ALIMENTAZIONE NEL 1° ANNO DI VITA:

LATTI FORMULATI

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Codex Alimentarius

- Commissione creata nel 1963 dalla FAO e dal WHO per sviluppare standard di composizione degli alimenti e linee guida rifacendosi ai programmi unificati FAO/WHO
- Finalità: proteggere la salute del consumatore, promuovere il coordinamento degli standard alimentari a livello internazionale (governi, istituzioni, n.g.o.)

Codex Alimentarius e formule per l'infanzia

- Precedente risoluzione adottata nel 1981 sulla base delle conoscenze degli anni '70
- Iniziativa a distanza di vent'anni per aggiornare le indicazioni alle nuove conoscenze scientifiche
- Coinvolgimento del Comitato di Nutrizione dell'ESPGHAN alla fine del 2004

Oltre 25 anni dopo la risoluzione del Codex Alimentarius sulle formule per l'infanzia……

Journal of Pediatric Gastroenterology and Nutrition
41:584–599 © November 2005 ESPGHAN Committee on Nutrition

Medical Position Paper

Global Standard for the Composition of Infant Formula: Recommendations of an ESPGHAN Coordinated International Expert Group

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Le formule non possono ricopiare la composizione biochimica del latte materno

Data on the composition of human milk of healthy, well-nourished women can provide some guidance for the composition of infant formulae, but gross compositional similarity is not an adequate determinant or indicator of the safety and nutritional adequacy of infant formulae. Human milk composition shows remarkable variation. Moreover, there are considerable differences in the bioavailability and metabolic effects of similar contents of many specific nutrients in human milk and formula.

Quale "riferimento" usare?

Therefore, the adequacy of infant formula composition should be determined by a comparison of its effects on physiological (e.g. growth patterns), biochemical (e.g. plasma markers) and functional (e.g. immune responses) outcomes in infants fed formulae with those found in populations of healthy, exclusively breast-fed infants.

Riferimento: non la composizione biochimica del latte materno ma la crescita ed i marker biochimici e funzionali dell'allattato al seno

Component	Unit	Minimum	Maximum
Energy	kcal/100 ml	60	70
Proteins			
Cows' milk protein	g/100 kcal	1.8*	3
Soy protein isolates	g/100 kcal	2.25	3
Hydrolyzed cows' milk protein	g/100 kcal	1.8†	3
Lipids			
Total fat	g/100 kcal	4.4	6.0
Linoleic acid	g/100 kcal	0.3	1.2
α-linolenic acid	mg/100 kcal	50	NS
Ratio linoleic/α-linolenic acids		5:1	15:1
Lauric + myristic acids	% of fat	NS	20
Trans fatty acids	% of fat	NS	3
Erucic acid	% of fat	NS	1
Carbohydrates			
Total carbohydrates‡	g/100 kcal	9.0	14.0

†Formula based on hydrolyzed milk protein with a protein content less than 2.25 g/100 kcal should be clinically tested.

Energia

- Desità energetica del latte materno: circa 65 kcal/dL → 5-10% meno di quanto indicato in precedenza
- Anche la spesa energetica del lattante inferiore ai valori indicati in precedenza

Proteine

Valutare e documentare adeguatamente ogni fonte proteica (animale e/o vegetale)

Fattore di conversione: proteine (g)=azoto (g) x 6.25

Utilizzo di uno score basato sulla media di contenuto di un aminoacido per g di azoto nel latte materno

Non necessario indicare un valore massimo di azoto non proteico (NPN)

Se idrolisati di proteine: valutare clinicamente ogni prodotto con proteine del latte idrolisate < 2.25 g/100 kcal , e considerare valori minimi più elevati se la fonte proteica è diversa

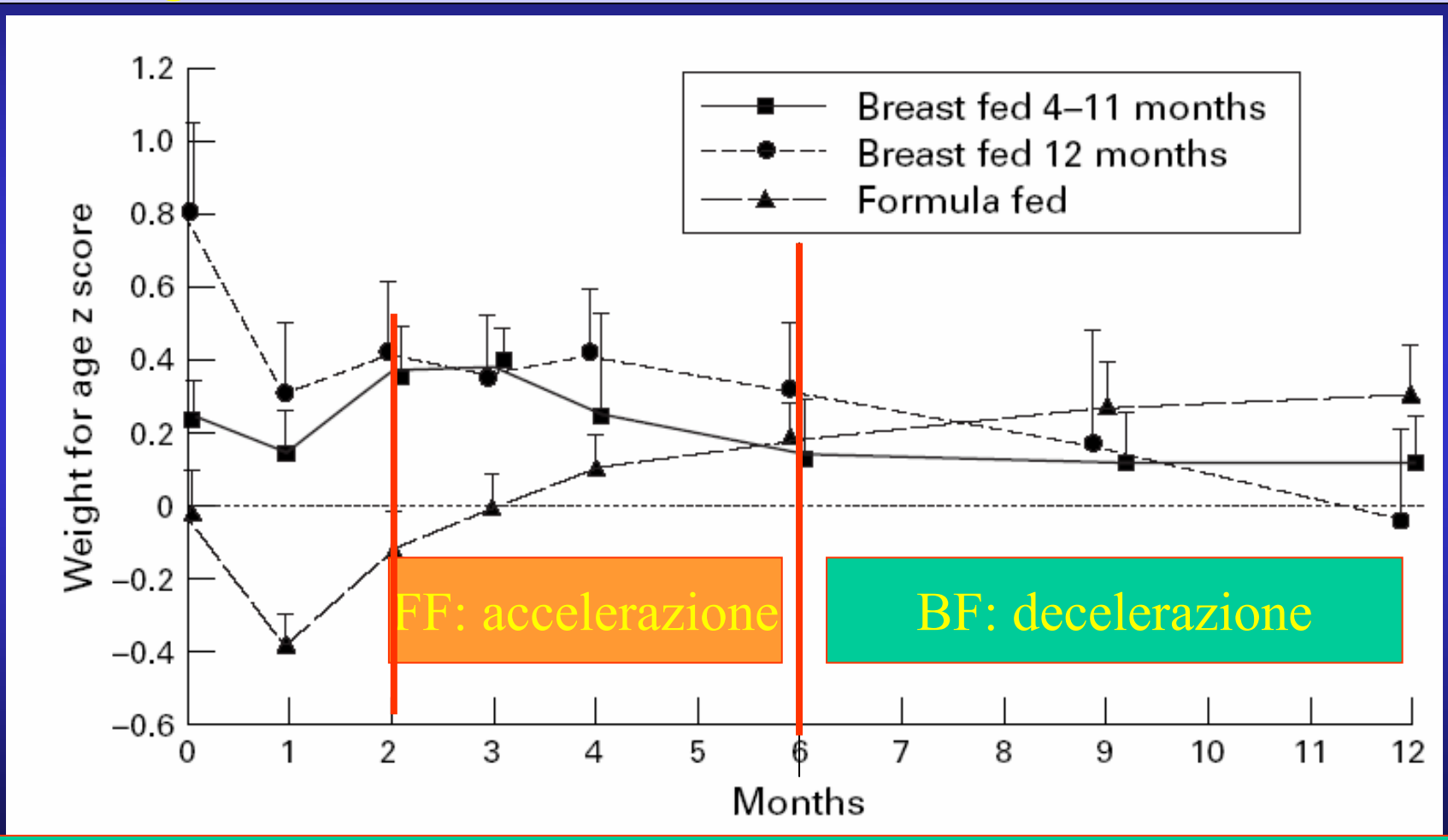
in ogni caso: trial clinici adeguati!

tilizzo di *specifiche sieroproteine* *(alfa-lattoalbumina attoferrina, ricche di cys e trp)* e *nuove tecniche d razionamento* con riduzione quota di glicomacropeptid GMP, ad elevato contenuto di thr)

migliorare la *qualità proteica* delle formule e ridurr l'apporto proteico, garantendo adeguato tasso di crescita minor stress metabolico e *profilo aminoacidico pi isiologico*

Growth patterns of breastfed and formula-fed Italian infants: an Italian Study

Agostoni C et al, Arch Dis Child 1999; 81: 395



Dati consistenti con l'unico disegno di studio "randomizzato"

Kramer et al. Pediatrics 2002;110:343

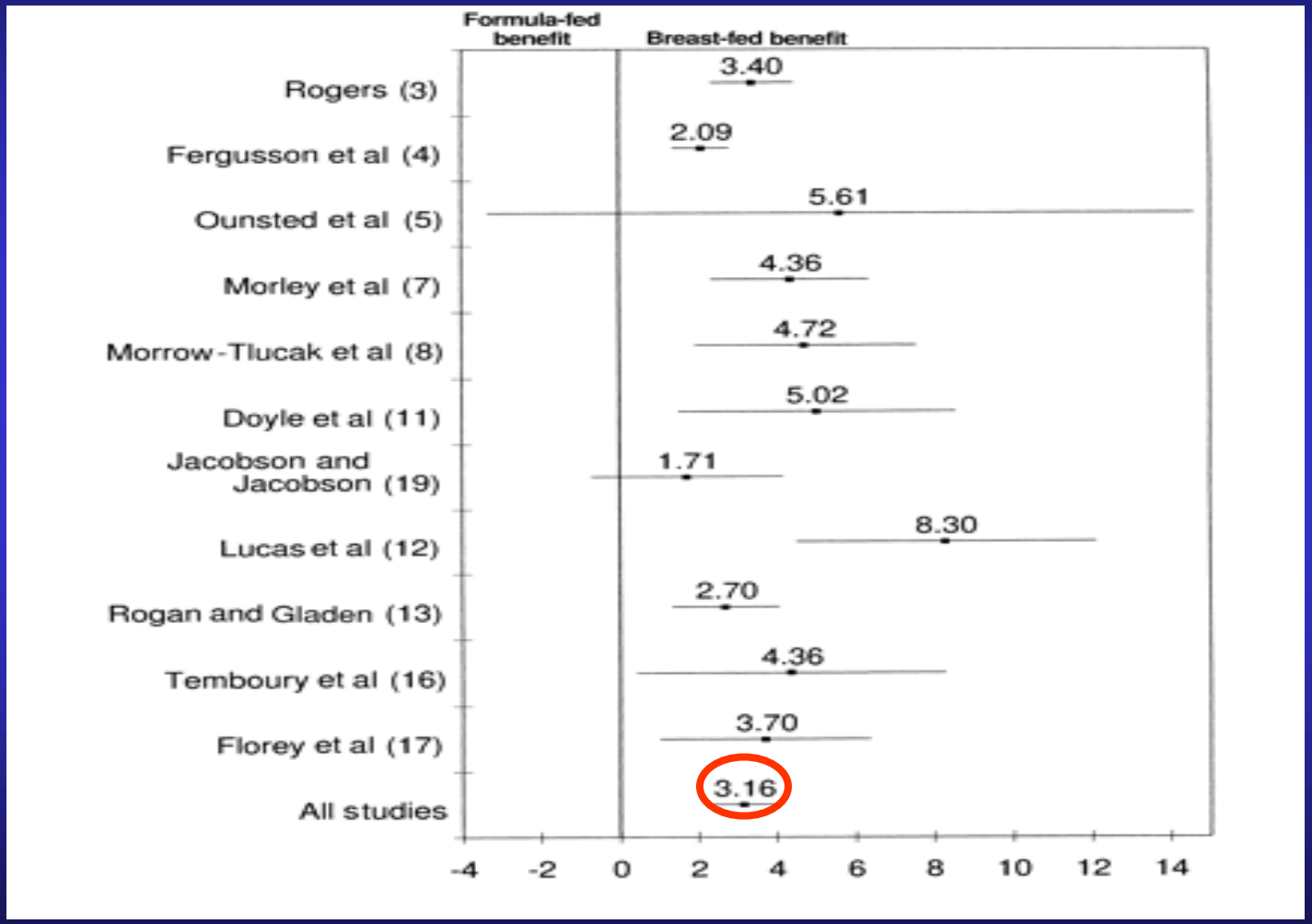
quali spiegazioni?

- Quantità e qualità proteica
- Composizione aminoacidica
- Leptina e molecole ormono-simili
- Tutte insieme, in associazione ad altri composti bio-attivi
- Capacità di autoregolarsi dell'allattato al seno

Grassi

- Acido linoleico: non > 1200 mg/100 kcal (circa 11% apporto energetico totale)
- Acido alfa-linolenico: non < 50 mg/100 kcal (circa 0.45% apporto energetico totale), non > comunque a 240 mg/100 kcal.
- Perché alfa-linolenico? → precursore di DHA
- Rapporto linoleico/alfa-linolenico: tra 5 e 15 a 1

BF and IQ – Meta-analysis



Anderson JW et al. AJCN 1999; 70:525

JAMA 2002;287:2365-71

ORIGINAL CONTRIBUTION

The Association Between Duration of Breastfeeding and Adult Intelligence

Erik Lykke Mortensen, PhD
Kim Fleischer Michaelsen, MD, ScD
Stephanie A. Sanders, PhD
June Machover Reinisch, PhD

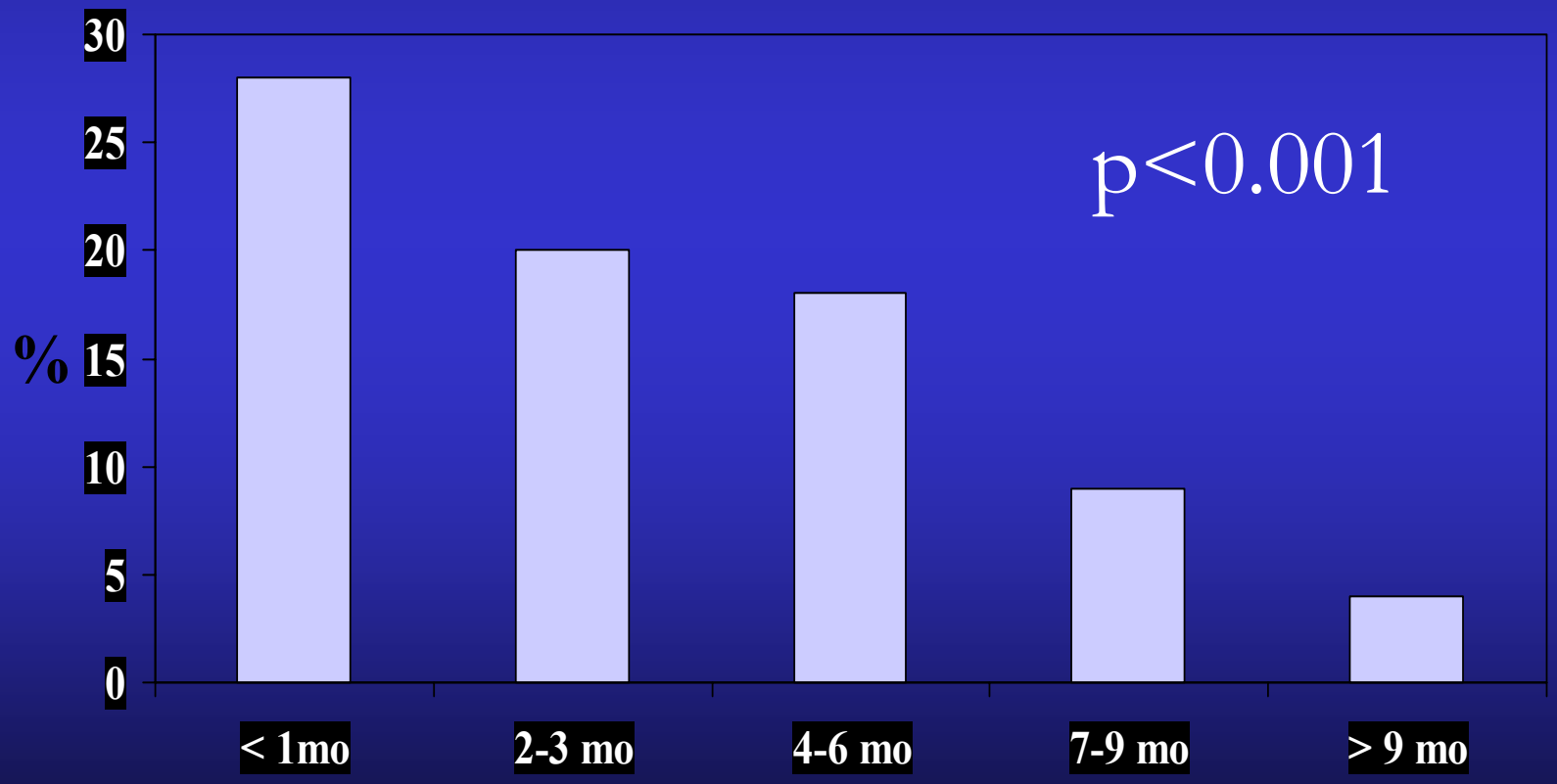
Context A number of studies suggest a positive association between breastfeeding and cognitive development in early and middle childhood. However, the only previous study that investigated the relationship between breastfeeding and intelligence in adults had several methodological shortcomings.

Objective To determine the association between duration of infant breastfeeding and intelligence in young adulthood.

Design, Setting, and Participants Prospective longitudinal birth cohort study conducted in a sample of 973 men and women and a sample of 2280 men, all of whom were born in Copenhagen, Denmark, between October 1959 and December 1961. The samples were divided into 5 categories based on duration of breastfeeding, as assessed by physician interview with mothers at a 1-year examination.

A NUMBER OF STUDIES HAVE SUGgested a positive association between breastfeeding and cognitive and intellectual development in early and middle childhood.[1,2] However, studies of correla-

% of subjects with suboptimal (<90) Full Scale WAIS IQ score



quali spiegazioni?

- Acidi grassi polinsaturi a catena molto lunga (acido arachidonico, ma soprattutto acido docosaesaenoico)
- Composizione aminoacidica
- “Ambiente familiare” dell’allattato al seno

Carboidrati

- Lattosio: importante ruolo funzionale per la fisiologia intestinale→ effetto prebiotico, feci più morbide, facilita assorbimento di acqua, sodio e calcio
- Glucosio: non più raccomandato per aumento dell'osmolalità (1 g/100ml: 58 mOsm/kg)
- Fruttosio e saccarosio: non più raccomandati per i possibili effetti nel caso di lattanti affetti da intolleranza ereditaria al fruttosio (1:20000)
- Amidi: precotti o gelatinizzati, fino al 30% CHO totali (2 g / 100 ml)

Vitamine liposolubili/micronutrienti

Di base: The IEG sees no reason to add to infant formulae excessive amounts of any nutrient that do not serve any nutritional purpose or provide any other benefit, and the effects of which have not been evaluated. Therefore, the contents of water-soluble vitamins in infant formulae generally should not exceed five times the minimum level.

Ferro: 0.3 – 1.3 mg/100 kcal

Livelli di assunzione più bassi (rispetto a precedenti indicazioni) sufficienti per i fabbisogni del lattante

Tassi di assorbimento del ferro più elevati dalle modern formule, e comparabili a quelli del ferro dal latte matern (15-20%)

Col livello minimo proposto si calcola un assorbimento 4 10 volte superiore comunque rispetto all'allattato al seno

Rischi potenziali associati ad assunzioni di ferro elevate minore tasso di crescita in lunghezza, incidenza più elevat di diarrea e (marginalmente) di infezioni respiratorie alte

Incremento di ferro nei depositi→rischio ossidativo?

Optional ingredients	Unit	Minimum	Maximum
Taurine	mg/100 kcal	0	12
Total added nucleotides	mg/100 kcal	0	5
Cytidine 5′-monophosphate (CMP)	mg/100 kcal	0	2.5
Uridine 5′-monophosphate (UMP)	mg/100 kcal	0	1.75
Adenosine 5′-monophosphate (AMP)	mg/100 kcal	0	1.5
Guanosine 5′-monophosphate (GMP)	mg/100 kcal	0	0.5
Inosine 5′-monophosphate (IMP)	mg/100 kcal	0	1.00
Phospholipids	mg/100 kcal	0	300
Docosahexaenoic acid*	% of fat	0	0.5

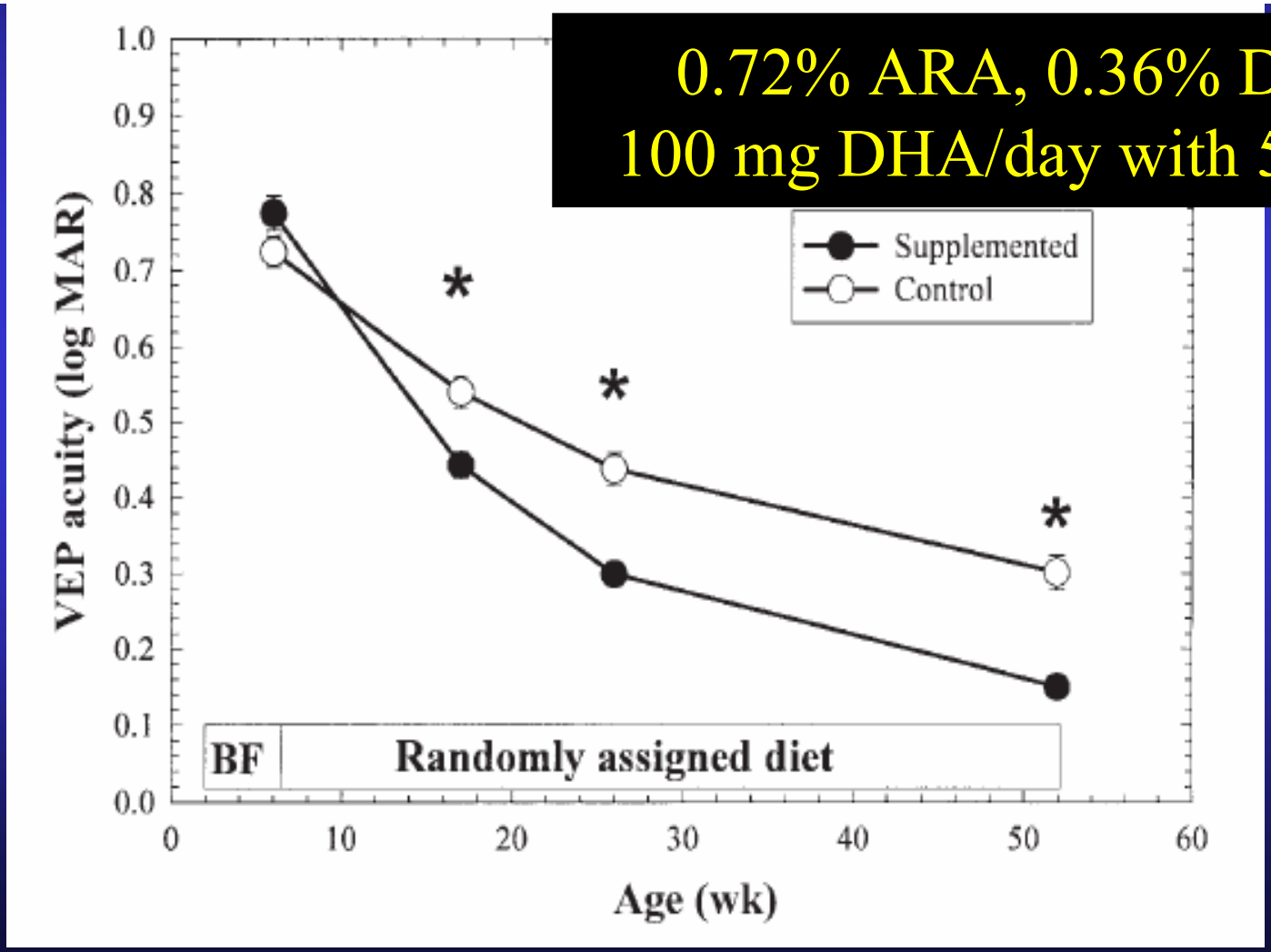
*If docosahexaenoic acid (22:6n-3) is added to infant formula, arachidonic acid (20:4n-6) contents should reach at least the same concentration as DHA. The content of eicosapentaenoic acid (20:5n-3) should not exceed the content of docosahexaenoic acid.

Effetti funzionali dell'apporto di LCPUFA nell'uomo

- Contributo globale allo sviluppo e alla maturazione della retina (e di altre aree cerebrali?)
- Ridotti processi infiammatori e aggregazione piastrinica
- influenza sull'elasticità delle pareti arteriose e sulla pressione ematica

randomized controlled trial of long-chain polyunsaturated fatt
cid supplementation of formula in term infants after weaning a
wk of age[1–3]

leen E Birch, Dennis R Hoffman, Yolanda S Castañeda, Sherry L Fawcett, David G Birch , and Ricardo D Uauy



LCP : Conclusioni

Formule supplementate con LCP nei primi 12 mes portano a differenze visive

Il periodo critico durante il quale l supplementazione con LCPUFA garantisc differenze funzionali (visive) in lattant precedentemente allattati al seno si estende oltre i 4°- 6° mese → cioè nel periodo del divezzamento

Effetti visivi strettamente correlati ai livelli ematic di DHA

→ OSSERVAZIONI: solo a breve termine
Non differenze nella visione sterica a 12 mesi

Long-Chain Polyunsaturated Fatty Acids (LC-PUFA)

addition of DHA should not exceed 0.5% of total fat intake, and AA contents should be at least the same concentration as DHA, whereas the content of EPA in infant formula should not exceed the DHA content.

"optional addition"

Nucleotides

at a maximum total content of 5 mg/100 kcal as well as maximal levels of 2.5 mg/100 kcal CMP, 1.75 mg/100 kcal UMP, 1.5 mg/100 kcal AMP, 0.5 mg/100 kcal GMP, and 1.0 mg/100 kcal IMP are recommended.

"optional addition"

Fattori di difesa del latte materno: una classificazione

. Agenti ad azione antiinfettiva diretta

Molecole Glucidiche, Azotate (Lattoferrina, Lisozima, Immunoglobuline, Glutamina) e Lipidiche utilizzate a scopo FUNZIONALE

. Promotori della crescita di microrganismi protettivi

Fattore bifidogeno identificato da Gyorgy nel 1974 (glicoproteine, glicopeptidi e oligosaccaridi)

. Cellule

Neutrofili e macrofagi (in fase di attivazione), Linfociti (80% T linfociti)

. Molecole ad azione antiinfiammatoria

EGF, Antiossidanti, Prostaglandine, Poliamine, Cortisolo, Attivatori dell'attività piastrinica, AA liberi

. Immunomodulatori

Interferone alfa, Interleuchine, TNF, GSF, ***Nucleotidi***

I LATTI FORMULATI

i nucleotidi

LV e latti formulati praticamente privi di nucleotidi

Direttive CEE: valori max nucleotidi monomerici (5'P cit.,urid.,aden uan.,inos.) nei latti formulati: **5 mg/100Kcal**

FFETTI BIOLOGICI:

sviluppo e maturazione funzionale del sistema immunitario nell rima infanzia (attività NK, IL-2, cellulo-mediata e difes ntibatteriche)

trofismo e riparazione epitelio intestinale con miglior ssorbimento nutrienti (post-enterite e pre-diarrea)

migliore recupero ponderale negli SGA

protezione contro dislipidemie (stimolo sulle desaturasi co

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Editorial

The Composition of Infant Formula: A Worldwide Approach

*Alfredo Guarino, MD and †Stefano Guandalini, MD

a crucial concept of the present recommendations is that it concerns all children of the world, being produced by experts from all over the world. The second important implication of this paper we want to stress is that it involves the delicate matter of the relationship between Scientific Societies, Regulating Agencies and Industry, and clearly states the preeminence of Science in this relationship.

In this scenario, the recommendations are inevitably "conservative" in that they are rigidly evidence-based, i.e. based purely on consolidated scientific information

Non menzione a chiare lettere dei "nutrienti funzionali"
(in particolare: prebiotici, probiotici)
ma apertura sulla inclusione in documenti futuri

Journal of Pediatric Gastroenterology and Nutrition
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Editorial

Infant Formulae: From ESPGAN Recommendations Towards ESPGHAN-coordinated Global Standards

*Carlo Agostoni and †Magnus Domellöf

Many potential new ingredients, not mentioned in the IEG recommendations, are presently investigated as possible future additions to infant formulae: Probiotics, prebiotics (nondigestible oligosacharides), structured triglycerides, recombinant proteins (e.g. lactoferrin), enzymes (e.g. bile salt stimulated lipase), hormones (e.g. insulin), growth factors, polyamines

….altri?

Probiotici – nuova definizione

Preparazioni di cellule microbiche o componenti di cellule microbiche che hanno effetto benefico sulla salute ed il benessere dell′ospite (e.g. lattobacilli, bifidobatteri)

Salminen 1999

Journal of Pediatric Gastroenterology and Nutrition
38:365–374 © April 2004 Lippincott Williams & Wilkins, Philadelphia

Medical Position Paper

Probiotic Bacteria in Dietetic Products for Infants: A Commentary by the ESPGHAN Committee on Nutrition

ESPGHAN Committee on Nutrition: *Carlo Agostoni, †Irene Axelsson, ‡Christian Braegger, §Olivier Goulet, ‖Berthold Koletzko, #Kim F. Michaelsen, **Jacques Rigo, ††Raanan Shamir, ‡‡Hania Szajewska, §§Dominique Turck, and ‖‖Lawrence T. Weaver

CONCLUSIONS

Our review of available clinical trials found only limited data on the safety and clinical effects probiotic preparations added to infant formulas, follow-up formulas, and special medical foods. There is no published evidence for any long-term clinical benefit of infant formulas supplemented with probiotic bacteria. No data are available on possible long-term effects on intestinal colonization and its effects on long-term gastrointestinal and immune functions. Acquisition of such data would be highly desirable given the suggestion that bacteria ingested during early infancy are more likely to permanently colonize the intestine than those ingested during later life (84). There are some data supporting a short-term benefit of some probiotic strains in infants and young children with infectious diarrhea.

The working group recommends that nutritional, physiological and therapeutic effects be demonstrated by appropriate clinical studies described in detail. Formulae with added probiotic microorganisms should be labelled with the exact name of the strain and its concentration (number of microorganisms per weight unit of formula as ready for consumption). The label should include recommendations as to the amount and duration of consumption, and on storage and preparation.

Follow-on formulae with added bacteria regarded as probiotics have been for since abou three years. The Committee has no reason to object to the addition of bacteria regarded as probiotics to follow-on formulae, provided the requirements described below are fulfilled.
Only bacterial strains with identity and genetic stability demonstrated by cultural and molecular methods should be used, if they can be considered as generally safe when added to the individual food and have been shown to survive the gastrointestinal passage, have the capacity to proliferate in the gut for the duration of consumption and can modify the intestinal milieu (for example pH, short chain fatty acids). The identity of the probiotic strain should be described by molecular methods in a dossier and be available to the food control authorities. The content of viable bacteria should be such throughout shelf-life as to achieve 10^6 to 10^8 colony forming units per gram of formula prepared as ready for consumption. Processing, packaging and storage should not impair the viability of the bacteria.

Prebiotici

Ingredienti alimentari non digeribili che influenzano positivamente l'ospite stimolando selettivamente la crescita o l'attivita' di un numero limitato di batteri nel colon

(es, oligosaccaridi non digeribili: lattulosio, inulina, frutto-oligosaccaridi FOS, galatto-oligosaccaridi GOS)

Gibson & Roberfroid J Nutr 1995; 125: 1401-12

MOLECOLE GLUCIDICHE OLIGOSACCARIDI

- sono note più di 100 molecole
- costituiscono il terzo componente del latte umano dal punto di vista quantitativo
- hanno struttura lineare o ramificata
- contengono glucosio, galattosio, N-acetil-glucosammina, mannosio, fucosio, acido sialico

OLIGOSACCARIDI
caratteristiche

- inibiscono l'adesione dei batteri patogeni e delle tossine all'epitelio. Tale azione sembra essere associata in particolare ai gangliosidi che includono acido sialico
- la maggior parte degli oligosaccaridi contenuta nel latte materno non è idrolizzata dagli enzimi del tratto intestinale superiore e raggiunge intatta il grosso intestino
- favoriscono lo sviluppo della flora bifidogena a livello dell'apparato digerente creando un ambiente sfavorevole alla proliferazione di ceppi patogeni

I LATTI FORMULATI

LV e formule pressocchè prive di oligosaccaridi!!

i prebiotici

- galatto-oligosaccaridi (GOS) a corta catena derivati d
rodotti caseari fermentati e frutto-oligosaccaridi (FOS)
atena lunga derivati da piante.

- fermentazione batterica colonica con produzione d
SCFA ed idrogeno

- basso contenuto energetico con utilizzo locale

- FOS: in vitro ed in vivo stimolazione crescita d
ifidobatteri a spese di batterioidi, clostridi e coliform
onché listeria, shigella, salmonella e v.cholerae

- GOS: stimolazione crescita di bifidobatteri e lattobacil
el colon prossimale

Prebiotic Inulin Enriched with Oligofructose in Combination with the Probiotics *Lactobacillus rhamnosus* and *Bifidobacterium lactis* Modulates Intestinal Immune Functions in Rats[1]

Monika Roller, Gerhard Rechkemmer[2] and Bernhard Watzl[2]

ABSTRACT Probiotics (PRO) modulate systemic immunity in animals and humans. In contrast, the effects of prebiotics (PRE) on systemic and intestinal immunity have not been investigated. Whether the combined application of PRO and PRE [synbiotics (SYN)] has synergistic or additive effects is presently unknown. Therefore, PRO (*Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb12), PRE (inulin enriched with oligofructose), and SYN (combination of PRO and PRE) were fed to F344 rats for 4 wk as supplements to a high fat diet. Functions of immune cells isolated from peripheral blood mononuclear cells (PBMC), spleen, mesenterial lymph nodes and Peyer's patches (PP) were investigated. The SYN supplement increased secretory immunoglobulin A (sIgA) production in the ileum compared with controls fed the high fat diet alone ($P < 0.05$), and decreased the oxidative burst activity of blood neutrophils ($P < 0.05$) compared with rats fed PRO. The PRE supplement enhanced the production of interleukin-10 ($P < 0.05$) in PP as well as the production of sIgA in the cecum ($P < 0.05$), compared with controls. The PRO supplement modestly affected immune functions, whereas systemic immunomodulatory effects were observed in rats fed SYN. The PRE supplement primarily acted at the level of the gut-associated lymphoid tissue. The combined application of PRO and PRE has different effects from those of the individual supplements, but does not simply result in additive or synergistic effects. J. Nutr. 134: 153–156, 2004.

In conclusion, the Committee reaffirms its previous statement that is has no major concerns on the inclusion of up to 0.8 g/100 mL of a combination of 90% oligogalactosyl-lactose and 10% high molecular weight oligofructosyl-saccharose to infant formulae and follow-on formulae. It also reaffirms its previous comment that further information should be gathered on safety and benefits of this combination as well as other forms of oligosaccharides in infant formulae and follow-on formulae.

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Prebiotic Oligosaccharides in Dietetic Products for Infants: A Commentary by the ESPGHAN Committee on Nutrition

ESPGHAN Committee on Nutrition: *Carlo Agostoni, †Irene Axelsson, ‡Olivier Goulet, §Berthold Koletzko, ‖Kim F. Michaelsen, ¶John W. L. Puntis, #Jacques Rigo, **Ra urck

*University of Milano, Mi s-Malades, Paris, France; §Ludwig-Maximilians-U iversity, Frederiksberg, Denmark; ¶The Gener n; **Meyer Children's Hospital of Haifa, Ha iversity of Lille, Lille,

CONCLUSIONS AND RECOMMENDATIONS

- Currently there are only limited published data on the evaluation of prebiotic substances in dietetic products for infants. Therefore, no general recommendation on the use of oligosaccharide supplementation in infancy for preventive or therapeutic purposes can be made.
- During the time of their administration prebiotic oligosaccharides in dietetic products have the potential to increase the total number of bifidobacteria in feces and to soften stools.
- There is no published evidence of other clinical benefits of adding prebiotic oligosaccharides to dietetic products for infants.
- The available data on the oligosaccharide mixtures in infant formulae do not demonstrate adverse effects.
- Validated clinical outcome measures of prebiotic effects in infants should be characterized in further well-designed and carefully conducted randomized controlled trials with relevant inclusion/exclusion criteria and adequate sample size. Such trials should also define the optimal quantities, types and intake durations and safety of different oligosaccharides.
- Further evaluation is required before the general use of prebiotics in premature infants and/or infants with special conditions (e.g., immune deficiency).

Nei trigliceridi del latte materno…

Acido grasso	posizione (% sul totale dei trigliceridi)		
	1	**2 (beta)**	**3**
Miristico	3	7	7
Palmitico	16	58	6
Palmitoleico	3	4	7
Stearico	15	3	2
Oleico	46	12	49
Linoleico	11	7	14
Alfa-linolenico	0.4	0.6	1.5
Arachidonico	tracce	0.9	0.3

adattato da Breckenridge, J Lipid Res 1967;8:473

BETA-PALMITATO: FISIOLOGIA

- La lipasi pancreatica rilascia gli acidi grassi in posizione 1 e 3 nell'intestino. I due acidi grassi ed il risultante monogliceride sono così resi assorbibili.
- La lipasi stimolata dai sali biliari (BSSL) è in grado di idrolizzare il monogliceride ad acido grasso più glicerolo, ma questo processo è ancora dubbio nell'allattato al seno.
- Gli acidi grassi a lunga catena non esterificati (per es., l'acido palmitico) hanno un punto di fusione superiore alla temperatura corporea e, se vi è calcio sufficiente nel lume intestinale, formano saponi di calcio insolubili.
- L'acido palmitico nella forma di 2-monogliceride non è disponibile a formare saponi di calcio. Questo fenomeno puo' in parte spiegare il maggiore assorbimento di acido palmitico esterificato in posizione 2 in confronto all'acido palmitico esterificato nelle posizioni 1 e 3.

Lopez A et al. Early Hum Dev 2001;65: S83-94

Migliore assorbimento di acido palmitico

Migliore assorbimento *in toto* dei grassi

Migliore assorbimento di calcio

I latti formulati: oggi e domani

- Latte materno: anche durante il divezzamento
- Se il latte materno viene a mancare introdurre una formula adeguata dal punto di vista nutrizionale e funzionale almeno fino al dodicesimo mese di vita
- Testare adeguatamente ogni nuovo nutriente
- …..un solo tipo di formula senza più la “storica” divisione tra “starting” e “follow-up”?

EUROPEAN COMMISSION
HEALTH and CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions
C2 - Management of scientific committees; scientific co-operation and networks

Scientific Committee on Food

SCF/CS/NUT/IF/65 Final
18 May 2003

Report of the Scientific Committee on Food on the Revision of Essential Requirements of Infant Formulae and Follow-on Formulae

(adopted on 4 April 2003)

FORMULE DI SEGUITO

Requirements for Infant Formulae and Follow-on Formulae

SUMMARY TABLE OF RECOMMENDATIONS ON THE COMPOSITION OF INFANT FORMULAE AND FOLLOW-ON FORMULAE

	Infant Formulae	Follow-on Formulae
Energy density (kcal/100 mL)	60-70	60-70
Nutrients (per 100 kcal, unless otherwise stated)		
Protein[1]		
Cow's milk protein	1.8-3 g[2]	1.8-3 g
Soy protein	2.25-3 g	
Protein hydrolysates		
L-carnitine addition to soy protein and protein hydrolysates formulae	≥1.2 mg	no requirement
Addition of taurine	≤12 mg	
Nucleotides, if added[3]	≤ 5 mg	
Choline	7-30 mg	no requirement
Fat		
Total fat	4.4-6 g	4.0-6.0 g
Phospholipids	≤1 g/L	
Inositol	4-40 mg	no requirement
Lauric and myristic acids	Together ≤20% of total fatty acids	
Linoleic	0.5-1.2 g	
Formulae without added LCPUFA		
α-linolenic	≥100 mg	
Linoleic/α-linolenic ratio	5-15	
Formulae with added LCPUFA		
α-linolenic[4]	≥50 mg	
Linoleic/α-linolenic ratio[4]	5-20	
n-6 LCPUFA	≤2% of total fatty acids	
Arachidonic acid	≤1% of total fatty acids	
n-3 LCPUFA	≤1% of total fatty acids	
Ratio EPA/DHA (wt/wt)	<1	
Cottonseed/sesame oils	No use of these type of oils	
Conjugated linoleic acid (CLA)	No intentional addition	
Trans fatty acids	≤3% of total fatty acids	
Erucic acid	≤1% of total fatty acids	

[1] Calculation of protein content: N x 6.25, non-protein nitrogen (formulae made from intact protein) ≤15% of total nitrogen.
[2] Infant formulae containing 1.8 g/100 kcal should be clinically evaluated.
[3] Maximum content per nucleotide as specified in the text.

	Infant Formulae	Follow-on Formulae
Carbohydrates		
Total carbohydrates	9-14 g	
Lactose in cows' milk protein- and protein hydrolysates formulae	≥4.5 g	
Lactose in soy protein formulae	No requirement	
Saccharose	None in cows' milk protein and soy protein formulae ≤20% of total carbohydrates in protein hydrolysates formulae	Sum of saccharose, fructose, honey ≤20% of total carbohydrates
Fructose	None	
Glucose	No intentional addition to formulae based on intact proteins, ≤2 g in formulae based on protein hydrolysates	
Maltose, maltodextrins	Unrestricted	
Starches	≤30% of total carbohydrates (≤2 g/100 mL) as precooked or gelatinised naturally gluten-free starches No starches modified by enzymatic cross-linking or stabilisation	Gluten-free carbohydrates only

Assunzione di nutrienti tra 8 e 24 mesi in Paesi Europei

Paese	Età (mesi)	P g/kg	P %	Lip%	Cho%
Spagna	9	4.4	15.7	26.4	58
Francia	10	4.3	15.6	27.1	57
Italia	12	5.1	19.5	30.5	50
Danimarca	12-36	3.3	15	28	57

Rolland-Cachera et al. Acta Paed 1999; 88:365

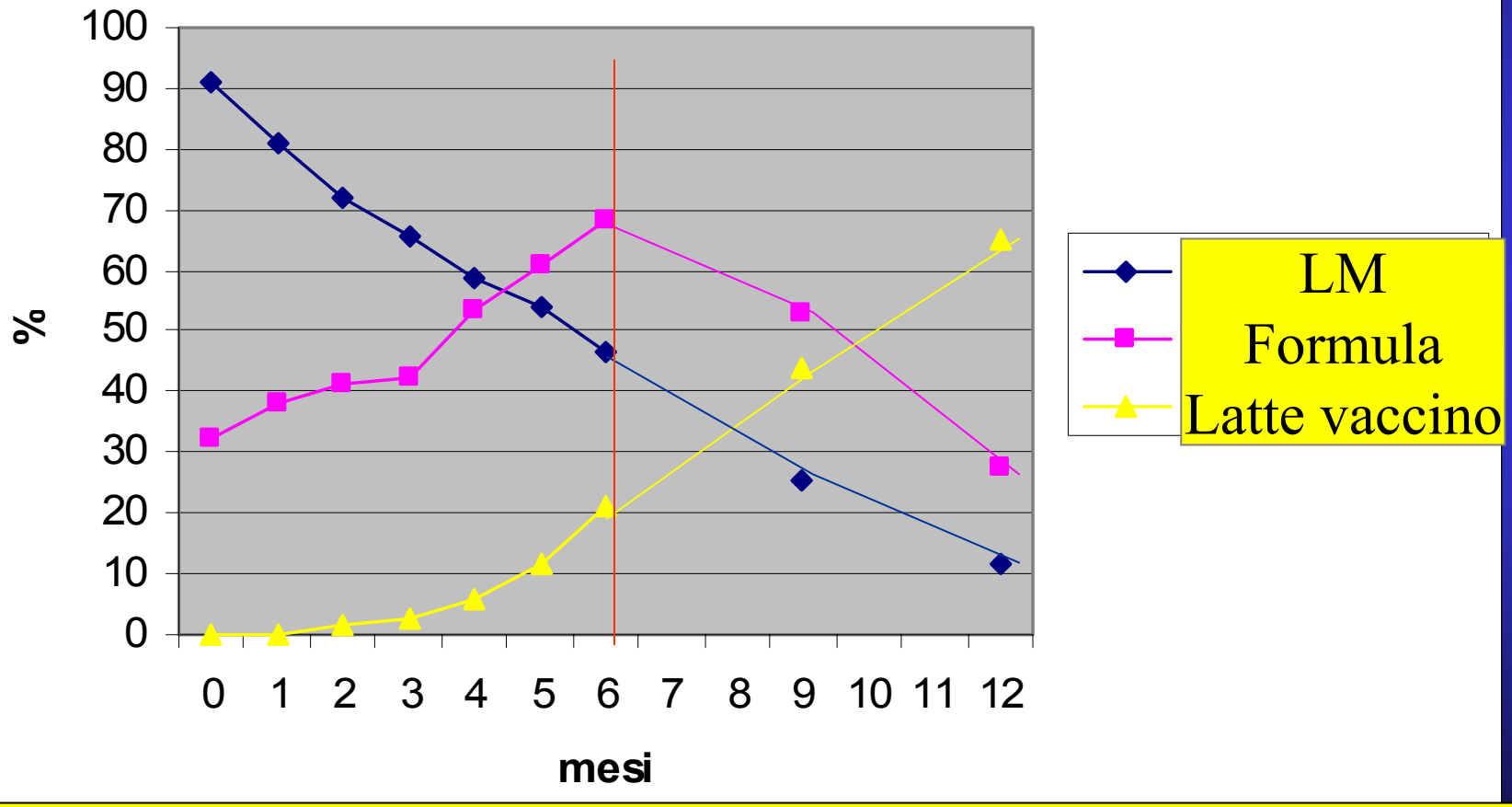
LARN Italiani - Revisione del 1996

Età	En kcal, range	Proteine (corrette per qualità		
ms	min F/M→max F/M	g/kg/d	%*	(x kg)
6-9	653/710 → 950/1027	2.0	8	(x 8)
9-12	739/797 → 1133/1056	1.8	7.6	(x 10)
12-18	854/922 → 1190/1277	1.4	6	(x 11)
18-24	950/1008 → 1306/1382	1.4	6	(x 12)

*calcolato

Assunzione di latte nei primi 12 mesi in Italia

(Puer Project: Giovannini M et al, Acta Paediatr 2003; 92: 357)



500 ml latte vaccino = 18 grammi proteine

= 7.2% energia in una dieta di 1000 kcal(vs 1.4% LM e 3.6% F2)

Proteine : effetto positivo su crescita o aumento del rischio di obesità?

Aumento della assunzione di proteine → aumento della secrezione di insulina e fattori di crescita→ in particolare IGF-I

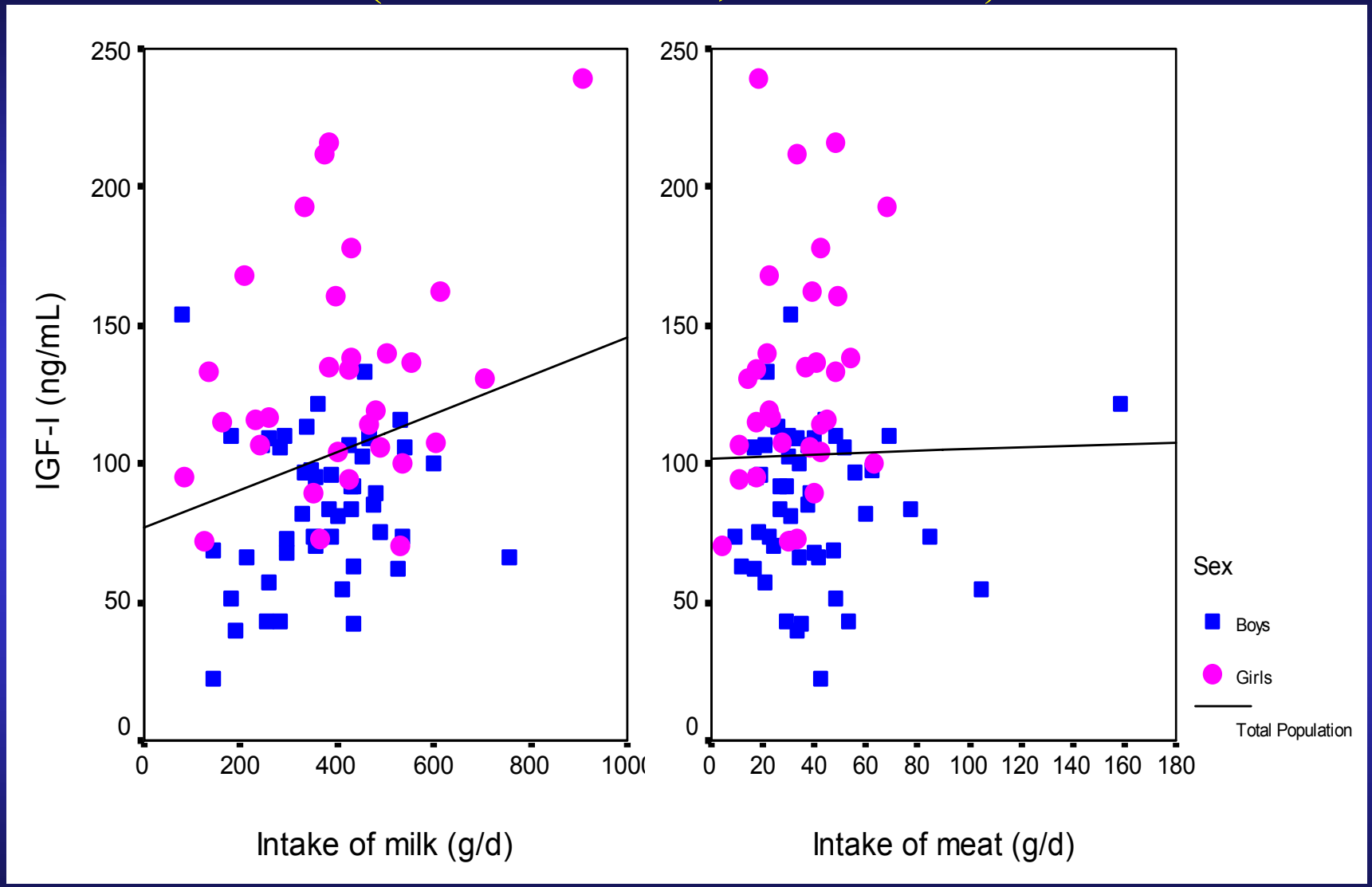
Nelle fasce a più elevata assunzione proteica tra 8 e 24 mesi→ ripresa dell'aumento del BMI (kg/m^2) a 2-3 anni (precoce "adiposity rebound", normalmente osservato a 5-6 anni)

Associazioni proteine/obesità

Autore	Prot%	Età	Osservazione:	P
olland-Cachera 1995 nt J Obes 19:573	16.6	24 ms	EAR	<0.05
caglioni 2000 nt J Obes 24:777	22	12 ms	5 anni	<0.05
Dorosty 2000 ediatrics 105: 1115	14	18 ms	EAR	NS
Gunnarsdottir 2003 nt J Obes 23:1523	17, M	9-12 ms	6 anni	<0.05
Hoppe 2004 m J Clin Nutr 79:494	13,F, 14,M	9 ms	10anni	NS
caglioni 2004 cta Paediatrica 93:1596	14	12 mos	8anni	NS

EAR: early adiposity rebound

Osservazione su 90 bambini danesi a due anni e mezzo (Michaelsen et al, AJCN 2004)



r=0.24, p=0.03 r=0.12, p=0.31

Aumento del consumo di latte da 200 a 600 ml = 30% aumento di IGF-1

Iron supplemented formula milk related to reduction in psychomotor decline in infants from inner city areas: randomised study

BMJ 1999;318:693–8

Objective To compare the effect of unmodified cows' milk and iron supplemented formula milk on psychomotor development in infants from inner city areas when used as the main milk source.

Design Double blind, randomised intervention trial.

Setting Birmingham health centre.

Subjects 100 infants, mean age 7.8 months (range 5.7 to 8.6 months), whose mothers had already elected to use unmodified cows' milk as their infant's milk source.

Intervention Changing to an iron supplemented formula milk from enrolment to 18 months of age, or continuing with unmodified cows' milk.

Main outcome measures Developmental assessments using Griffiths scales at enrolment and at 18 and 24 months

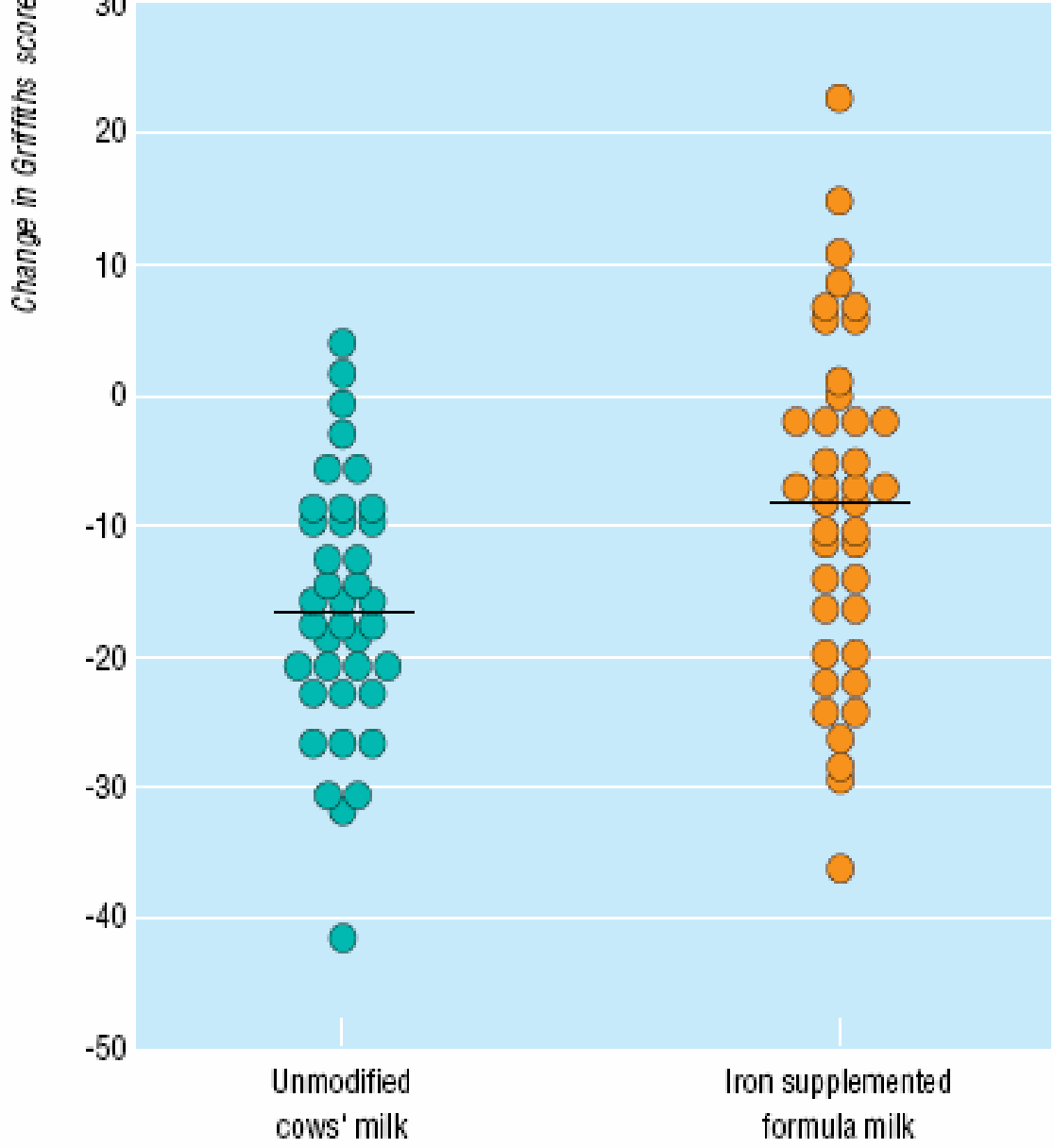


Fig 2 Changes in Griffiths general quotient score between enrolment and 24 months of age in infants receiving unmodified cows' milk or iron supplemented formula milk (P=0.02)

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Editorial

Infant Formulae: From ESPGAN Recommendations Towards ESPGHAN-coordinated Global Standards

*Carlo Agostoni and †Magnus Domellöf

….. the present standard of composition of formulae should ensure the best possible nutrition, leading to optimal growth, development and future health.

… Paediatricians should carefully study the composition of any formula, since these standards, and their evolution, will produce formulae with very different characteristics, not just influencing nutrient content but, more importantly, the functional outcomes for infants.

The child is the father of the man.

Pediatricians should be more interested in adult disease.

L.T.Weaver