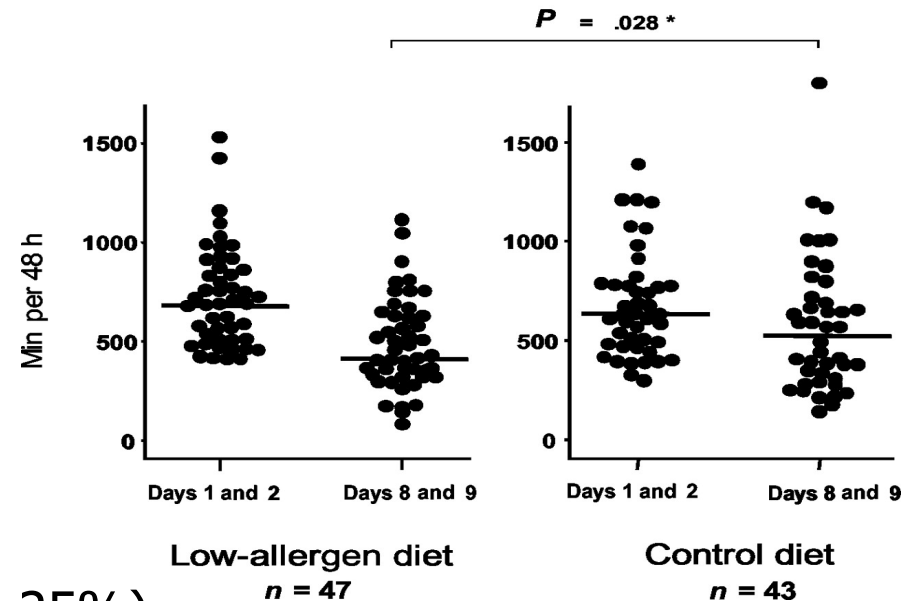
Studio RCT su 107 lattanti
(M 5 wk) con coliche (≥ 3 h/die x 3 gg)
Le madri venivano randomizzate per
dieta libera o di esclusione (7 gg) per:

- latte
- uovo
- pesce
- frutta secca
- soja
- grano



Più frequente diminuzione del pianto ($\geq 25\%$)
nel gruppo a dieta di esclusione (74% vs 37%)

Diminuzione significativa dei min. di pianto/irritabilità
($\downarrow 21\%$) nel gruppo dieta di esclusione





A chi

TERAPIA
CON I LATTI
FORMULA

Quali

Per quanto
tempo



Formula consigliata per la supplementazione	Soja Idrolisato spinto Miscele AA	Idrolisato spinto Miscele AA
Evitare idrolisati parziali	Si	Si
Evitare latte di mammiferi (capra, pecora)	Si	Si



*AAP. Committee on Nutrition.
Pediatrics 2000;106:346-9*



[...] infants with **IgE-associated symptoms** of allergy may benefit from a **soy formula**, ***either*** as the initial treatment ***or*** instituted **after 6 months** of age after the use of a therapeutic hydrolysate formula

[...] soy ***is not recommended*** for the treatment of infants with ***non-IgE-associated syndromes***



*Joint Statement ESPACI-ESPGHAN
Arch Dis Child 1999;81:80-4*

[...] in general, formulae based on **intact soy protein** isolates ***are not recommended*** for the initial treatment of food allergy in infants, although a proportion of infants with cows'milk protein allergy tolerates soy formula.

Allergy to soya formula and to extensively hydrolyzed whey formula in infants with cow's milk allergy: a prospective, randomized study with a follow-up to the age of 2 years

Klemola, J Pediatr 2002;140:219

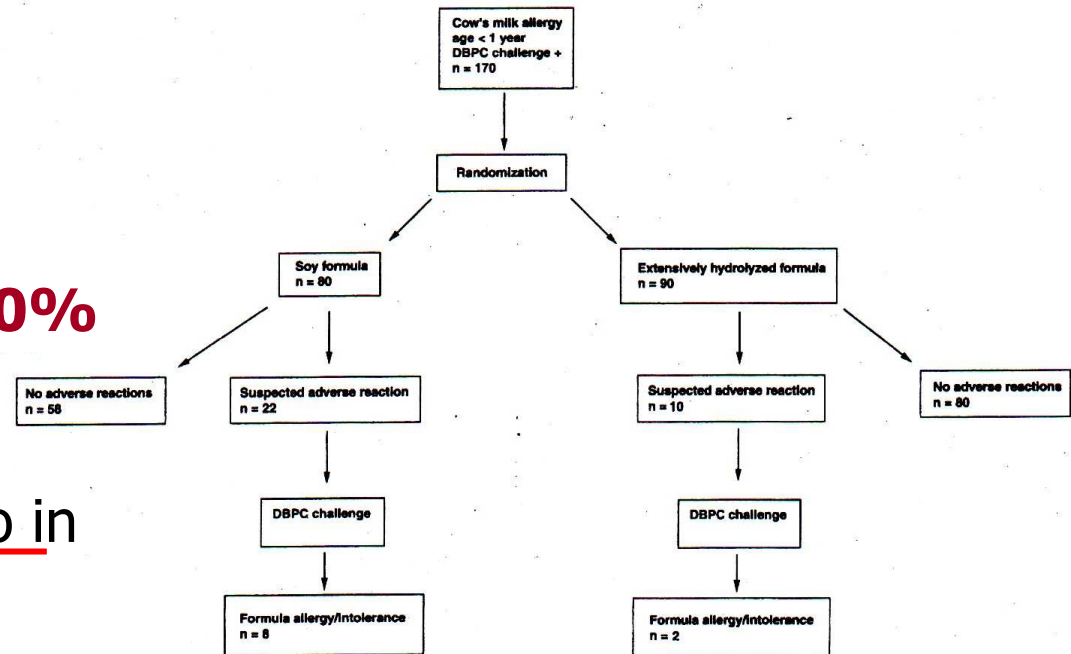
170 bb < 12 m. con APLV
randomizzati per eHF o soya



DBPCFC+ per la **soja** al nel **10%**
DBPCFC+ per **eHF** nel **2%**

Presenza di IgE per la soya solo in 1/4 dei bb con DBPCFC+

Reazioni alla soya più frequenti
in bb < 6 mesi



Detection and identification of a soy protein component that is cross-reactive with caseins from cow's milk

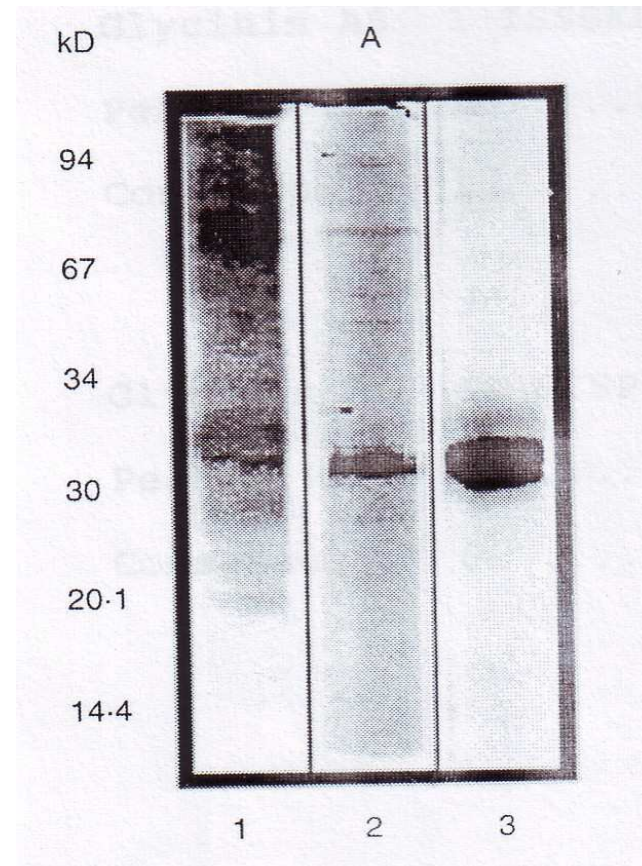
Rozenfeld P, Clin Exp Immunol 2002;130:49-58

Studio di cross-reattività tra
soja e LV con immunoblot
ed ELISA inibizione



Componente p.m. 30 kD
responsabile di cross-reattività
tra **soja** e **caseina**

Componente della banda 30 kD
= dipeptide ***glicinina A5-B3***
(66% omologia)





La probabilità di allergia alla soia in bambini con APLV è dell'**8-14%** (anafilassi estremamente rara)

Zeiger, J Pediatr 1999;134:614

Klemola, J Pediatr 2002; 140: 219

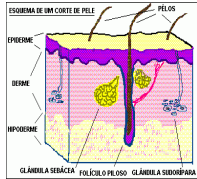
AA Vari, Pediatrics 2000;106:346-9

La percentuale di allergia alla soia nei bambini con **proctocolite** o **enterocolite allergica** è del **25-60%**

Powell, Compr Ther 1986;12:28

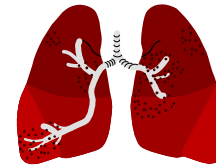
AA Vari, Pediatrics 2000;106:346-9

QUANDO NON SOMMINISTRARE LA SOJA NELL' ALLERGIA AL LATTE?



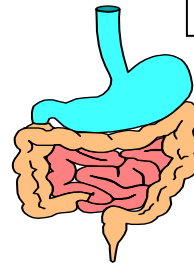
CUTE

- Orticaria-Angioedema acuto
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- Anafilassi
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- Sindrome Orale Allergica ("Pollen-Food Allergy S.")
- Ipersensibilità GI immediata ("Anafilassi GI")
- **Patologie allergiche GI ad eosinofili**
- **FPIES**
- **Proctocolite da proteine alimentari**
- **Enteropatia da proteine alimentari**
- Stipsi cronica (?)
- Coliche del lattante (?)



TRIADE

**DISTURBI DELL'ALVO
e/o SANGUE FECI**

**MECCANISMO
CELLULO-MEDIATO**

**INFIAMMAZIONE CRONICA
INTESTINALE**

CARATTERI DIFFERENZIALI DI ALCUNE FORME CLINICHE DI ALLERGIA ALIMENTARE GASTRO-INTESTINALE

	Gastroenterite eosinofila	Proctocolite da proteine alimentari	Enterocolite da proteine alimentari (FPIES)	Enteropatia da proteine alimentari
Meccanismo	IgE-med. e/o cellulo-med.	cellulo-med.	cellulo-med.	cellulo-med.
Età	tutte	lattante	lattante	lattante
Eosinofilia tissutale	+++ (anche periferica)	+	no	+/-
Sangue feci	++	+++ (macroscopico)	+/-	Generalmente no
Deficit di accrescimento	++	No	+	++
Altro	Anemia, DAR, perdita di proteine, SPT e RAST +/-	Diarrea +/-	Collasso, metemoglobinememia, ↑ GB (PMN)	Depositi IgA Appiattimento mucosa

Enterocolite allergica da proteine (*Food Protein-Induced Enterocolitis Syndrome: FPIES*)

- ✓ Meccanismo cellulo-mediato
- ✓ Insorgenza semi-ritardata (\approx 1-3 h)
- ✓ Possibile a tutte le età (più frequente nel lattante)
- ✓ Allergeni più frequenti: latte, soia, cereali, pesce
- ✓ Manifestazioni cliniche: vomito a getto, collasso, diarrea (\pm sangue), letargia, disidratazione, distensione addominale, ritardo di crescita, metemoglobinemia, acidosi, ipoalbuminemia
- ✓ Manifestazioni cutanee assenti
- ✓ SPT e RAST negativi; \uparrow PMN
- ✓ Diagnosi è clinica

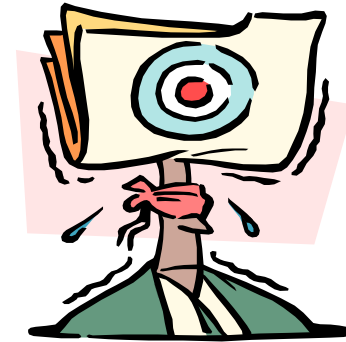
Sicherer SH, JACI 2005; 115: 149-56

IPOALLERGENICITA' "IN VIVO" DEGLI IDROLISATI

FORMULA	Sampson J Pediatr 1991	Wahn J Pediatr 1992	Ragno Eur J Pediatr 1993	Halken PAI 1993	Martin- Esteban JPGN 1998	Gianpietro PAI 2001	Caffarelli CEA 2002	Klemola J Pediat 2002
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Alimentum	100	-	90	-	-	-	-	-
Prophylac	-	-	87	100	-	94	-	-
Pregomin	-	87	-	-	-	-	-	-
Nutrilon Pepti	-	-	-	-	-	97	-	-
Alfarè	-	75	-	-	-	-	-	-
Hypolac	-	-	-	-	-	-	82	-
Damira					94			
Peptiditutteli	-	-	-	-	-	-	-	98
Nidina HA	-	-	55	-	-	-	-	-
Humana HA	-	-	-	-	-	-	71	-

Terracciano, AAI 2002;89(suppl):86 (modif)

Tenere bene a mente che....



“[...] Only pure amino acid mixtures
are considered to be
non-allergenic ...”



*Joint Statement ESPACI-ESPGHAN
Arch Dis Child 1999;81:80-4*

The efficacy of amino acid-based formulas in relieving the symptoms of cow's milk allergy: a systematic review

Hill, Clin Exp Allergy 2007;37:808

Table 3. Results of randomized controlled cross-over challenge trials comparing amino acid-based formula (AAF) vs. cow's milk/cow's milk-based formula (CM/CMF) vs. hydrolysed formula (HF) vs. soy-based formula (SF) in patients with confirmed or suspected cow's milk allergy (CMA)

Outcome measures	Sampson et al. [10]			Hill et al. [8]				Caffarelli et al. [35]					
	AAF	eHF	CMF	AAF	eHF	SF	CMF	AAF	pHF (whey)	eHF (casein)	eHF (whey)	SF	
Time to resolution of symptoms	-	-	-	< 2 weeks	-	-	-	-	-	-	-	-	-
Patients with improvement of symptoms	-	-	-	18/18	-	-	-	-	-	-	-	-	-
Patients with vomiting	0/28	1/28	-	0/18	4/10	2/7	1/1	0/16	0/17	0/16	1/16	0/16	
Patients with diarrhoea	-	-	-	0/18	5/10	1/7	0/1	0/10	0/17	1/16	0/16	0/20	
Patients with GI symptoms	0/28	-	8/22	-	-	-	-	-	-	-	-	-	
Patients with eczema	-	-	-	0/18	1/10	4/7	0/1	2/10	4/17	0/16	1/16	0/20	
Patients with rash/'skin symptoms'	0/28	1/28	17/22	-	-	-	-	0/10	3/17	1/16	1/16	0/20	
Patients with 'respiratory symptoms'	0/28	1/28	16/22	-	-	-	-	0/10	2/17	0/16	0/16	0/20	
Patients with irritability	-	-	-	0/18	6/10	4/7	1/1	-	-	-	-	-	
Patients with hypotension	-	-	-	-	-	-	-	0/10	2/17	0/16	0/16	0/20	
Patients with 'growth failure'	-	-	-	0/18 post-AAF treatment	2/10 before AAF treatment	2/7 before AAF treatment	0/1 before AAF treatment	-	-	-	-	-	

eHF, extensively hydrolysed formula; pHF, partially hydrolysed formula; GI, gastro-intestinal; -, data not reported.

Metanalisi di 20 studi di confronto tra FAA, eHF, soja



FAA e eHF egualmente efficaci

Maggiori benefici con FAA in specifici sottogruppi:

- Allergia GI non IgE-mediata con ritardo di crescita
- DA atopica severa
- Sintomi durante allattamento materno esclusivo



A chi

TERAPIA
CON I LATTI
FORMULA

Quali

Per quanto
tempo

Review article

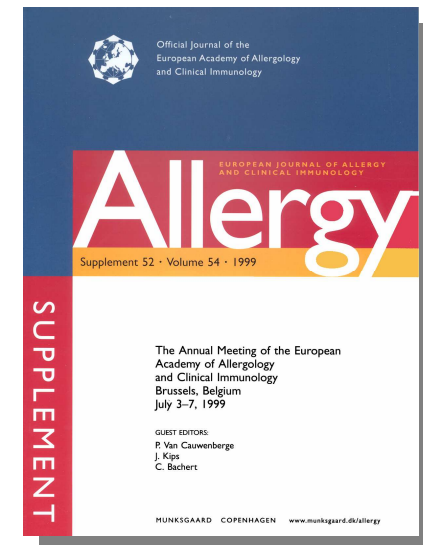
Standardization of food challenges in patients with immediate reactions to foods – position paper from the European Academy of Allergology and Clinical Immunology

Bindslev-Jensen et al, Allergy 2004;59:690

Inclusion criteria

Patients of any age with a history of adverse reaction to a food:

- For establishment or exclusion of the diagnosis of food intolerance/allergy
- For scientific reasons in clinical trials
- For determination of the threshold value or degree of sensitivity
- For assessment of tolerance. Once diagnosed, when a patient is suspected to have outgrown his clinical allergy – especially in children, whose food allergies normally outgrow during childhood, e.g. cow's milk or hen's egg allergies.



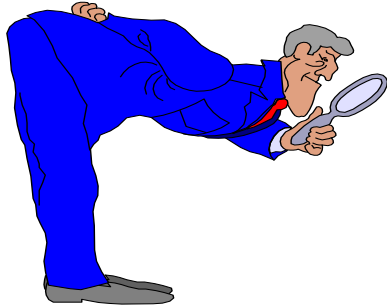


...what about other mammalian milks ?





Formula consigliata per la supplementazione	Soja Idrolisato spinto Miscele AA	Idrolisato spinto Miscele AA
Evitare idrolisati parziali	Si	Si
Evitare latte di mammiferi (capra, pecora)	Si	Si



LATTE DI CAPRA: LE RAGIONI DEL NO ...



Frequente presenza di IgE-specifiche in bb con APLV anche in assenza di precedenti assunzioni di latte di capra

Gjesing, Allergy 1986; 41: 51-56

Frazioni α s1 e α s2 della caseina bovina, della capra e della pecora presentano l'87-98% di omologia nella sequenza AA

Spuergin, Allergy 1997; 52: 293

Probabilità molto alta (\approx 95%) di positività del challenge con latte di capra in bb allergici al LV

Bellioni-Businco, JACI 1999; 103: 1191

Anaphylaxis to sheep's milk cheese in a child unaffected by cow's milk allergy

Calvani, Eur J Pediatr 1998; 157:17-19



Table 1. Skin prick tests, prick-prick tests and RASTs responses to different cow's milk protein and cheese

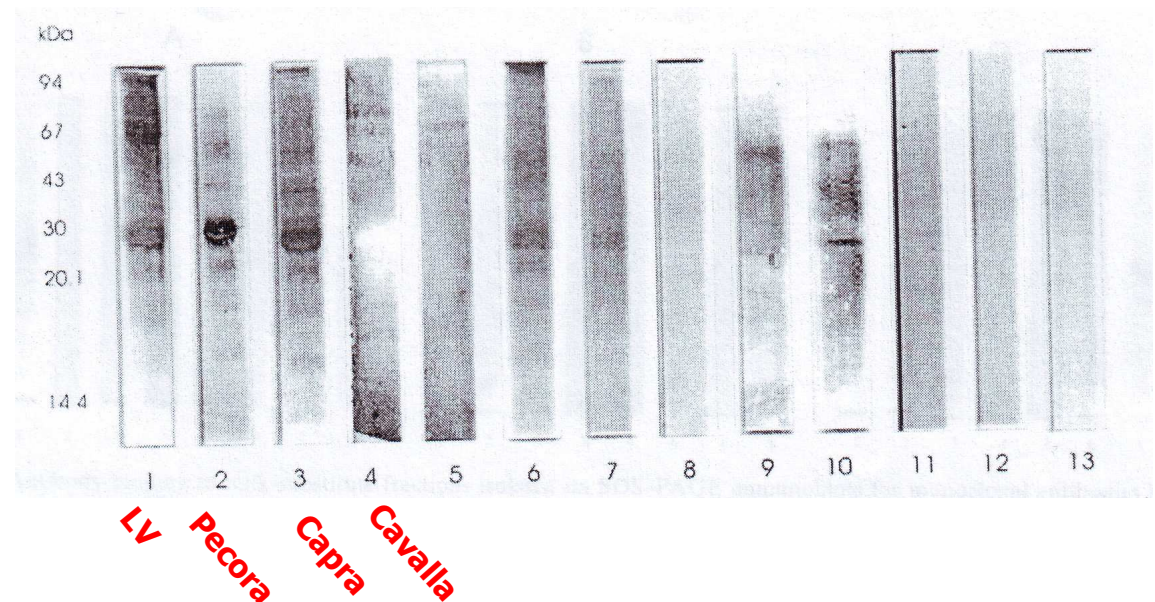
	Skin prick test	Prick-prick test	RAST
Cow's α -lactalbumin	neg		neg
Cow's casein	neg		neg
β -lactoglobulin	neg		neg
Pasteurized cow's milk	neg		neg
Milk mixture	+++		
Goat's milk formula	++++		
Fresh sheep's milk	+++		
Sheep's cheese "pecorino"		+++	
Sheep's "buttermilk curd"		+++	
Cow's cheese		neg	
Cow's cheese "cheddar"			neg
Cow's cheese "fermented"			neg

Evaluation of the residual antigenicity and allergenicity of cow's milk substitutes by in vitro tests

Docena, Allergy 2002;57:83

Antigenicità valutata mediante ELISA, EAST e immunoblot di:

- Latte di cavalla
- Latte di capra
- Latte di pecora
- pHF-C+W (Humana HA, Aptamil HA)
- pHF-W (NAN HA, BEBA HA)
- pHF-C (KAS 1000)
- eHF-C (Pregestimil)
- Formula AA (Neocate)



Residua attività antigenica
in tutti gli idrolisati, eccetto il Neocate

Tra i latti di mammiferi, cavalla meno immunogenico

Allergenicity of mares' milk in children with cow's milk allergy

Businco, JACI 2000;105:1031

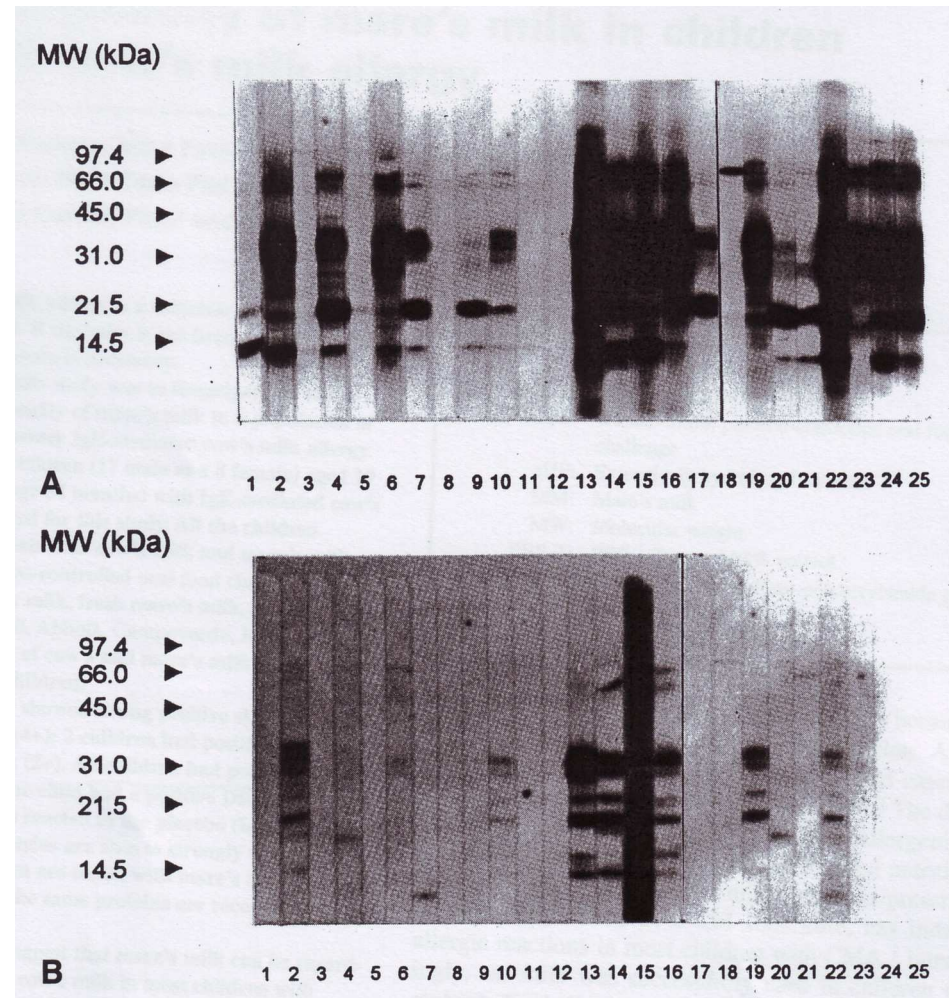


20 bb (M 34 m.) con APLV
IgE-mediata
SPT pos (++++) per LV in 20/20
SPT pos per LCav in 2/20



DBPCFC+ con LV in 20/20
DBPCFC+ con LCav in 1/20

Pattern di reattività immunoblot sensibilmente diverso nel LCav rispetto al LV



Use of ass' milk in multiple food allergy

Iacono, JPGN 1992;14:177



Intolerance to hydrolysed cow's milk proteins in infants: clinical characteristics and dietary treatment

Iacono, Clin Exp Allergy 2000;30:1597

Efficacy of donkey's milk in treating highly problematic cow's milk allergic children: an in vivo and in vitro study

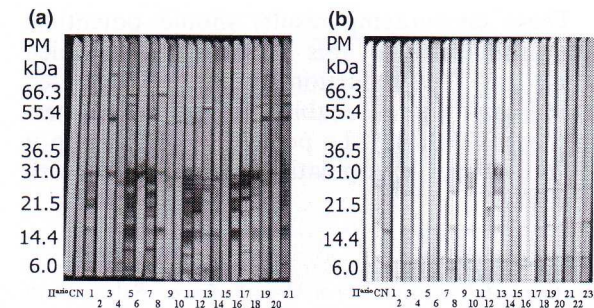
Monti G, Pediatr Allergy Immunol 2007;18:258

Efficacy of donkey's milk in treating highly problematic cow's milk allergic children: an in vivo and in vitro study



Monti G, Pediatr Allergy Immunol 2007;18:258

46 bb (età m. 12 m) con APLV
 IgE-mediata e non IgE-mediata
 confermata mediante DBPCFC
 76% allergici alla soia
 15% intolleranti a eHF



DBPCF con LAs
 Studio con immunoblot



LAs tollerato dal 82% dei bb
 (78% APLV con IgE+ e
 100% APLV con IgE-)
 e da 10/11 bb non tolleranti eHF

Table 1. Temporal Z-score variations in weight and length/stature

	T_1	T_2	T_3	T_4	T_5	T_6
Time from T_0 (months)	1	2-3	3-6	7-12	13-18	19-24
Cases (n)	30	27	23	19	7	4
Weight (ΔZ -score)	0.06 (0.16)*	0.07 (0.28)	0.18 (0.31)*	0.18 (0.42)*	0.37 (0.34)*	0.37 (0.79)
Length/stature (ΔZ -score)	0.11 (0.29)*	0.14 (0.46)	0.26 (0.52)*	0.17 (0.46)	0.13 (0.51)	0.25 (0.47)

Data presented as mean (s.d.).
 *p < 0.05 compared with Z-score at T_0 .

Catch-up growth a seguito rialimentazione con LA

... e le formule a
base di idrolisati di riso?



A hydrolised rice-based formula is tolerated by children with cow's milk allergy: a multi-centre study

Fiocchi A, Clin Exp Allergy 2006;36:311-6

100 bb (età m. 3.1 aa) con sospetta APLV confermata mediante DBPCFC (84/100) o con anafilassi da LV

SPT, UniCAP e immunoblot per LV, riso e idrolisato di riso (eHF-R)
DBPCFC con LV e eHF-R

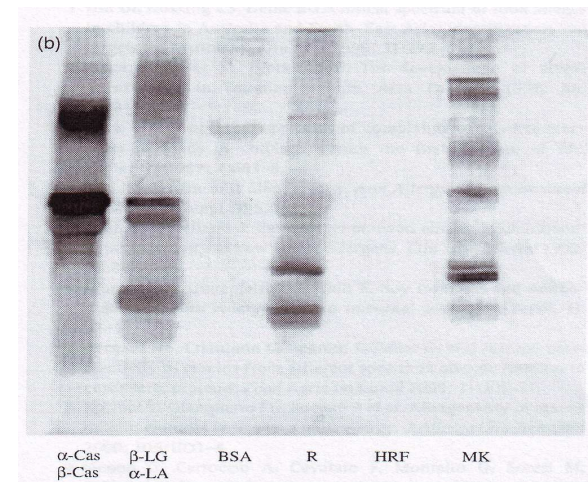


Positività UniCAP per eHF-R in 4/91 pz
Positività immunoblot per eHF-R in 6/96 pz

DBPCFC per eHF-R negativo nel 100/100 dei pz

Table 2. Sensitization indices in 100 children with CMA

	SPT+	CAP+	Immunoblotting+
CM	85/99*	80/93 [†]	92/96 [†]
ALA	72/99	61/91	57/96
BLG	73/99	61/91	20/96
α -Cas			54/96
β -Cas	74/99	63/91	38/96
BSA			61/96
Rice	4/99	21/91	70/96
HRF	3/99	4/91	6/96



Z-score of weight for age of infants with atopic dermatitis and cow's milk allergy fed with a rice-hydrolysed formula during the first two years of life

Savino F, Acta Paediatr 2005;94(suppl):115

54 bb (età m 3.2 m) con DA e APLV alimentati con eHF-C, soja o eHF-R

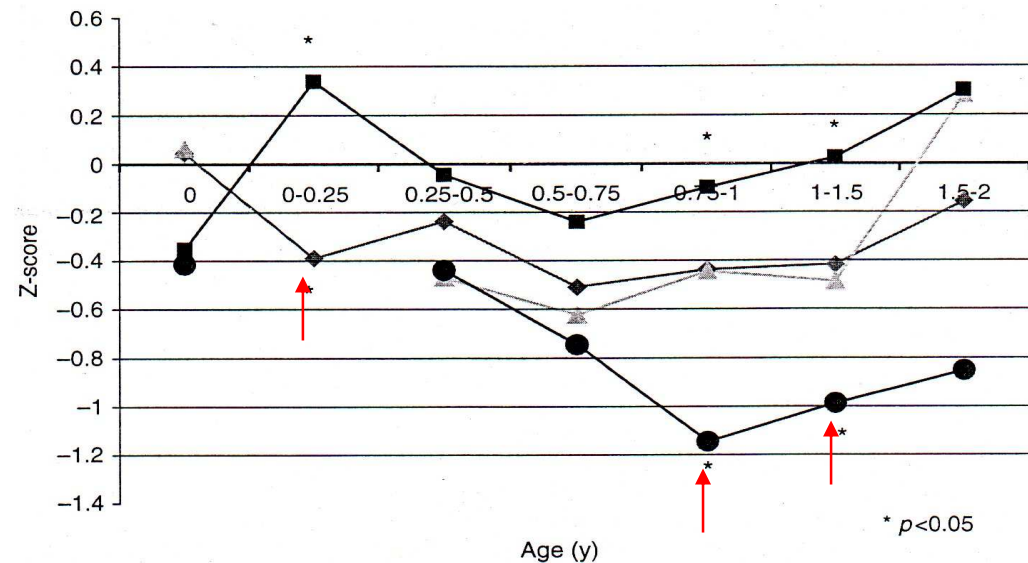
30 bb con sola DA (controlli)



Follow-up (media 17 m)

Nel gruppo eHF-R z-score peso ↓ a 9-12 mesi e 12-18 mesi rispetto ai controlli

Nel gruppo eHF-C z-score peso ↓ a 0-3 mesi rispetto ai controlli



“Take-home messages”

Prevenzione con le formule ipoallergeniche



- ✓ Lattanti con familiarità biparentale
- ✓ Opportune ulteriori conferme di efficacia
- ✓ Maggiore efficacia idrolisati spinti
- ✓ No soja
- ✓ Dati insufficienti sulla durata (primi 6 mesi?)

“Take-home messages”

Terapia con le formule ipoallergeniche

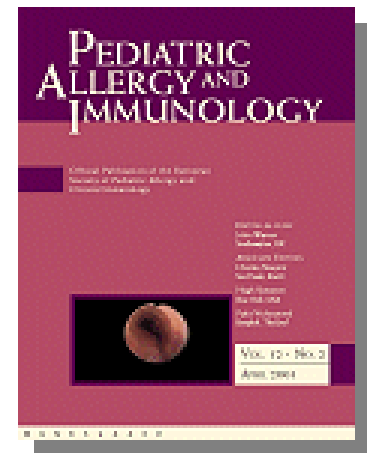


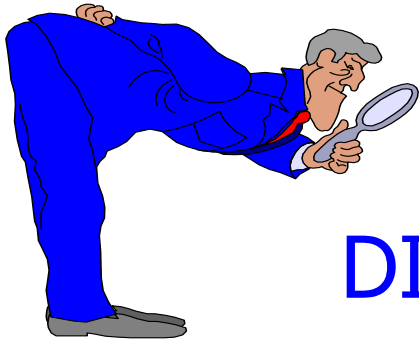
- ✓ Solo bambini con APLV dimostrata
- ✓ Idrolisati estensivi (o soja dopo i 6 mesi e nei casi senza sintomi intestinali non IgE-mediati)
- ✓ Formule elementari AA nei non responder
- ✓ Latti di cavalla/asina e idrolisati riso: pochi dati (poss. alternativa se formule elementari non accettate)
- ✓ Adeguatezza nutrizionale soja e eHF soddisfacente (cavalla/asina e idrolisati riso?)
- ✓ Fabbisogno di Ca^{++} e vit. D non soddisfatto dopo i 6 m.

- Non esiste una formula sostitutiva “ideale”
- Il latte va scelto caso per caso di fronte al “singolo” bambino
- Ciascuna formula “alternativa” deve dimostrarsi efficace sotto il profilo allergologico e nutrizionale

Wahn U.

“Aspects of nutritional management of food allergy”
Pediatr Allergy Immunol 2001;12(suppl.14):75-7





DIETA DI ELIMINAZIONE PER PROTEINE DEL LATTE

L'utilizzo di formule sostitutive migliora il valore nutrizionale delle diete, tuttavia i fabbisogni di *calcio* e *vitamina D* non sono soddisfatti

Salman, J Allergy Clin Immunol 2002
Henrikssen, Acta Paediatr 2000;89:272

Per il pediatra, la velocità di crescita è l'indice più sensibile per monitorare lo stato nutrizionale e identificare precocemente i possibili deficit

necessità di utilizzare strumenti idonei a valutare l'intake dietetico

Shideh Mofidi et al.

“Nutritional management of pediatric food hypersensitivity” Pediatrics 2003