

# 34 Congresso Nazionale di **ANTIBIOTICOTERAPIA** in età pediatrica

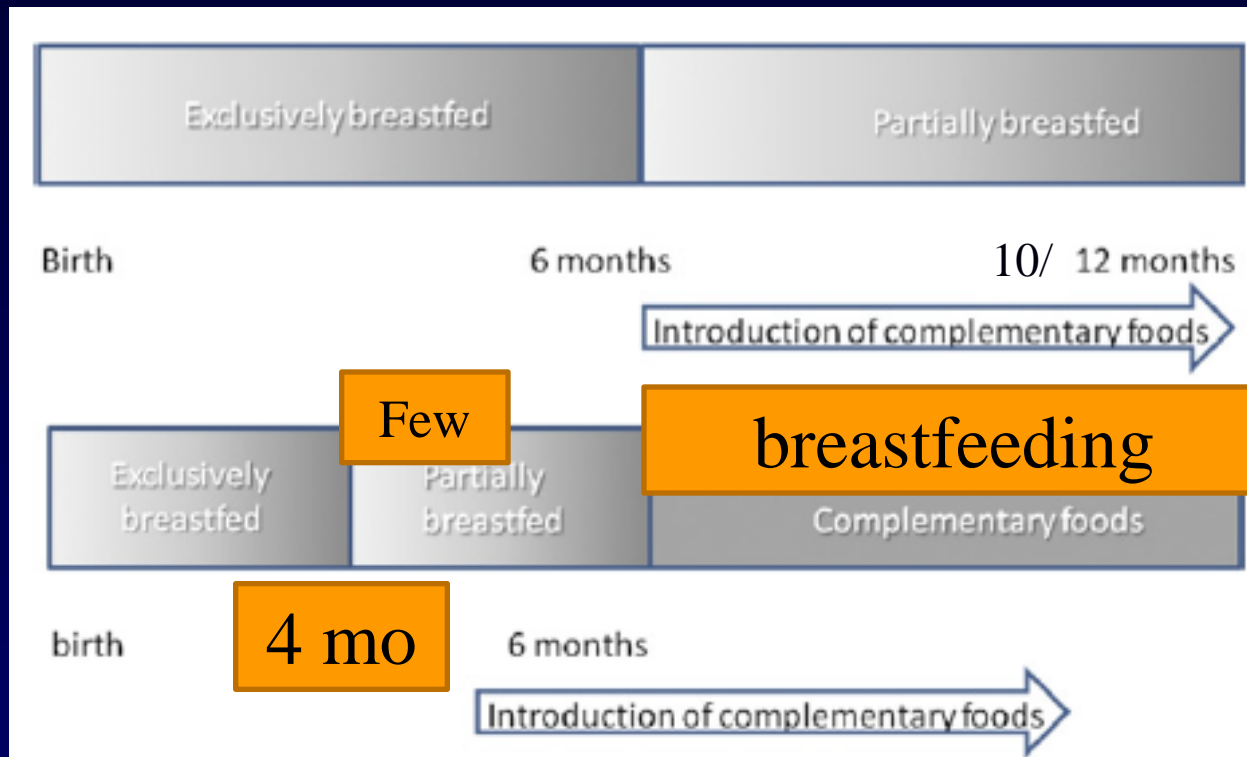
## **Le formule adattate per il lattante attualmente in commercio: differenze e significato**

*C. Agostoni, Milano*

# Benefits from Longer Breastfeeding: Do We Need to Revise the Recommendations?

*Curr Probl Pediatr Adolesc Health Care* 2011;41:240-243

Michael B. Krawinkel, MD



**FIG 1.** Different time schemes for breastfeeding and introduction of complementary foods in the first year of life. Sharp time limits are only set for clear presentation. When advising mothers, those limits are always to be kept flexible and appropriate for the individual mother-child pair.

## SCIENTIFIC OPINION

### Scientific Opinion on the essential composition of infant and follow-on formulae<sup>1</sup>

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)<sup>2,3</sup>

European Food Safety Authority (EFSA), Parma, Italy

There is no necessity to add ARA, EPA, chromium, fluoride, taurine, nucleotides, non-digestible oligosaccharides, “probiotics” or “synbiotics” to IF and FOF. There is also no necessity to use PL as a source of LCPUFAs instead of TAG in IF and FOF or to use TAG with palmitic acid predominantly esterified in the *sn*-2 position in IF and FOF instead of TAG from other fat sources. For FOF, in contrast to IF, the addition of L-carnitine, inositol and choline is not necessary.

# Evidenza

- Quantità delle proteine
- *Form* delle proteine (intere, idrolisi, aminoacidi)
- Grassi (qualità grassi insaturi)


# Lower protein content in infant formula reduces BMI and obesity risk at school age: follow-up of a randomized trial<sup>1-5</sup>

*Martina Weber, Veit Grote, Ricardo Closa-Monasterolo, Joaquín Escribano, Jean-Paul Langhendries, Elena Dain, Marcello Giovannini, Elvira Verduci, Dariusz Gruszczyński, Piotr Socha, and Berthold Koletzko for The European Childhood Obesity Trial Study Group*

Am J Clin Nutr 2014; 99:1041

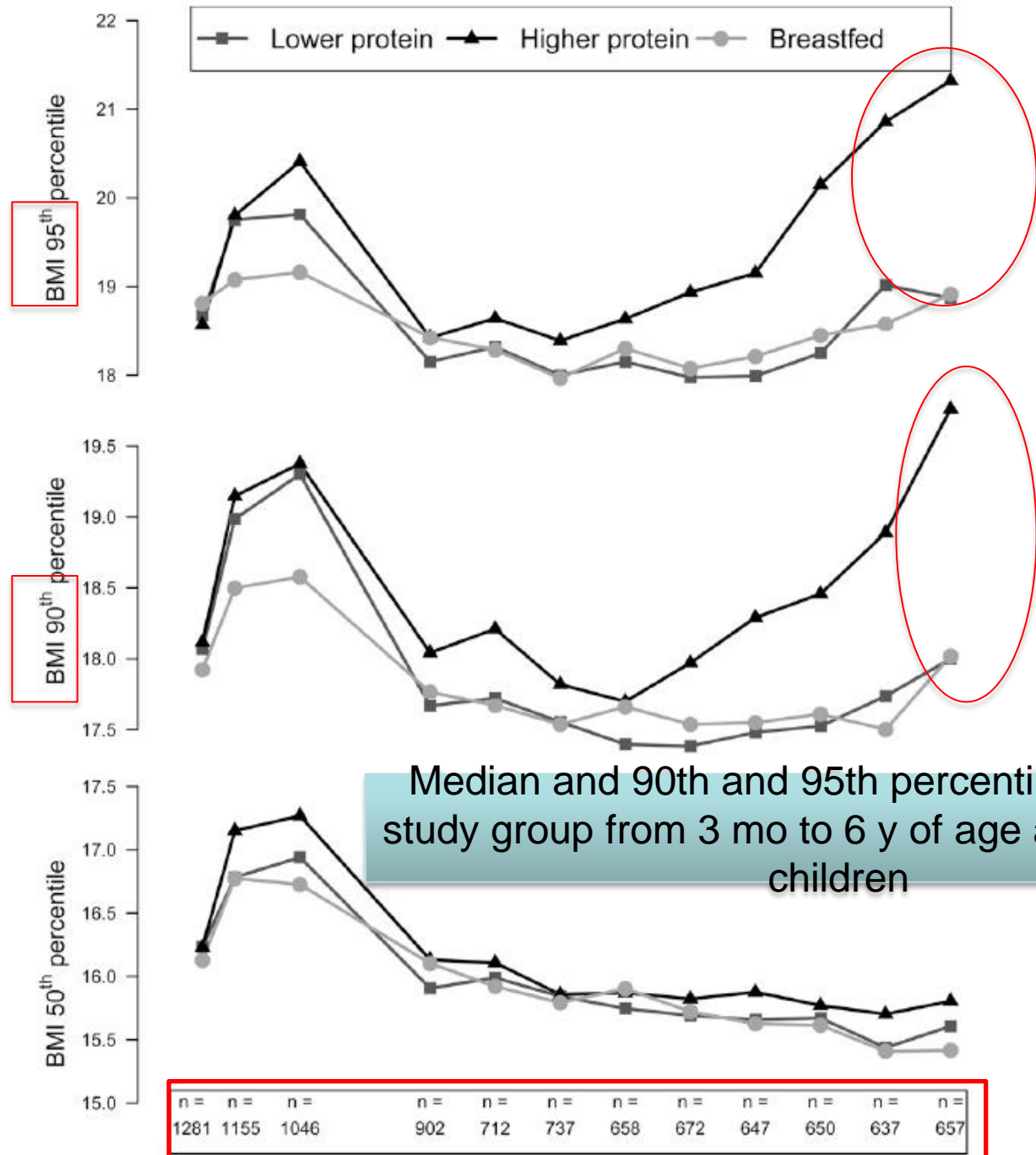
	Infant formulas		Follow-on formulas		Human milk <sup>2</sup> (n = 58)
	Lower protein	Higher protein	Lower protein	Higher protein	
Whey:casein ratio	1:4	1:4	1:4	1:4	
Energy (g/100 mL)	69.9	69.8	72.7	72.5	70 ± 6.7
Proteins (g/100 mL)	1.25	2.05	1.6	3.2	1.2 ± 0.2
Proteins (g/100 kcal)	1.77	2.9	2.2	4.4	—
Proteins (% of energy)	7.1	11.7	8.8	17.6	—

# FORMULA TYPE AND PROTEIN INTAKE g/d (SD)En%

Time	HP 	LP	P	1993 EU rec. g/d		
T1	14 (3) 11	9 (1) 7	0.001	T4-T6 → 14		
T2	16 (2) 11	9 (1) 7	0.001	T7-T9 → 15		
T3	17 (3) 11	10 (1) 7	0.001	T12-T18 → 14		
T4	18 (3) 11	11 (2) 7	0.001	T24 → 14.5		
T5	21 (5) 13	13 (2) 7	0.001			
T6	24 (5) 14	15 (4) 8	0.001			
T7	28 (6) 15	20 (5) 10	0.001			
T8	30 (7) 15	22 (6) 11	0.001			
T9	30 (7) 15	24 (7) 11	0.001	BF	P vs HP	P vs LP
T12	35 (9) 15	29 (8) 13	0.001	31 (9) 14	0.001	0.028
T18	42(12) 16	42 (12) 16	0.626	39 (10) 15	0.004	0.013
T24	45(12) 16	45 (13) 16	0.679	43 (11) 16	0.025	0.073

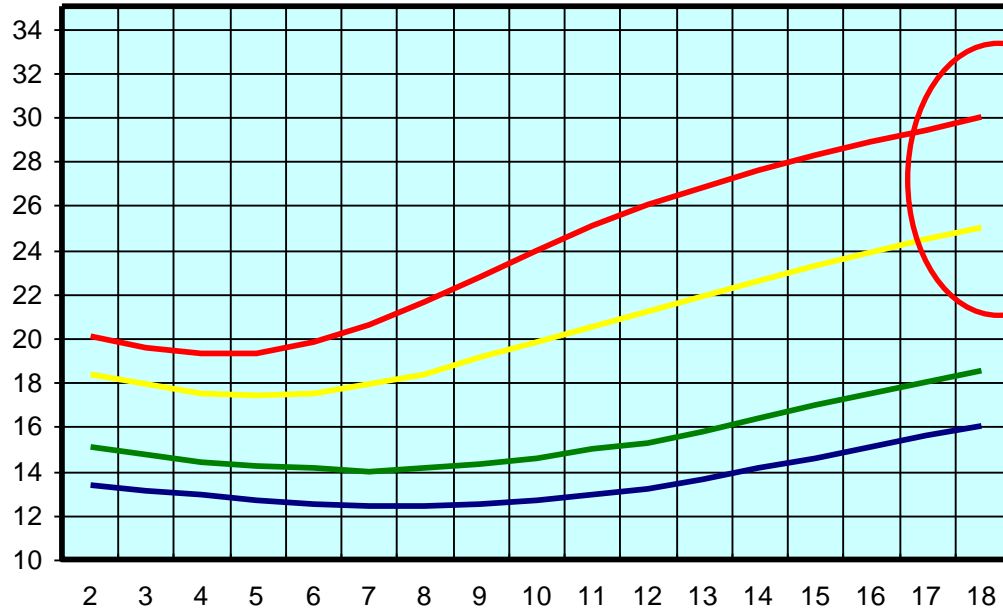
# FORMULA TYPE AND ENERGY INTAKE kcal/day

Time	HP	LP	EFSA 2013 AR		BF
			M	F	
T1	509.9 (118)	512.46 (110)			
T2	563. (117)	559.2 (113)			
T3	595.7 (116)	588.9 (118)			
T4	631.1 (113)	632.3 (116)			Circa 20% energia in più dell'AR raccomandato
T5	667.0 (115)	678.8 (131)			
T6	700.9 (140)*	726.6 (147)*			
T7	754.4 (143)	765.7 (153)	636	573	
T8	791.4 (155)	810.2 (162)	661	599	
T9	814.8 (155)	837.8 (188)	688	625	
T12	891.5 (184) <sup>a</sup>	881.9 (176) <sup>a</sup>	777	712	792.5(224) <sup>b</sup>
T18	1043.3 (223)	1045.1 (223)			988.8 (195)
T24	1119.7 (240)	1112.6 (253)	1028	946	1079.4 (222)





maschi

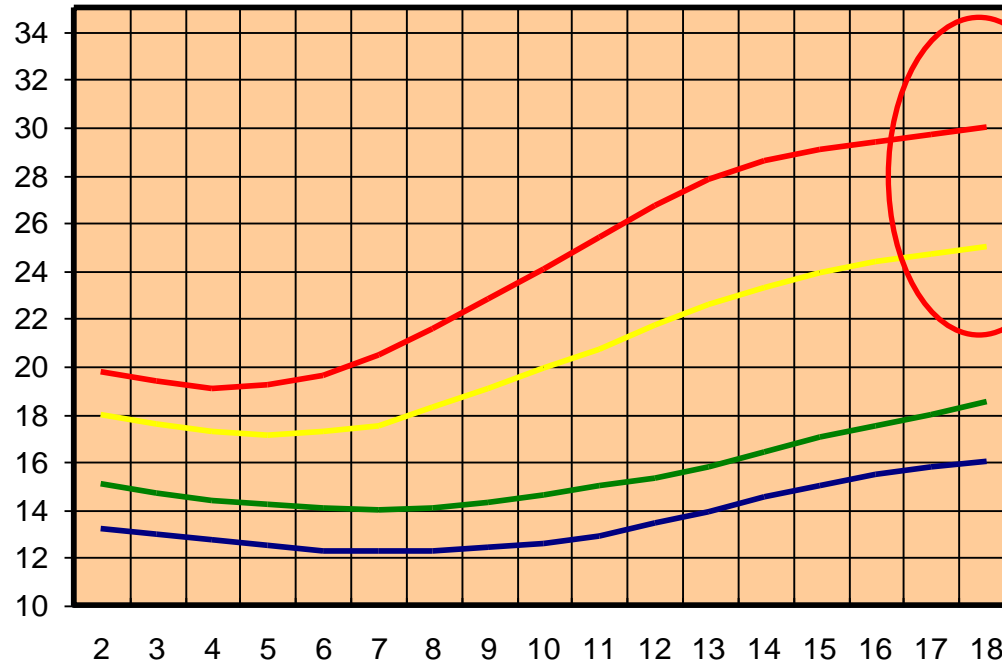


**BMI = peso / altezza<sup>2</sup>**  
(peso in Kg, altezza in m)

- limite magrezza grave
- limite magrezza
- limite sovrappeso
- limite obesità

Standard Internazionali per obesità, sovrappeso e magrezza

femmine



- limite magrezza grave
- limite magrezza
- limite sovrappeso
- limite obesità

Cole et al. BMJ 2000;320:1240  
Cole et al. BMJ 2007; 335:194

# Evidenza

- Quantità delle proteine
- Form delle proteine (intere, idrolisi, aminoacidi)
- Grassi (qualità grassi insaturi)

# Definitions

- Low- or medium grade of hydrolysis, (seroproteins) → up to more than 10.000 Dalton
- High degree of hydrolysis (seroproteins, casein, vegetal proteins → soy, rice) → limit of 1500 Daltons

Indications:  
cow's milk allergy  
premature infants?

YES

Dietary treatment of cows' milk protein allergy in childhood

If the child is not breast fed or the mother cannot or no longer wishes to breast feed, the first choice is an extensively hydrolysed formula (eHF) of CMP, the efficacy of which has been demonstrated by scientifically sound

Committee on Nutrition -French Society of Paediatrics, Br J Nutr 2012;107:325

NO

There is little evidence to support the use of extensive and partial protein hydrolysate formulas for preterm infants. High quality, long-term trials are required before these formulas should be offered routinely in preference to other types of formula for preterm infants. (consistent with the conclusions of a 2006 Cochrane CD003664 )

Szajewska H 2007; JPGN 45: S183

# Breast-feeding of allergic infants

*Erika Isolauri, MD, Annette Tahvanainen, RN, Terttu Peltola, MSc, and Taina Arvola, MD*

**Conclusions:** Breast-feeding should be promoted for primary prevention of allergy, but breast-fed infants with allergy should be treated by allergen avoidance, and in some cases breast-feeding should also be stopped. This particularly applies to infants with atopic eczema who also have impaired growth. (J Pediatr 1999;134:27-32)

Therefore the premature cessation of breast-feeding should not be advised, unless the evidence indicates that breast-feeding is responsible for medical problems or unless there is insufficient social support to continue breast-

Comment, A Goldmann

Table 4. Six to 12 months differences for WA ( $\Delta$  WA), LA ( $\Delta$  LA), and WL ( $\Delta$  WL) z-scores for all the groups (mean and 95% CI)

	Soy (n = 32)	CHy (n = 31)	RHy (n = 30)	BF (n = 32)
$\Delta$ WA	-0.16 (-0.36 to 0.04) <sup>a</sup>	0.16 (-0.05 to 0.38) <sup>b</sup>	0.18 (-0.02 to 0.38) <sup>b</sup>	-0.10 (-0.28 to 0.07)
$\Delta$ LA	0.11 (-0.14 to 0.37)	0.23 (-0.10 to 0.58)	0.24 (0.01-0.47)	0.01 (-0.20 to 0.23)
$\Delta$ WL	-0.18 (-0.50 to 0.14)	0.08 (-0.17 to 0.33)	0.21 (-0.17 to 0.59)	-0.09 (-0.40 to 0.20)

Different superscripts (<sup>a</sup>, <sup>b</sup>) indicate significant between-group comparisons at bivariate analysis.

## OBSERVATIONS

- All groups showed low WA and LA z-scores at 6 months of age.
- Infants fed hydrolyzed products showed a trend toward higher WA z-score increments in the 6- to 12-month period.
- Further research should be aimed at optimizing the dietary needs and feeding regimens for infants with CMA.

Short- and long-term effects of feeding hydrolyzed protein infant formulas on growth at  $\leq 6$  y of age: results from the German Infant Nutritional Intervention Study<sup>1-3</sup>

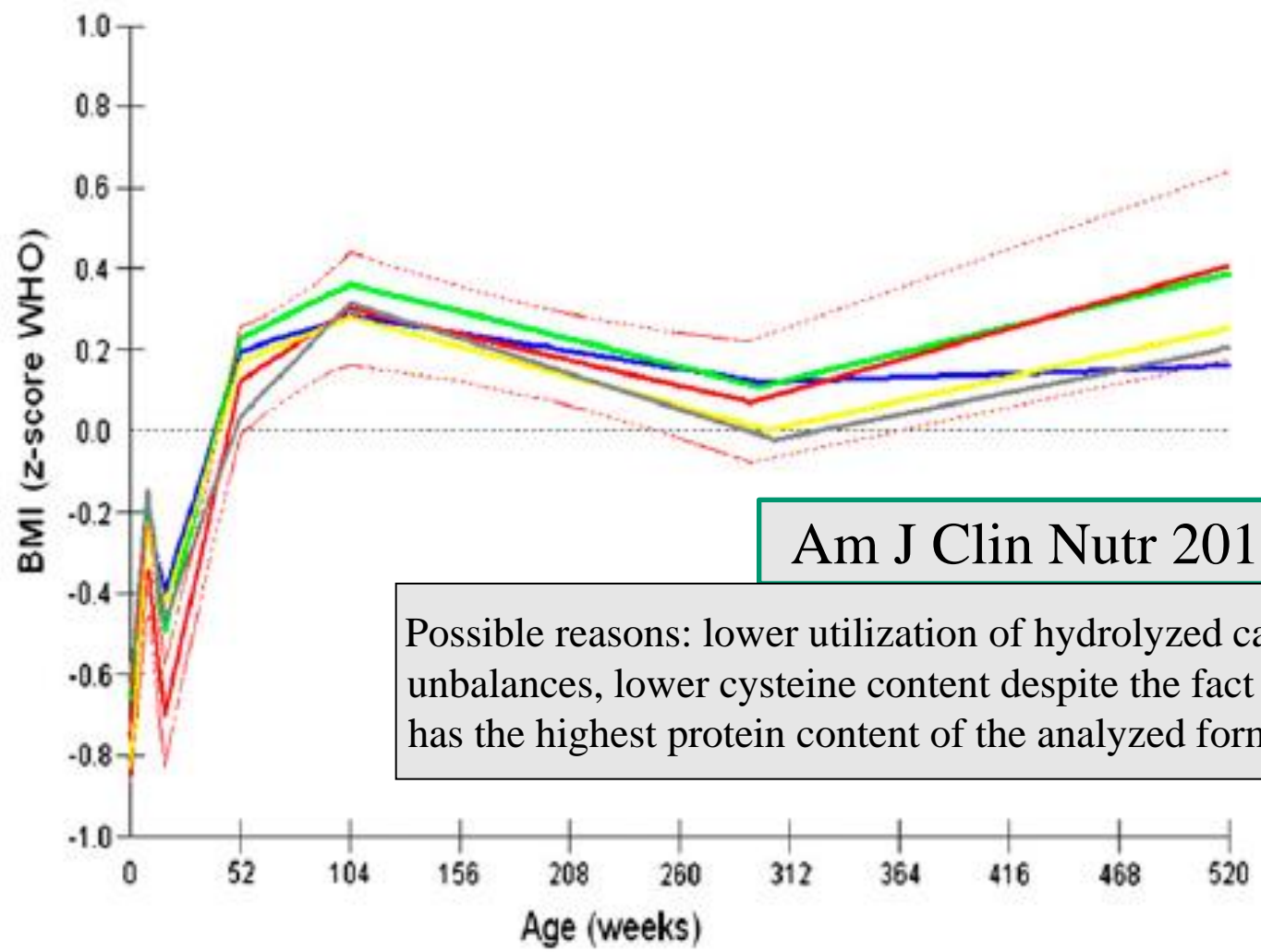
*Am J Clin Nutr* 2009;89:1846-56.

The main objective of the trial was to investigate whether feeding 4 different formulas would prospectively influence the manifestation of atopic diseases in 2252 high-risk children fed with:

- partially hydrolyzed whey (pHF-W), 67 kcal/100 mL
- extensively hydrolyzed whey (eHF-W), 67 kcal/100 mL
- extensively hydrolyzed casein (eHF-C), 68 kcal/100 mL
- cow milk formula (CMF), 66 kcal/100 mL
- infants exclusively breastfed for the first 16 wk of life.

# Long-term effects of hydrolyzed protein infant formulas on growth—extended follow-up to 10 y of age: results from the German Infant Nutritional Intervention (GINI) study<sup>1-6</sup>

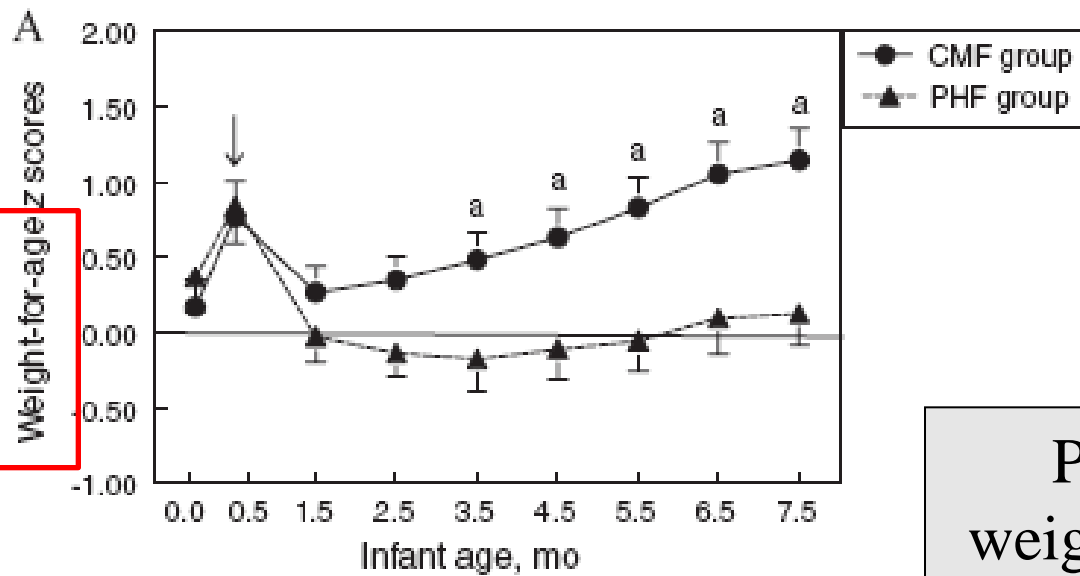
Peter Rzehak, Stefanie Sausenthaler, Sibylle Koletzko, Dietrich Reinhardt, Andrea von Berg, Ursula Krämer, Dietrich Berdel,



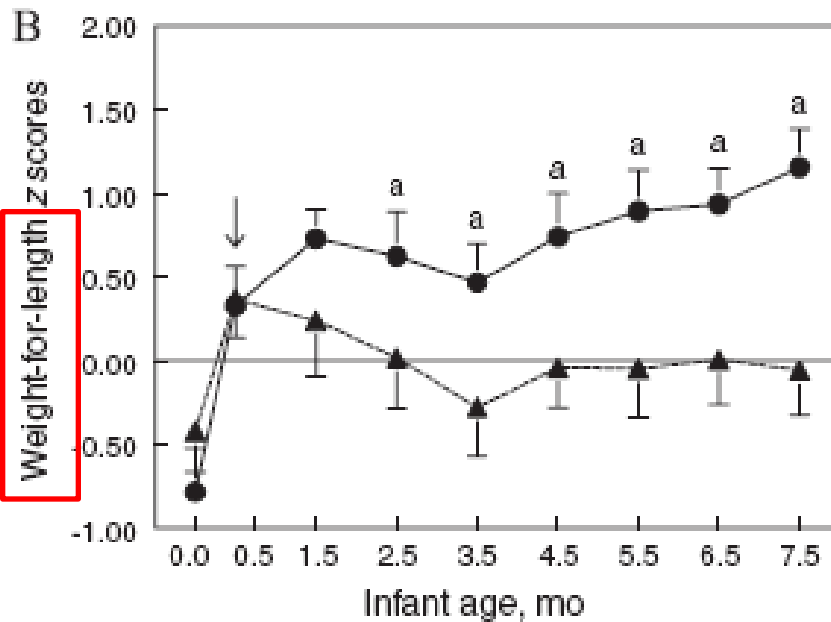
Am J Clin Nutr 2011;94:1803S

Possible reasons: lower utilization of hydrolyzed casein, amino acid unbalances, lower cysteine content despite the fact that this formula has the highest protein content of the analyzed formulas in the study





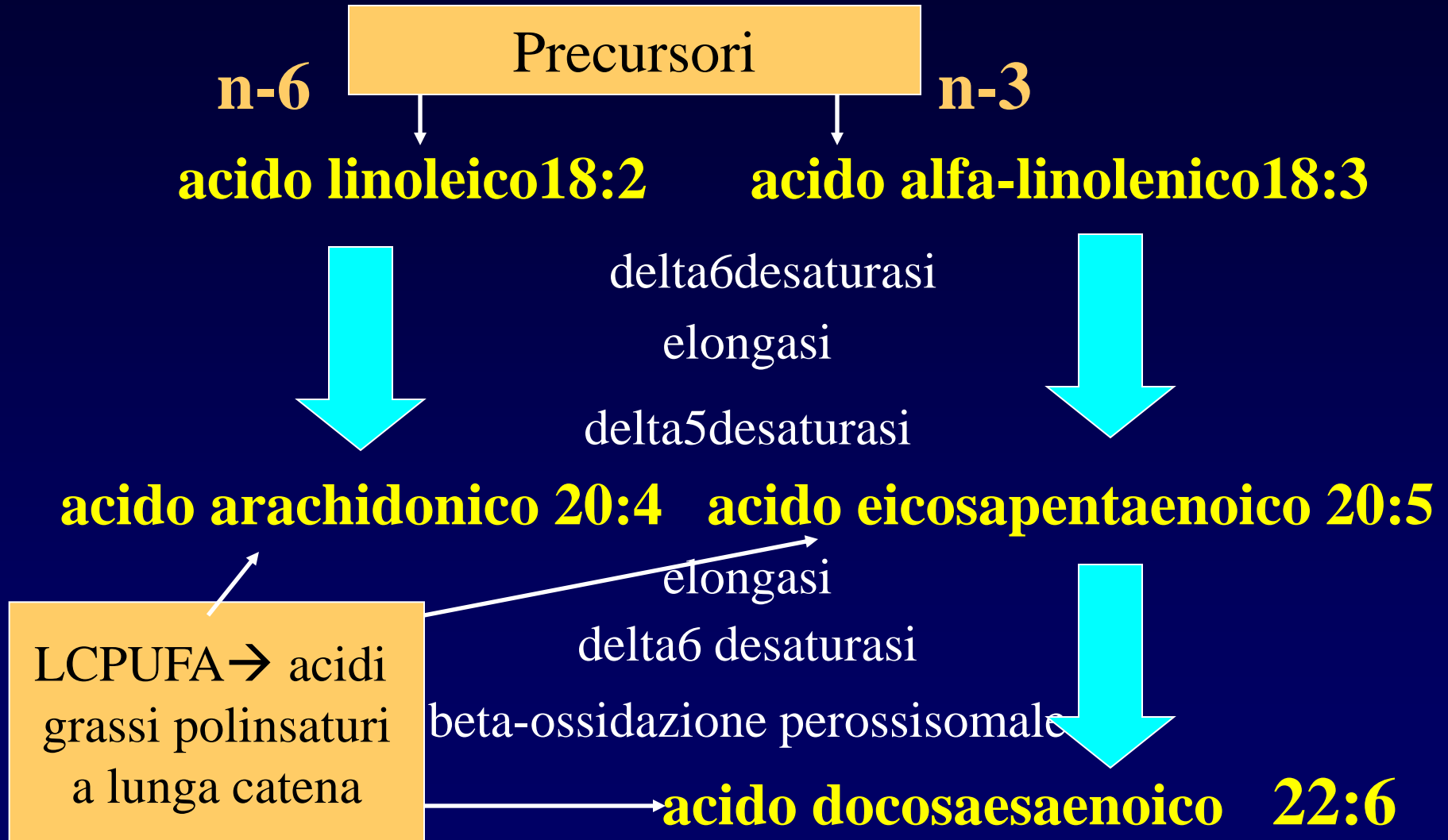
PhF → lower  
weight rate increase  
 $F = 6.60, P < 0.05$



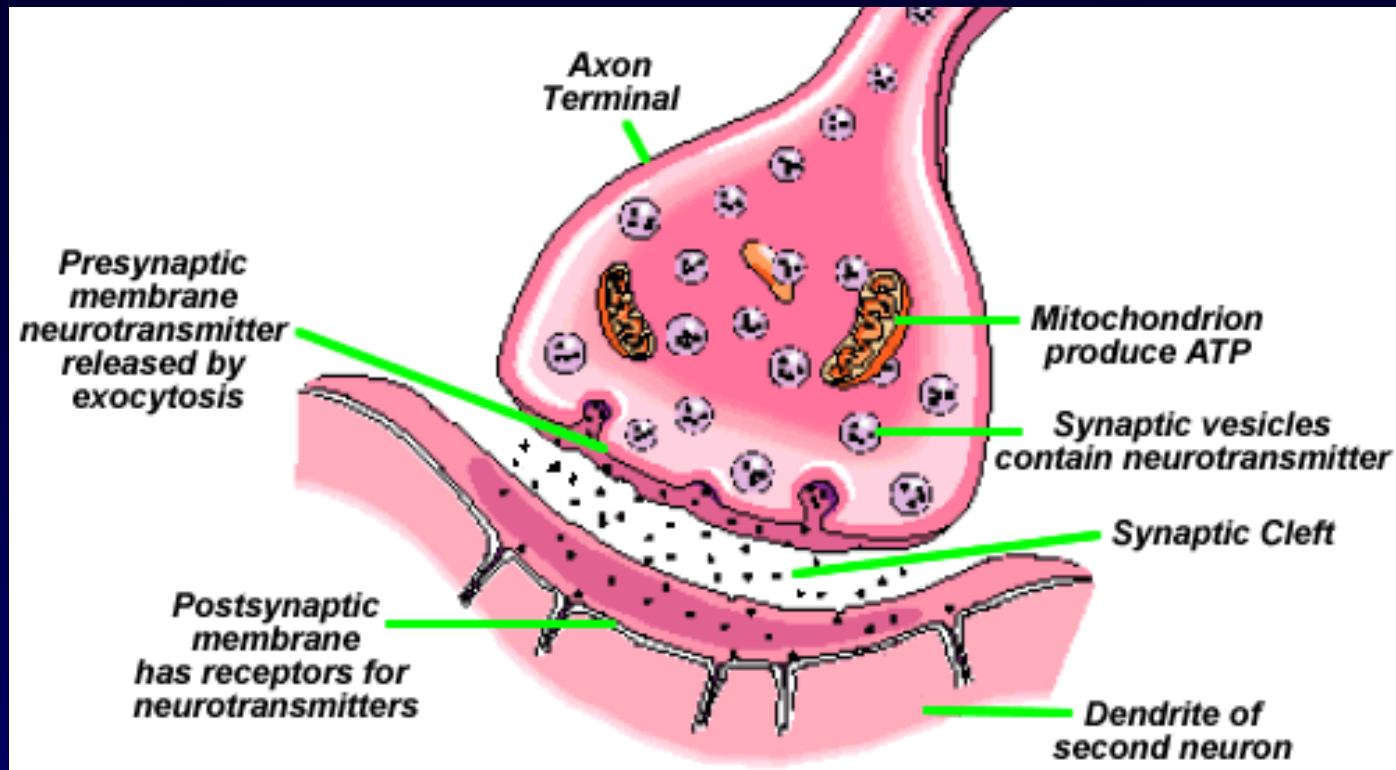
# Evidenza

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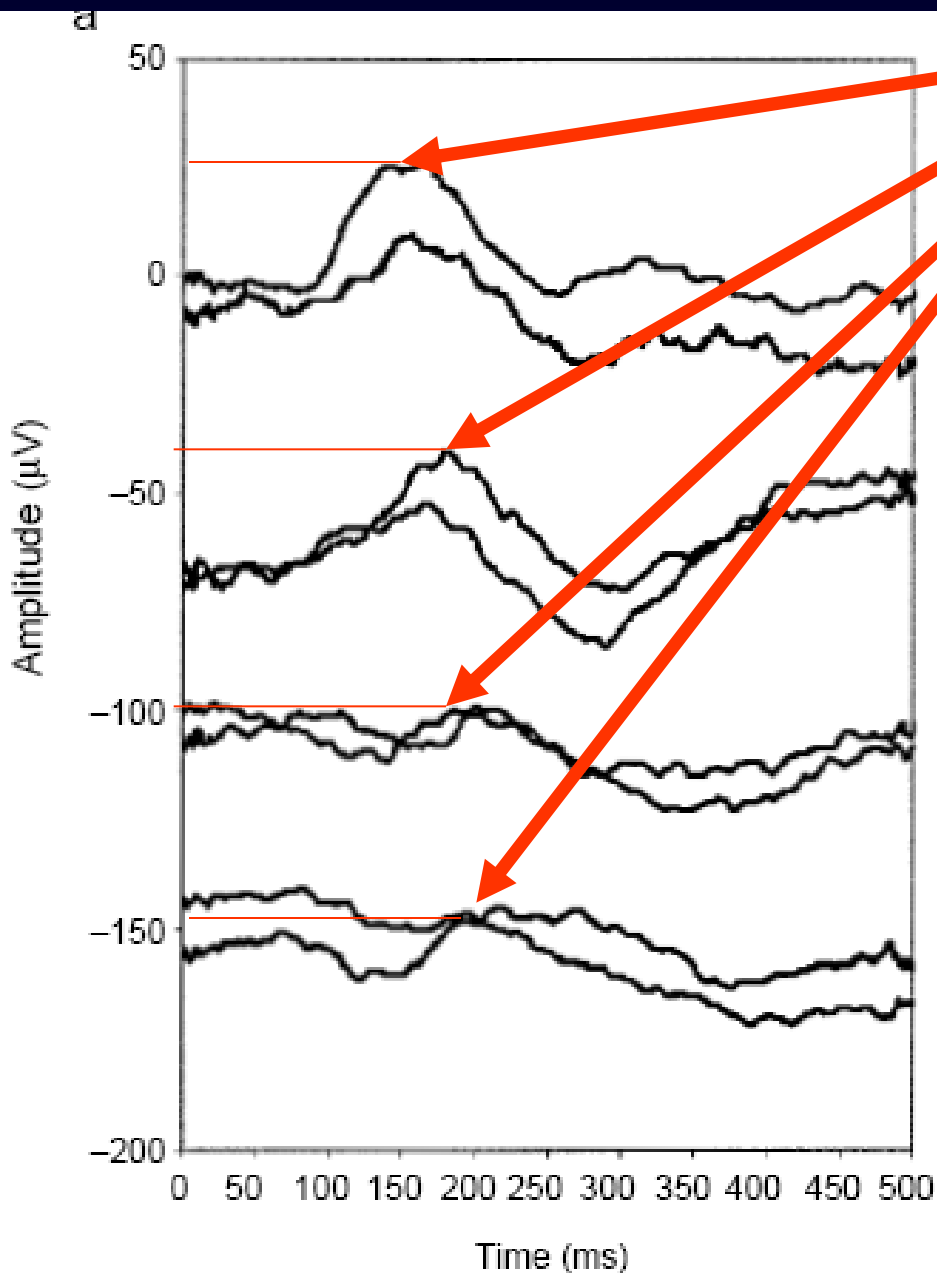
# ACIDI GRASSI POLINSATURI



# Il DHA agisce a livello delle sinapsi neuronali



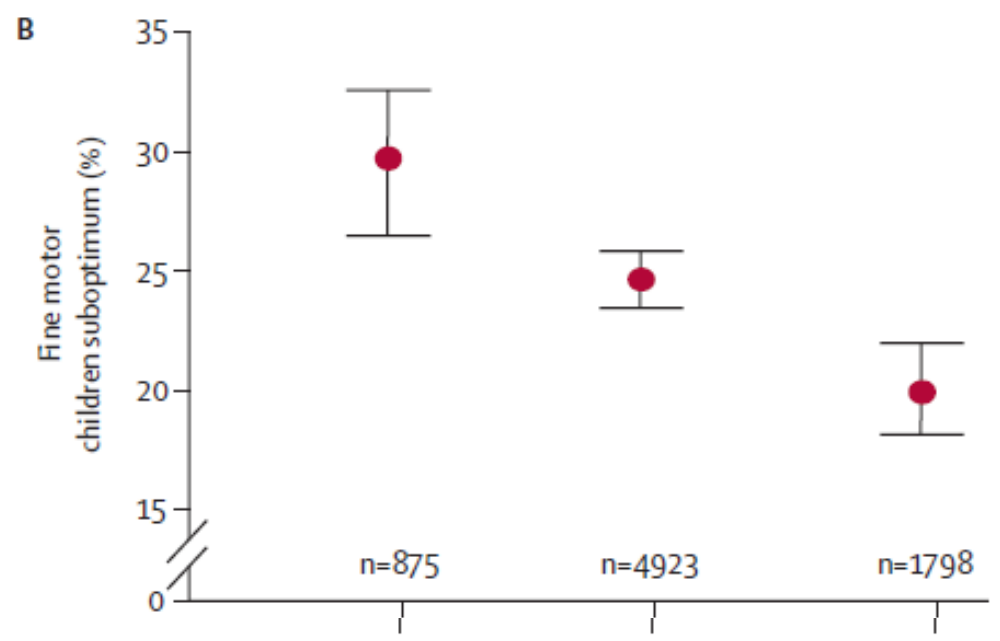
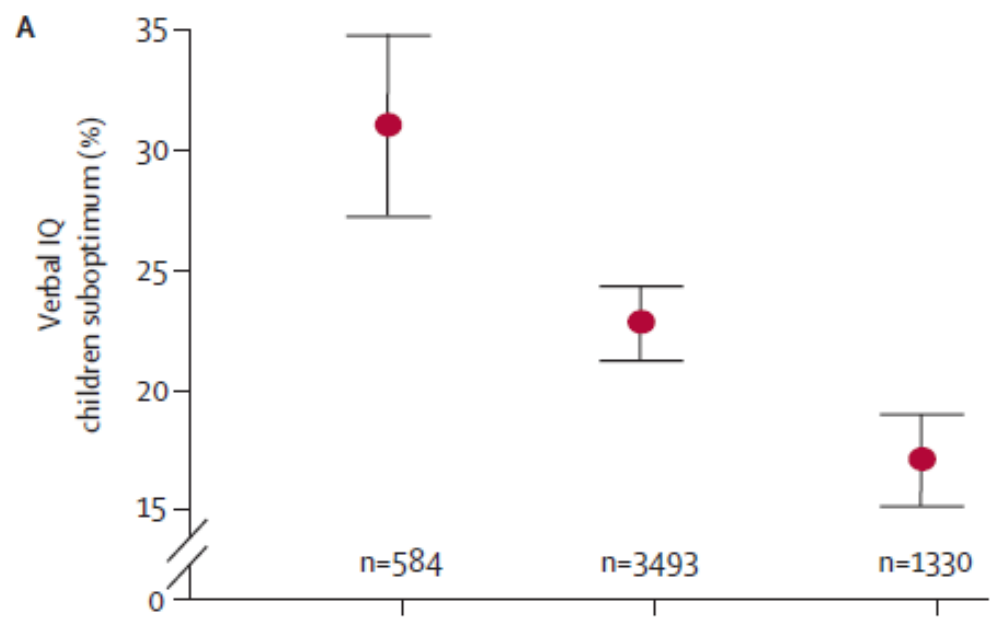
- Il DHA modula il rilascio di neurotrasmettitori
- Variazioni di DHA a questo livello si possono associare al comportamento ed all'apprendimento



VEPs  
 (potenziali evocati visivi)  
 Latenza dell'onda P  
 (lattanti di 3 mesi)

<i>Check size<sup>a</sup></i>	<i>n</i>	<i>Mean (SD)</i>
120'	20	152.8 (22.6)
60'	18	167.4 (20.1)
30'	17	194.6 (34.2)
24'	13	203.1 (34.7)

Livelli perinatali di DHA  
ed effetti della supplementazione materna



Maternal seafood consumption in pregnancy    None    0-340 g per week    >340 g per week

Supplementazione con DHA

dopo la gravidanza/periodo perinatale :  
i pretermine



# Longchain polyunsaturated fatty acid supplementation in preterm infants (Review)

Simmer K, Schulzke S, Patole S



**THE COCHRANE  
COLLABORATION®**

**Available data do not support supplementation**

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2008, Issue 4

<http://www.thecochranelibrary.com>

# Neurodevelopmental outcomes of preterm infants fed high-dose docosahexaenoic acid: a randomized controlled trial

JAMA 2009 ;301:175-82 Makrides M et al.

- Randomized, double-blind controlled trial enrolling infants born < 33 weeks' gestation, follow-up to 18 months.
- High-DHA (approximately 1% total fatty acids) enteral feeds compared with standard DHA (approximately 0.3% total fatty acids) from day 2 to 4 until term corrected age.
- Bayley MDI at 18 months' corrected
- Of the 657 infants enrolled, 93.5% completed the follow-up.
- MDI among girls fed the high-DHA diet higher than girls fed standard DHA (unadjusted mean difference, 4.7; 95% CI, 0.5-8.8; adjusted mean difference, 4.5; 95% CI, 0.5-8.5).

# Acidi grassi polinsaturi a lunga catena nei pretermine

- Dati, disegni di studio e risultati eterogenei
- DHA associato in alcuni studi ad outcomes funzionali favorevoli a breve e medio termine, mai effetti negativi
- Apporto di DHA ottimale intorno all'1% ?
- Quale outcome funzionale per l'acido arachidonico?
- Mantenere il rapporto acido linoleico/alfa-linolenico < 10:1
- Forme biochimiche e fonti da definirsi
- “Nutrizione di genere?”

Supplementazione di DHA  
oltre il periodo perinatale:  
nati a termine

# Longchain polyunsaturated fatty acid supplementation in infants born at term (Review)

Simmer K, Patole SK, Rao SC

2008

- In most well-conducted RCTs no effects of supplementation on functional outcomes
- Some groups have found beneficial effects on VEP acuity and mental development
- Further research is needed

In nessun caso (pretermine e termine)  
aggiustamento per i livelli di DHA alla nascita

DIFFERENTI RISULTATI →  
→ Differenti potenzialità di sintesi endogena  
su base genetica?

*Human Molecular Genetics*, 2006, Vol. 15, No. 11 1745–1756  
doi:10.1093/hmg/ddl117  
Advanced Access Published on May 2, 2006

**Common genetic variants of the *FADS1 FADS2* gene cluster and their reconstructed haplotypes are associated with the fatty acid composition in phospholipids**

Linda Schaeffer<sup>1</sup>, Henning Gohlke<sup>1</sup>, Martina Müller<sup>1,2</sup>, Iris M. Heid<sup>1,2</sup>, Lyle J. Palmer<sup>3</sup>, Iris Kompauer<sup>1</sup>, Hans Demmelmair<sup>4</sup>, Thomas Illig<sup>1</sup>, Berthold Koletzko<sup>4</sup> and Joachim Heinrich<sup>1,\*</sup>

Il background genetico può avere un ruolo rilevante...

## Moderation of breastfeeding effects on the IQ by genetic variation in fatty acid metabolism

Avshalom Caspi<sup>\*†‡</sup>, Benjamin Williams<sup>\*</sup>, Julia Kim-Cohen<sup>§</sup>, Ian W. Craig<sup>\*</sup>, Barry J. Milne<sup>\*</sup>, Richie Poulton<sup>¶</sup>, Leonard C. Schalkwyk<sup>\*</sup>, Alan Taylor<sup>\*</sup>, Helen Werts<sup>\*</sup>, and Terrie E. Moffitt<sup>\*†</sup>

→ genes may work via the environment to shape the IQ, helping to close the nature versus nurture debate.

# Supplementazione col DHA nel divezzamento



# Maturation of Visual Acuity Is Accelerated in Breast-Fed Term Infants Fed Baby Food Containing DHA-Enriched Egg Yolk<sup>1,2</sup>

Dennis R. Hoffman,<sup>\* \*\*3</sup> Richard C. Theuer,<sup>‡4</sup> Yolanda S. Castañeda,<sup>\*</sup>  
Dianna H. Wheaton,<sup>\*</sup> Rain G. Bosworth,<sup>\*</sup> Anna R. O'Connor,<sup>\*5</sup> Sarah E. Morale,<sup>\*</sup>  
Lindsey E. Wiedemann,<sup>\*</sup> and Eileen E. Birch<sup>\*†</sup>

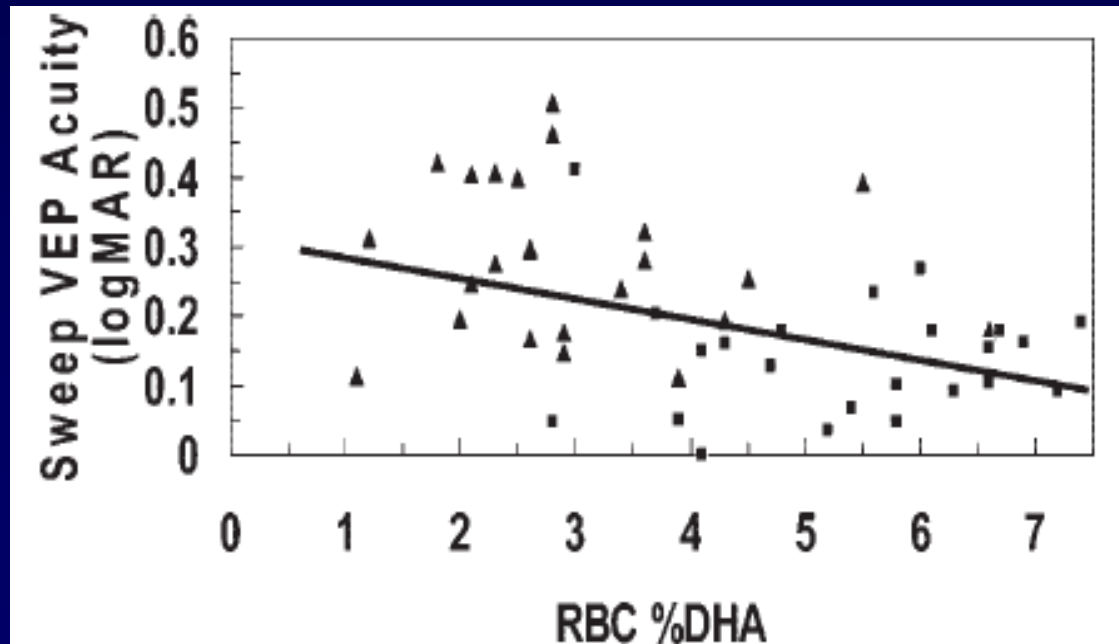
J. Nutr. 134: 2307–2313, 2004.

a 6ms, BF

1 vasetto al giorno con rosso  
d'uovo arricchito con  
circa 130 mg DHA, N = 25

1 vasetto controllo, N = 26

12 ms  
durata media BF =  
9 ms



## **DHA and ARA and brain development**

**Scientific substantiation of a health claim related to docosahexaenoic acid (DHA) and arachidonic acid (ARA) and brain development pursuant to Article 14 of Regulation (EC) No 1924/2006<sup>1</sup>**

**Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies**

**(Question No EFSA-Q-2008-212)**

**Adopted on 13 March 2009**

On the basis of the data presented, the Panel concludes that the data presented are insufficient to establish a cause and effect relationship between the intake of infant and follow-on formula supplemented with DHA at levels around 0.3% of the fatty acids and a ratio ARA:DHA between 1.4:1 and 2:1 and the contribution to normal brain development in infants and young children from birth to three years of age.

**NO → brain development**

## **DHA and ARA and visual development**

**Scientific substantiation of a health claim related to docosahexaenoic acid (DHA) and arachidonic acid (ARA) and visual development pursuant to Article 14 of Regulation (EC) No 1924/2006<sup>1</sup>**

**Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies**

**(Question No EFSA-Q-2008-211)**

**Adopted on 22 January 2009**

The following wording reflects the scientific evidence: “DHA contributes to the visual development of infants”.

In order to bear the claim a formula should contain at least 0.3% of the total fatty acids as docosahexaenoic acid. Such amounts can be easily consumed as part of a balanced diet.

The target population is infants (formula-fed infants born at term from birth up to 12 months and breastfed infants after weaning up to 12 months).

**SI' → visual development**

Health economic potential of early nutrition programming: a model calculation of long-term reduction in blood pressure and related morbidity costs by use of long-chain polyunsaturated fatty acid-supplemented formula<sup>1-4</sup>

The cost-effectiveness analysis showed an increased life expectancy of 1.2 quality-adjusted life-years and an incremental cost-effectiveness ratio of -630 Euros (discounted to present value) for the LC-PUFA formula in comparison with standard formula. LC-PUFA nutrition was the superior strategy even when the blood pressure-lowering effect was reduced to the lower 95%

Straub N et al, Am J Clin Nutr 2011 ;94:2030S

# Le formule adattate per il lattante : differenze e significato

- Quantità delle proteine → adiposità in gruppi geneticamente predisposti anche a lungo termine
- *Form* delle proteine (intere, idrolisi, aminoacidi) → effetti su crescita ponderale a breve termine
- Grassi (qualità grassi insaturi) → sviluppo funzionale visivo (nervoso?) a breve-medio termine
- Altre differenze in composizione → non evidenza di effetti funzionali