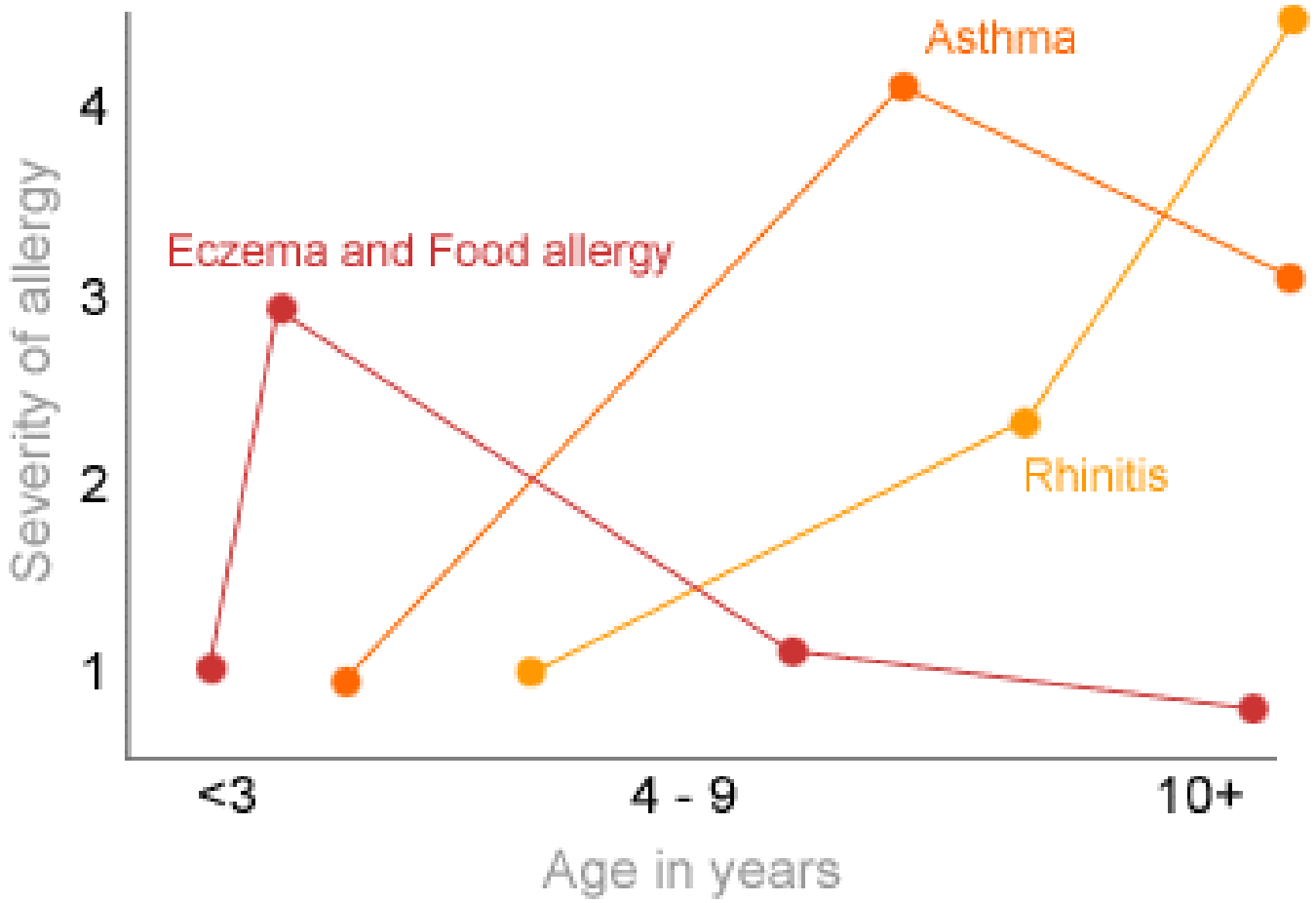
Allergia megelőzés és szoptatás

Dr. Réthy Lajos Attila (MD, PhD)

Országos Gyermekegészségügyi Intézet, Budapest,

European Academy of Allergology and Clinical Immunology,
Section of Pediatrics ETC

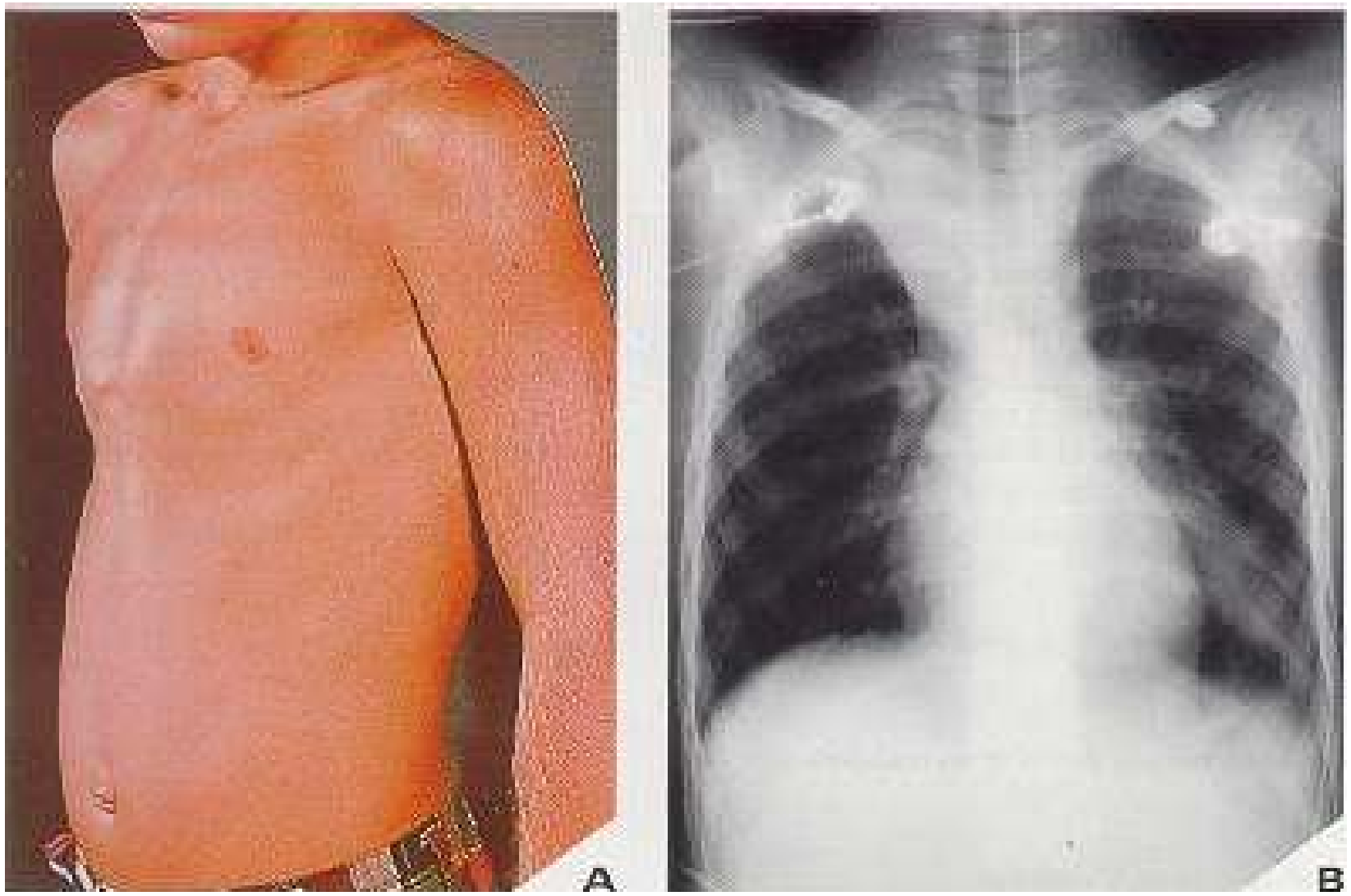
Allergiás menetelés, „allergic march”



Adapted from: Saarinen, Lancet 1995

Atopiás dermatitisz

Allergiás asztma



Allergiák:
Komplex (poligénes/multifaktoriális) betegségek

- Többféle **genetikai** tényező és
- **környezeti** faktorok

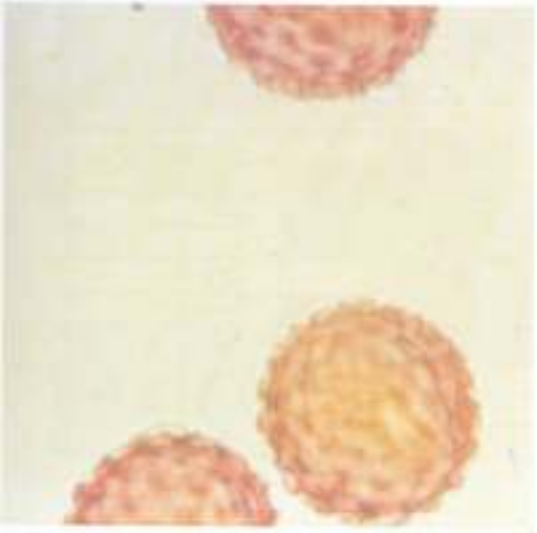
együttes hatása !

Poratka

Parlagfű és pollen

2.7 Giant Ragweed (*Ambrosia trifida*). One of the two common forms of ragweed in North America, this plant can reach heights of up to 12 feet (3.7 m).

2.8 Short Ragweed (*Ambrosia artemisiifolia*). More widespread than Giant Ragweed, this plant is now found in much of North America, proliferating in more temperate climates. The pollen may be airborne throughout the year in some regions; peak counts generally occur during August and September.



2.9 Ragweed pollen grains. Oil emersion photomicrograph, ×450. (Courtesy of Greer Laboratories.)

2.10 English Plantain. This plant pollinates during the same season as the grasses. It can trigger allergic rhinitis in some individuals, which may be confused with an allergic response to grass pollens.

Allergiák, öröklődési kockázat

Ha a családi anamnézis negativ:	10-20%
Ha egyik szülő allergiás:	30- 50 %
Ha mindkét szülő allergiás :	40-75 %

Allergia prevenció

- Előzmények:

- 1999, 2000 és 2004-es szakmai irányelvek
- (ESPGHAN, AAP, EAACI) után,

- **2008: Friss nemzetközi állásfoglalások**
  - **(EAACI, ESPGHAN, AAP)**
    - Cochrane adatbázis -és elvégzett meta-analizisek kiértékelése alapján

Pediatr Allergy Immunol 2008: 19: 1–4
DOI: 10.1111/j.1399-3038.2007.00680.x

PEDIATRIC ALLERGY AND IMMUNOLOGY

Review Up-date

Dietary prevention of allergic diseases in infants and small children

Amendment to previous published articles in Pediatric Allergy and Immunology 2004, by an expert group set up by the Section on Pediatrics, European Academy of Allergology and Clinical Immunology

Høst A, Halken S, Muraro A, Dreborg S, Niggemann B, Aalberse R, Arshad SH, von Berg A, Carlsen KH, Duschén K, Eigenmann PA, Hill D, Jones C, Mellon M, Oldeus G, Oranje A, Pascual C, Prescott S, Sampson H, Svartengren M, Wahn U, Warner JA, Warner JO, Vandenplas Y, Wickman M, Zeiger RS. Dietary prevention of allergic diseases in infants and small children.
Pediatr Allergy Immunol 2008: 19: 1–4.

Because of scientific fraud four trials have been excluded from the original Cochrane meta-analysis on formulas containing hydrolyzed protein for prevention of allergy and food intolerance in infants. Unlike the conclusions of the revised Cochrane review the export group set up by the Section on Paediatrics, European Academy of Allergology and Clinical Immunology (SP-EAACI) do not find that the exclusion of the four trials demands a change of the previous recommendations regarding primary dietary prevention of allergic diseases. Ideally, recommendations on primary dietary prevention should be based only on the results of randomized and quasi-randomized trials (selection criteria in the Cochrane review). However, regarding breastfeeding randomization is unethical, Therefore, in the development of recommendations on dietary primary prevention, high-quality systematic reviews of high-quality cohort studies should be included in the evidence base. The study type combined with assessment of the methodological quality determines the level of evidence. In view of some methodological concerns in the Cochrane meta-analysis, particularly regarding definitions and diagnostic criteria for outcome measures and inclusion of non peer-reviewed studies/reports, a revision of the Cochrane analysis may seem warranted. Based on analysis of published peer-reviewed observational and interventional studies the results still indicate that breastfeeding is highly recommended for all infants irrespective of atopic heredity. A dietary regimen is effective in the prevention of allergic diseases in high-risk infants, particularly in early infancy regarding food allergy and eczema. The most effective dietary regimen is exclusively breastfeeding for at least 4–6 months or, in absence of breast milk, formulas with documented reduced allergenicity for at least the first 4 months, combined with avoidance of solid food and cow's milk for the first 4 months.

Arne Høst[1], Susanne Halken[1], Antonella Muraro[2], Sten Dreborg[3], Bodo Niggemann[4], Rob Aalberse[5], Syed H. Arshad[6], Andrea von Berg[7], Kai-Håkon Carlsen[8], Karel Duschén[9], Philippe A. Eigenmann[10], David Hill[11], Catherine Jones[12], Michael Mellon[13], Göran Oldeus[14], Arnold Oranje[15], Cristina Pascual[16], Susan Prescott[17], Hugh Sampson[18], Magnus Svartengren[19], Ulrich Wahn[20], Jill A. Warner[12], John O. Warner[12], Yvan Vandenplas[20], Magnus Wickman[21] and Robert S. Zeiger[13]

[1]Department of Pediatrics, Odense University Hospital, Odense, Denmark, [2]Department of Pediatrics, University of Padua, Padua, Italy, [3]ESPACI Past President, Lerum, Sweden, [4]Department of Pneumology and Immunology, University Children's Hospital Charité, Humboldt University, Berlin, Germany, [5]Department of Allergy CLB, Amsterdam, The Netherlands, [6]Clinical Allergy Research Unit, St Mary's Hospital, Newport, Isle of Wight, UK, [7]Abt. für Kinderheilkunde, Marien-Hospital, Wesel, Germany, [8]Voksentoppen National Centre of Asthma, Allergy and Chronic, Lung Diseases in Children, Oslo, Norway, [9]Department of Paediatrics, University Hospital Linköping, Linköping, Sweden, [10]Allergologie/Pediatrie, University of Geneve, Geneve, Switzerland, [11]Department of Allergy, Royal Children's Hospital, North Melbourne, Victoria, Australia, [12]Child Health, Level G (803) Centre Block, Southampton General Hospital, Southampton, UK, [13]Kaiser Permanente San Diego, San Diego, CA, USA, [14]Department of Paediatrics, County Hospital Ryhov, Jönköping, Sweden, [15]Department of Dermatology and Venerology Pediatric Dermatology Unit, ErasmusMC-University Medical Center, Sophia Children's Hospital Rotterdam, Rotterdam, The Netherlands, [16]Servicio de Alergia, Hospital Infantil Universitario La Paz, Madrid, Espana, [17]Department of Paediatrics, University of Western Australia, Subiaco, Western Australia, [18]Department of Pediatrics, Division of Allergy and Immunology, Mount Sinai School of Medicine, New York, NY, USA, [19]Department of Public Health Sciences, Division of

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Effects of Early Nutritional Interventions on the Development of Atopic Disease in Infants and Children: The Role of Maternal Dietary Restriction, Breastfeeding, Timing of Introduction of Complementary Foods, and Hydrolyzed Formulas

Frank R. Greer, Scott H. Sicherer, A. Wesley Burks and and the Committee on Nutrition and Section on Allergy and Immunology
Pediatrics 2008;121;183-191
DOI: 10.1542/peds.2007-3022

ABSTRACT

This clinical report reviews the nutritional options during pregnancy, lactation, and the first year of life that may affect the development of atopic disease (atopic dermatitis, asthma, food allergy) in early life. It replaces an earlier policy statement from the American Academy of Pediatrics that addressed the use of hypoallergenic infant formulas and included provisional recommendations for dietary management for the prevention of atopic disease. The documented benefits of nutritional intervention that may prevent or delay the onset of atopic disease are largely limited to infants at high risk of developing allergy (ie, infants with at least 1 first-degree relative [parent or sibling] with allergic disease). Current evidence does not support a major role for maternal dietary restrictions during pregnancy or lactation. There is evidence that breastfeeding for at least 4 months, compared with feeding formula made with intact cow milk protein, prevents or delays the occurrence of atopic dermatitis, cow milk allergy, and wheezing in early childhood. In studies of infants at high risk of atopy and who are not exclusively breastfed for 4 to 6 months, there is modest evidence that the onset of atopic disease may be delayed or prevented by the use of hydrolyzed formulas compared with formula made with intact cow milk protein, particularly for atopic dermatitis. Comparative studies of the various hydrolyzed formulas also indicate that not all formulas have the same protective benefit. There is also little evidence that delaying the timing of the introduction of complementary foods beyond 4 to 6 months of age prevents the occurrence of atopic disease. At present, there are insufficient data to document a protective effect of any dietary intervention beyond 4 to 6 months of age for the development of atopic disease.

Journal of Pediatric Gastroenterology and Nutrition
46:99–110 © 2008 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and
North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

Medical Position Paper

Complementary Feeding: A Commentary by the ESPGHAN Committee on Nutrition

ESPGHAN Committee on Nutrition: *Carlo Agostoni, †Tamas Decsi, ‡[3]Mary Fewtrell, §Olivier Goulet, ¶Sanja Kolacek, ||[1]Berthold Koletzko, **[3]Kim Fleischer Michaelsen, ††Luis Moreno, ‡‡John Puntis, §§Jacques Rigo, ¶¶Raanan Shamir, ||||[2]Hania Szajewska, ***Dominique Turck, and †††Johannes van Goudoever

**San Paolo Hospital, University of Milano, Milano, Italy, †Department of Paediatrics, University of Pecs, Hungary, ‡Institut Child Health, London, UK, §Hôpital Necker Enfants-Malades, University of Paris Descartes, Paris, France, ¶Children's Hosp Zagreb Medical University, Croatia, ||Dr von Hauner Children's Hospital, University of Munich, Germany, **Department of Hu Nutrition, University of Copenhagen, Denmark, ††Escuela Universitaria de Ciencias de la Salud, Universidad de Zaragoz Zaragoza, Spain, ‡‡Leeds General Infirmary, Leeds, UK, §§CHR Citadelle, University of Liege, Liege, Belgium, ¶¶Meyer Childr Hospital of Haifa, Ruth and Bruce Rappaport School of Medicine, Technion, Haifa, Israel, ||||Medical University of Warsaw, Pol ***University of Lille, Lille, France, and †††Erasmus MC/Sophia Children's Hospital, Rotterdam, The Netherlands*

ABSTRACT

This position paper on complementary feeding summarizes evidence for health effects of complementary foods. It focuses on healthy infants in Europe. After reviewing current knowledge and practices, we have formulated these conclusions: Exclusive or full breast-feeding for about 6 months is a desirable goal. Complementary feeding (ie, solid foods and liquids other than breast milk or infant formula and follow-on formula) should not be introduced before 17 weeks and not later than 26 weeks. There is no convincing scientific evidence that avoidance or delayed introduction of potentially allergenic foods, such as fish and eggs, reduces allergies, either in infants source of iron and should not be used as the main drink be 12 months, although small volumes may be added to co lementary foods. It is prudent to avoid both early (<4 mon and late (≥7 months) introduction of gluten, and to introd gluten gradually while the infant is still breast-fed, inasmuc this may reduce the risk of celiac disease, type 1 diabetes mell and wheat allergy. Infants and young children receiving a v tarian diet should receive a sufficient amount (~500 mL breast milk or formula and dairy products. Infants and yo children should not be fed a vegan diet. ***JPGN 46:99–110, 2***

Key Words: Complementary feeding—Solid foods—Beiko

Az új állásfoglalások a következő nyitott kérdésekre adnak választ

Allergia-kialakulás szempontjából magas kockázatú csecsemőknél:

- Allergénkerülés:
  - Várandósság alatt ?
  - Szoptatás alatt ?
- Szoptatás -meddig ?
- Speciális tápszerek kérdése- mi legyen?
  - Extenziven v. részlegesen hidrolizált? Szója?
- Hozzátáplálás optimális kezdete?
- ----------

TABLE I. Dietary prevention recommendations/comments from several professional organizations

	Group/publication			
Definitions/interventions	AAP 2008 Clinical Report	AAP 2000 recommendations	ESPACI/ESPGHAN 1999, ESPGHAN 2008 recommendations	SP-EAACI, 2004, 2008 recommendations
Risk category: "high risk"	Parent or sibling with documented allergic disease	Biparental or parent plus sibling history of allergy	Parent or sibling affected (1999)	Parent or sibling with documented allergic disease
Pregnancy avoidance	Lack of evidence	Possibly peanut		No special diet*
Breast-feed "exclusively" until	Evidence for 3-4 mo (waiting 4-6 mo tied to introducing solids*)	6 mo	4-6 mo*	At least 4 mo, prefer 6 mo*
Maternal lactation avoidance of allergens	Some evidence for reduced atopic dermatitis	Peanuts, tree nuts and "consider" egg, milk, fish, and "perhaps other foods"		No special diet*
Prevention formulas	Compared with whole cow's milk protein, evidence for certain extensive hydrolysates, partial hydrolysates, but not soy (see text)	"Hypoallergenic formula" (extensive hydrolysate, possibly partial hydrolysate); not soy.	Confirmed reduced allergenicity (1999)	Extensively hydrolyzed until 4 mo of age (2004); documented reduced allergenicity (2008)
Types of "solids" and complementary foods	Evidence to wait 4 (to 6) mo; lack of convincing evidence for avoiding specific allergenic foods	Solids held to 6 mo Dairy products, age 1 y Egg, age 2 y Peanuts, nuts, fish, age 3 y	Not before 17 wk and no later than 26 wk; no convincing evidence for delaying potentially allergenic foods such as fish, egg (2008)*	No evidence of diet effect after 4-6 mo

ESPACI, European Society for Pediatric Allergology and Clinical Immunology; *ESPGHAN,* European Society for Pediatric Gastroenterology, Hepatology and Nutrition; *SP-EAACI,* Section on Pediatrics, European Academy of Allergology and Clinical Immunology.
*Advice that is the same for those not "high risk."

VÁRANDÓS KISMAMÁK DIÉTÁJA

- Cochrane adatbázis, meta-analzis, (4 klinikai tanulmány)
- Diétás antigen kerülés várandósság alatt:
  - atopia csökkentő hatás nem igazolódott
  - **Kiegyensúlyozott anyai/magzati tápanyag-ellátást veszélyezteti,**
  - **pl. LC-PUFA-idegrendszer**
    - Kramer: Cochrane Database Syst Rev 2006;3:CD000133.

- Földimogyoró fogyasztás:
  - Nem bizonyonyított a szenzibilizáló hatás a gyermekeknél
    - Lack: N Engl J Med 2003;348:977-85.
  - (És az anyák nem is tartották be a diétát…)
    - Dean T: J Hum Nutr Diet 2007

- AAP report, a fentiek szintéziseként:
  - **Nincs bizonyíték anyai diéta megelőző szerepére a várandósság alatt**

Tápszerek a megelőzésre

- Részben v. extenziven hidrolizált?
  - Cochrane report:
    - Osborn DA: Cochrane Database Syst Rev 2006;4:CD003664
  - German Infant Nutritional Intervention Study, a randomized double-blind trial
    - von Berg A et al: J Allergy Clin Immunol 2003

- Szintézis: Committee reviews-

  Csökkentett allergéntartalommal (részben vagy extenziven hidrolizált):

  - Atopiás Dermatitis(AD) megelőzhető

  - (extenziven hidrolizált kazein formula kissé hatékonyabb lehet)
    - Greer FR, Pediatrics 2008
    - Host A: Pediatr Allergy Immunol 2008
    - EAACI 2008

  - AAP 2008:
    - Költség szempontok miatt nem tesz különbséget a hidrolizált formák között,
    - Szója alapút elvet,
    - Aminosav-alapú formulák megelőző szerepéről nincsenek megfelelő vizsgálatok

Szoptatás alatti diéta:

- Cochrane meta-analizis
  - **Kevés bizonyíték az atopiás dermatitis (AD) csökkenésére diétával**,
  - További vizsgálatok szükségesek
    - Kramer MS: Cochrane Database Syst Rev 2006;3:CD000133

- Muraro et al, review: Pediatr Allergy Immunol 2004
  - több tanulmány alapján, de nem strukturáltan:
- **speciális diéta szoptatás alatt szükségtelen**

- AAP, EAACI, ESPGHAN 2008, egységes álláspont:
- **Nem szükséges a diéta szoptatás alatt**.

Szilárd étel bevezetése

- Potenciálisan szenzibilizáló allergének késleltetett bevezetése:
  - **Nincs meggyőző bizonyíték** hatékonyságára!

    - Greer: Pediatrics 2008;
    - Host : Pediatr Allergy Immunol 2008
    - Filipiak: J Pediatr 2007
    - Zutavern: Pediatrics 2008

Mi előzhető meg kizárólagos szoptatással?

- Gyermekkori atopiás dermatitis(AD): - **megelőzhető** (konszenzus)

- Allergiás eredetű asztma:

  2001, Meta analizis:
  - **5 éves korig preventív hatás**
    - Gdalevich M: J Pediatr 2001

  2007: Tasmania Asthma Study:
  - **7 éves korig inkább preventiv hatás**
  - **14 éves koron túl már nem véd,**
  - **44 év fölött már magasabb asztma kockázat** (korai infekciók hiánya?)
    - Matheson MC: J Allergy Clin Immunol 2007

- Ételallergia (Tehéntej)
  Peer-reviewed observational/interventional studies, Muraro, Ped.Allerg. Immunol 2004:
  - **Min. 4 hónapos exkluziv szoptatás: 18 hónapos korig csökkenti a tehéntej-fehérje allergia** előfordulását
  - Cochrane review: nincs védő hatás (de csak 1 tanulmány vak provokációval)

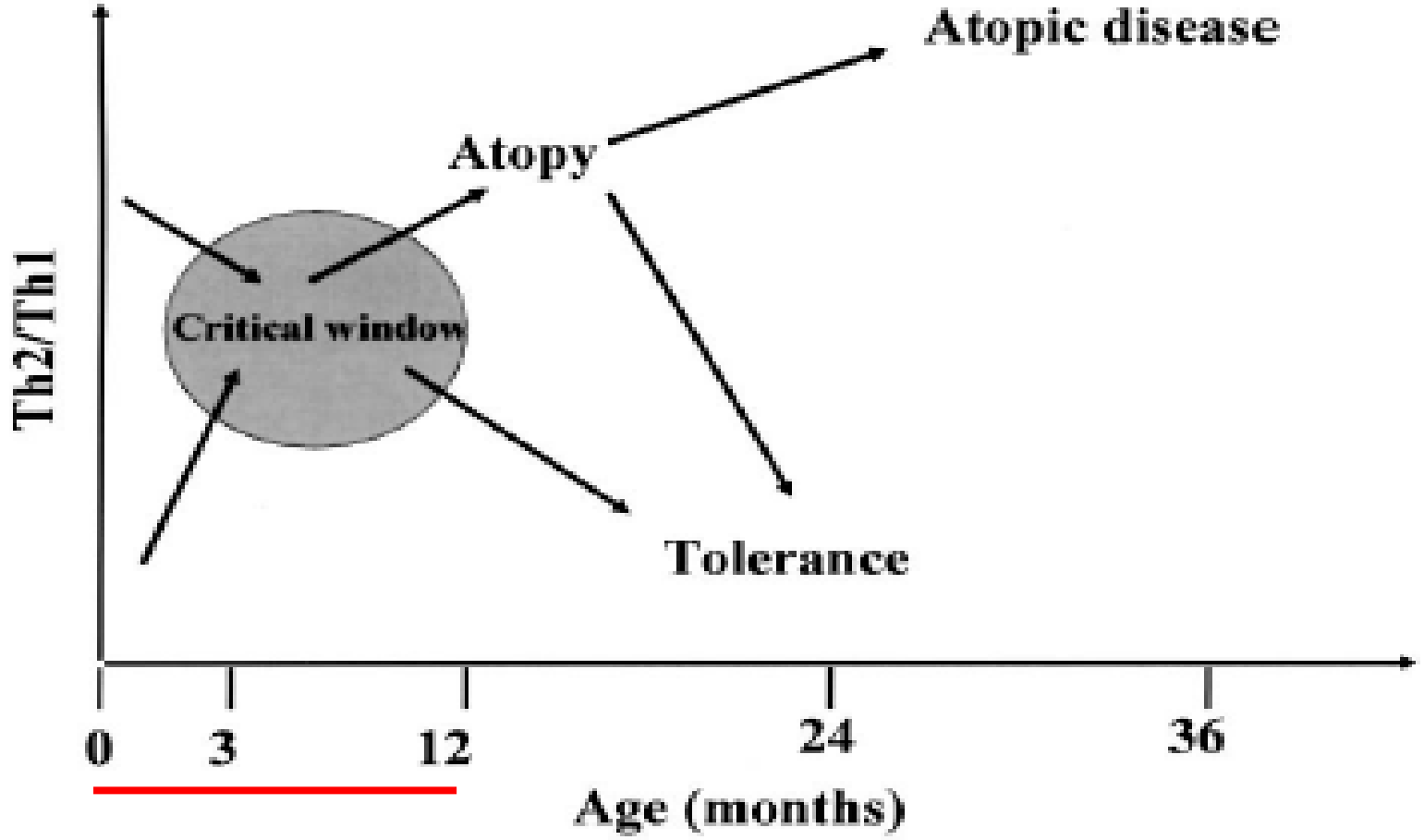
- **AAP 2008: Exkluziv szoptatás 4 hónapig: első 2 életévben csökkenti az ételallergia kumulativ incidenciáját**

Lambaréné, Gabon,
Schistosoma gyakori, allergia ismeretlen

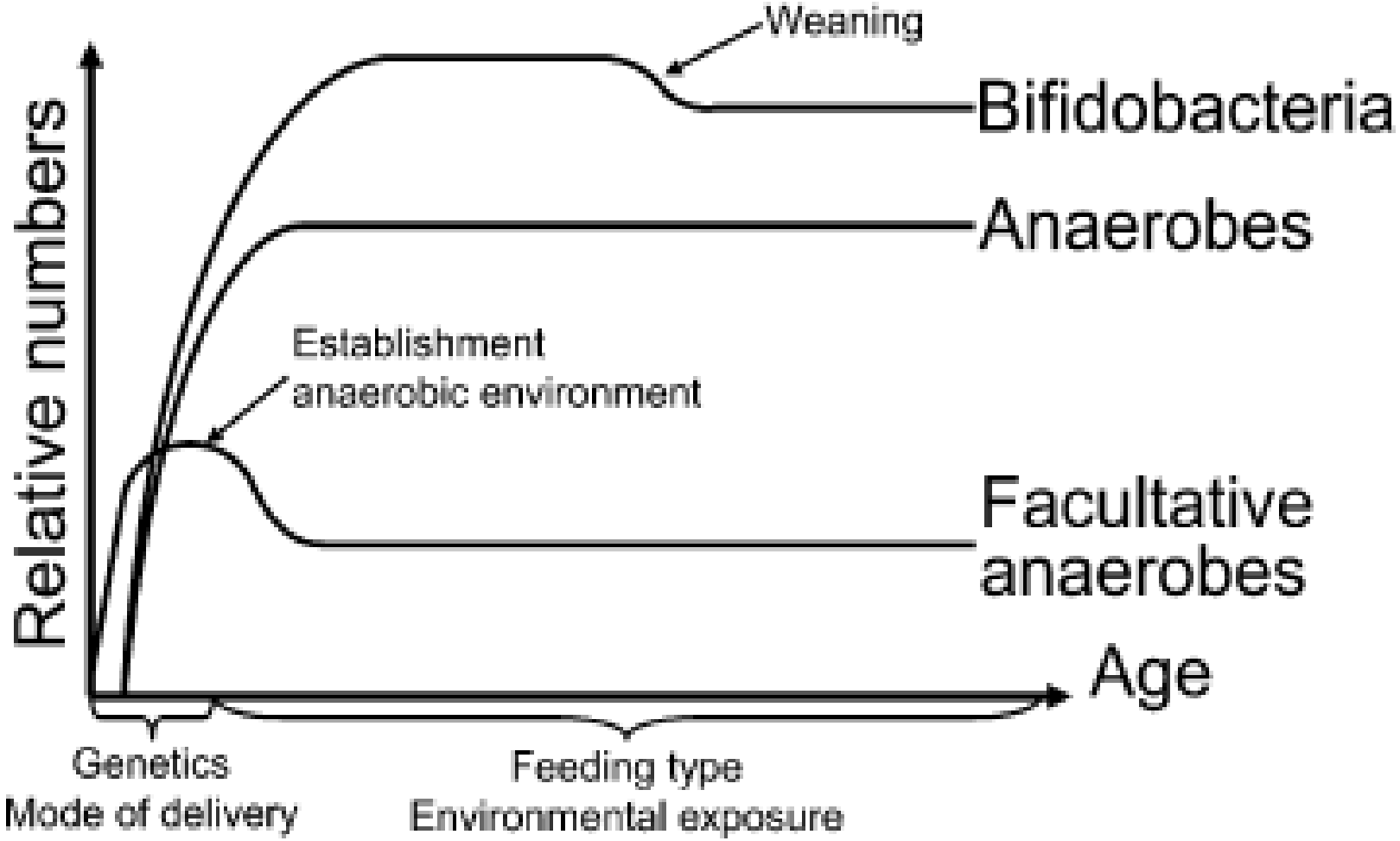
Schubert C, *Nature Medicine* **10**, 1271 - 1272 (2004)

- 

Az immunválasz kialakulása egészséges és atopiás gyermekekben (Rautava, J. Ped. Gastroent Nutr, 2004)



Ezzel egyidőben: A bélflóra kialakulásának menete: (Rautava, J. Ped. Gastroenterol Nutr, 2004)



Újszülött/csecsemőkori bélflóra

Egészséges gyermekekben

- Lactobacillusok aránya elhanyagolható
- Döntő hányad-Csecsemőkori bifidusok
  - Bifidobacterium breve,
  - Bifidobacterium infantis
  - Bifidobacterium longum

Allergiás kismamák csecsemőiben inkább:

  - Bifidobacterium adolescentis –

- B. adolescentis: gyakoribb allergiás csecsemőknél
  - Isolauri EJ Clin Gastroenterol 2008

Bélflóra és az immunválasz – Epidemiológiai vizsgálatok

- Svéd-Észt felmérés (csecsemők) :
  - Atopiás csecsemők: coliform-prevalencia
  - Egészséges kontrollok: bifidobaktérium prevalencia
    - (Bjorksten, JACI, 2001)
- Finnország:
  - Atopiás csecsemők:
    - több clostridium, kevesebb bifidobacterium az első 3 élethét során
    - A bifidobacterium prevalencia alacsonyabb az első életévben az egészségesekhez képest
      - (Kalliomaki, JACI, 2001,)

Farmercsaládok **gyermekei**: Csökkent asthma/atopia kockázat

Von Ehrenstein, O. S., (2000) Reduced risk of hay fever and asthma among children of farmers. *Clin. Exp. Allergy* **30,** 187–193.

Riedler, J., (2001)Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. *Lancet* **358,** 1129–1133.

Braun-Fahrlander, (2002) Environmental exposure to endotoxin and its relation to asthma in school-age children. *N. Engl. J. Med.* **347,** 869–877.

Védő faktor, pl: ”Farming lifestyle”

- 

Probiotikumok: Gyermekkori atopiás dermatitis prevencióban lehet szerep, terápiában nem igazolt!

Meta-analysis of clinical trials of probiotics for prevention and treatment of pediatric atopic dermatitis

Joohee Lee, AB,[b] David Seto, BA,[b] and Leonard Bielory, MD[a] *Newark, NJ*

Background: Prenatal and postnatal probiotic supplementation for prevention and treatment of pediatric atopic dermatitis (PAD) has been studied in clinical trials, but results have been mixed and hindered by heterogeneity of study design.
Objectives: To summarize and interpret quantitatively clinical trial findings on the efficacy of probiotics for PAD and to define key trial features correlating with high methodologic quality.
Methods: PubMed and Cochrane database searches yielded 21 trials (n = 1898; age 0-13 y) published between February 1997 and May 2007 for review and quality assessment. Ten double-blind randomized controlled clinical trials were meta-analyzed by using RevMan. Data from the 6 prevention studies (n = 1581) and 4 treatment trials (n = 299) were pooled by using fixed-effects and random-effects models of relative risk ratios and of weighted mean difference, respectively.
Results: Prevention corresponded with summary effect sizes of 0.69 (0.57, 0.83) and 0.66 (0.49, 0.89), respectively, supporting probiotics' PAD prevention potential, which decreased further to 0.61 after exclusion of the 1 trial of postnatal-only probiotics. The clinical significance of the treatment trial findings of intergroup Scoring Atopic Dermatitis (quantification of PAD severity) score reduction by –6.64 points (–9.78, –3.49) and –8.56 (–18.39, 1.28), and intragroup change of –1.06 (–3.86, 1.73) and –1.37 (–4.81, 2.07), is questionable.
Conclusion: Current evidence is more convincing for probiotics' efficacy in prevention than treatment of PAD.
(J Allergy Clin Immunol 2008;121:116-21.)

Abbreviations used
AD: Atopic dermatitis
CR: Clinical Relevance
ES: Effect size
FE: Fixed-effects
LGG: *Lactobacillus rhamnosus* GG
MQ: Methodological Quality
PAD: Pediatric atopic dermatitis
RE: Random-effects
RR: Risk ratio
SCORAD: Scoring Atopic Dermatitis
WMD: Weighted mean difference

clinical trials, but results have been mixed. Assessing probiotics' clinical efficacy in preventing or treating PAD is hindered by subtle but potentially significant heterogeneity of protocols, variety of studied strains, and small sample sizes.

Numerous systematic reviews of probiotics for PAD have been published.[2-5] Most of these publications have concluded that more work has to be done in this area before any clinical recommendations can be made. Our meta-analysis strives to take an additional analytic step beyond the qualitative assessments of systematic reviews. Although the various permutations of environment, host, probiotic strain, disease, and study design are obstacles for a robust quantitative synthesis, it is the premise of

Kiterjesztett higiéné hipotézis- Reguláló T sejtek szerepe az immunrendszer érésében

Rautava, JACI, 2005

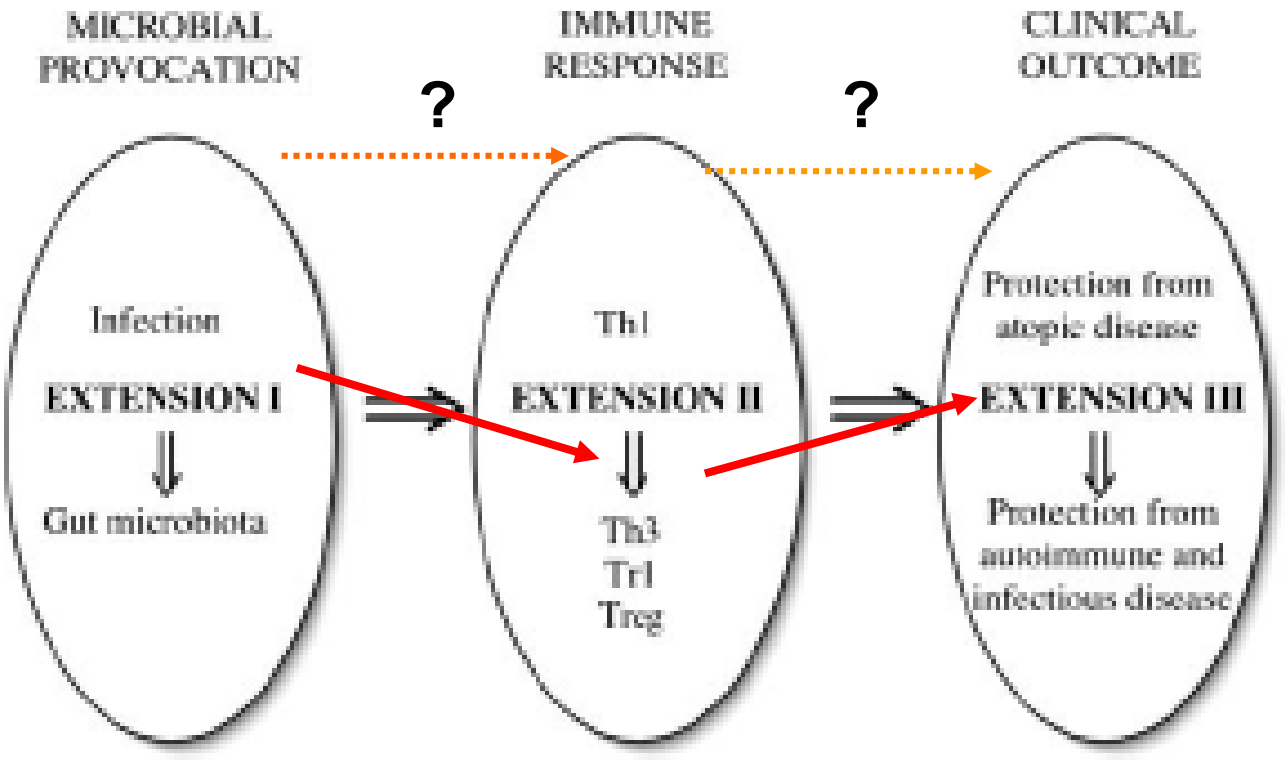


FIG 1. The extended hygiene hypothesis.

Konklúziók, atopia megelőzés csecsemő-és kisdedkorban I.

„Risk baby” (-családi pozitiv anamnézis)

- ‘‘Allergénkerülés várandósság ill. szoptatás alatt-
  - Várandósság alatt káros is lehet **(hiányállapotok!)**
  - szerepe a megelőzésben nem bizonyítható !
- Szoptatás (Kizárólagos/teljes) optimális időtartama:
  - 4-6 hónapig MINDEN CSECSEMŐNEK! (nem csak „high risk” bébiknek
- Speciális tápszerek: (Ha nincs elegendő anyatej)
  - Extenziven v. részlegesen hidrolizált is javasolható-
  - szója alapú nem javasolt
- Hozzátáplálás: Szilárd ételek ‘‘solids’’:
  - ESPGHAN 2008- 17,hét előtt korai, 26. hét után már túl késő a bevezetés;
  - Potenciális allergizáló ételek (pl. hal, tojás):
    - Evidencia káros hatásukra: Nincsen!
    - (ACAAI, Amer. Acad. Ped, EAACI 2007-2008)
  - Viszont pl. hal: LCPUFA **forrás- idegrendszeri fejlődés**!

Konklúziók, atopia megelőzés csecsemő -és kisdedkorban, II.

- Életmód, higiéné: Kiterjesztett higiéné hipotézis
- Anyatej: Bifidogén faktor(ok)
- Egyes Probiotikumok (pl. **csecsemőkori** bifidobacteriumok):

  - gyermekkori atopiás dermatitis ***megelőzésében*** szerepükre több –evidencia szintű- bizonyíték-
    - Egyéb allergiák, autoimmun betegségek megelőzésében inkább közvetett bizonyítékok (anyatej)
    - Vlsz. Reguláló T sejtekre hatnak

Probiotikumok ***terápiás szerepe*** egyelőre kérdéses, evidencia szinten nem bizonyított

Közös konklúzió: További hosszú távú, követéses vizsgálatok szükségesek!

Köszönöm a figyelmet !