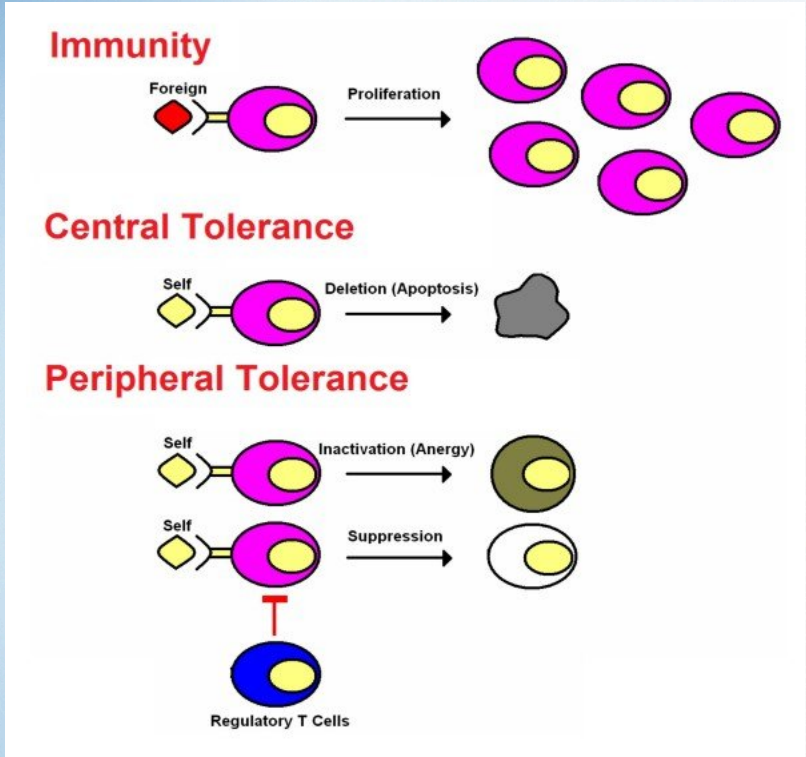
BESİN ALERJİSİNDE PÜF NOKTALARI VE PİRİNÇ PROTEİNİ

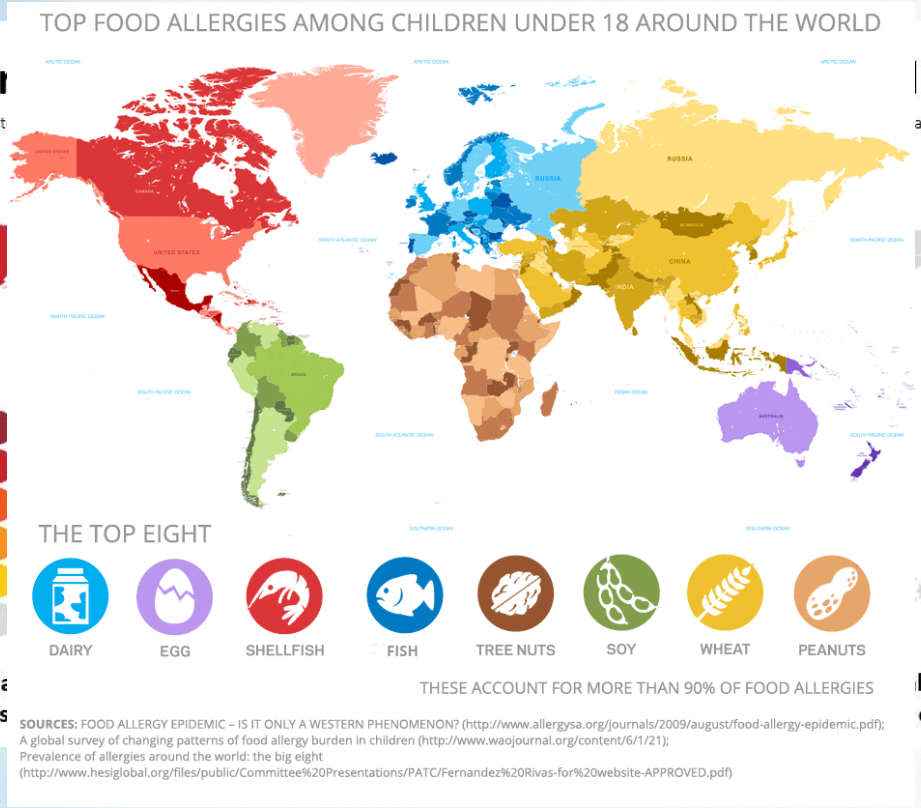
Dr. Funda ÇETİN


Immunity
Foreign
Proliferation
Central Tolerance
Self
Deletion (Apoptosis)
Peripheral Tolerance
Self
Inactivation (Anergy)
Self
Suppression
Regulatory T Cells


2387.09
CALCULATE
N
W
E
S

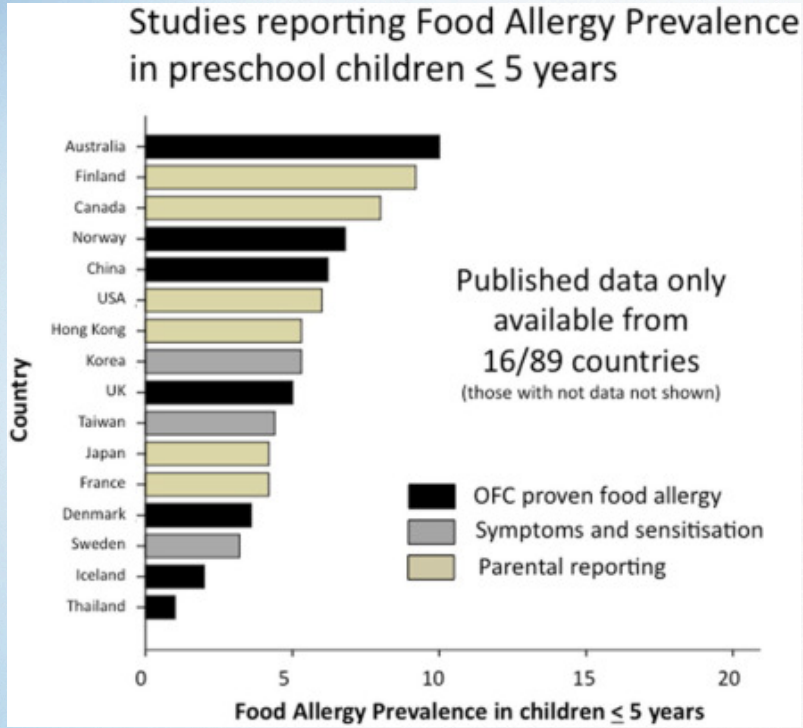
Dünyada en yaygın besin alerjisi→İSPA

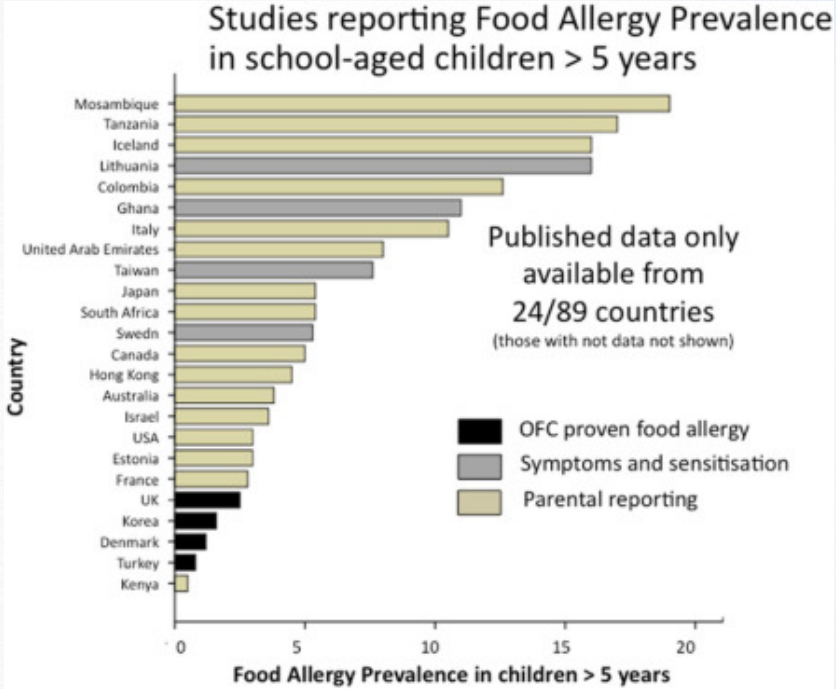
BESİN ALERJİSİ→NEDEN



- Sıklık →Artmaktadır!
  - Coğrafya
  - Beslenme
- İSPA→ %0.54-4.9

BESİN ALERJİSİ→NEDEN



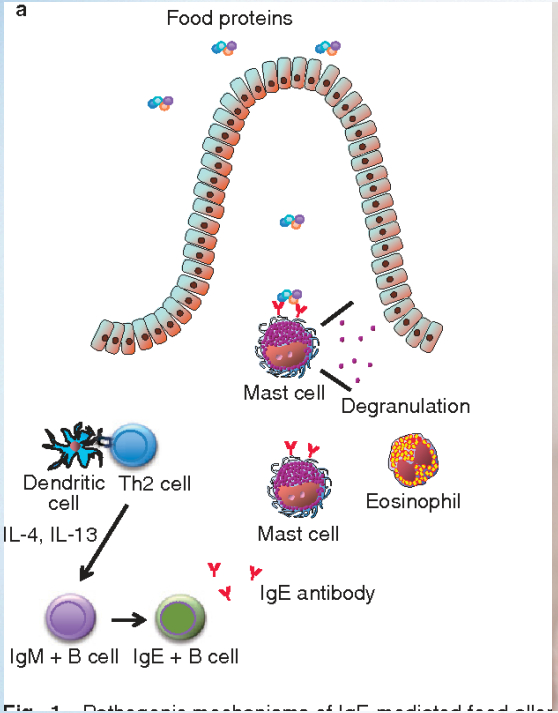


Presott SI, WAO J 2013

BESİN ALERJİLERİNDE PÜF NOKTALARI

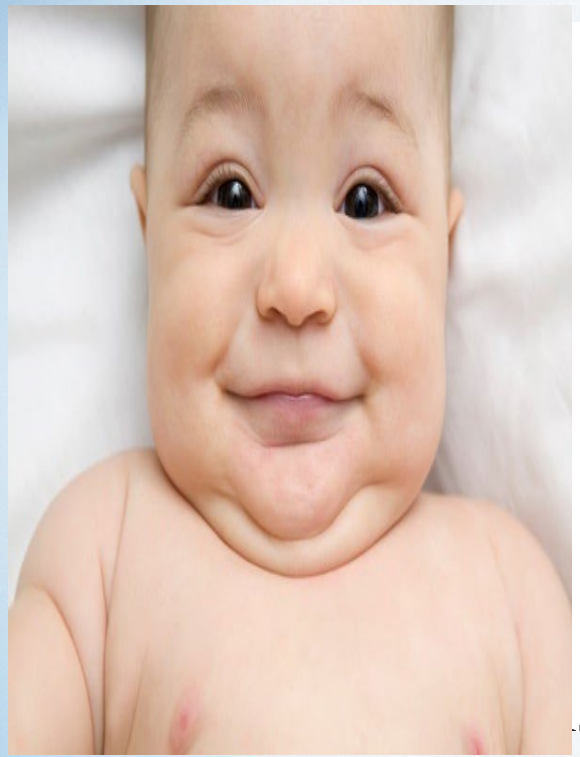
- Sıklığı giderek artmakta!

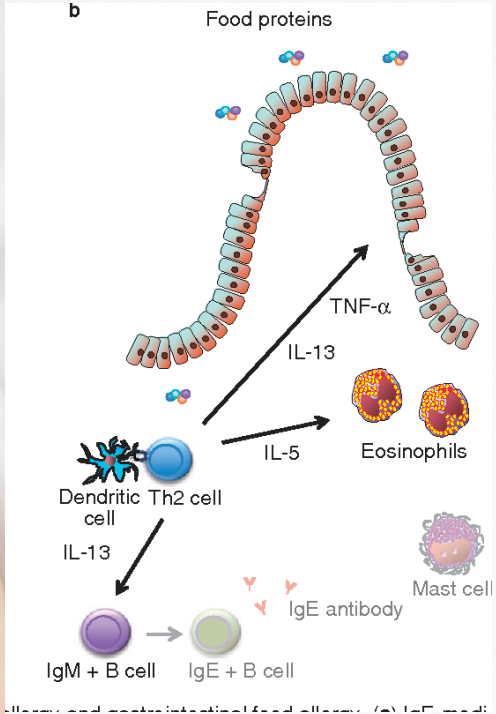
Ig E Aracılı İSPA → Tanısı kolay !



- İS →tüketiminden hemen sonra, hızlı
- Hedef organlar→
  - Hava yolu
  - Cilt
  - GİS
  - Sistemik bulgular
- Anaflaksi

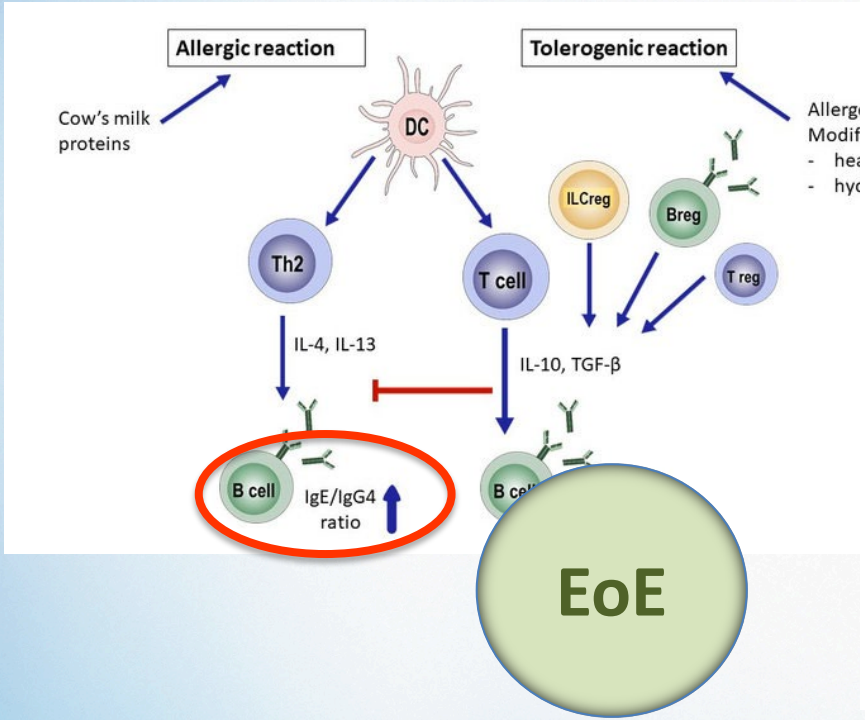
Non-Ig E Aracılı İSPA → Tanısı ZOR !

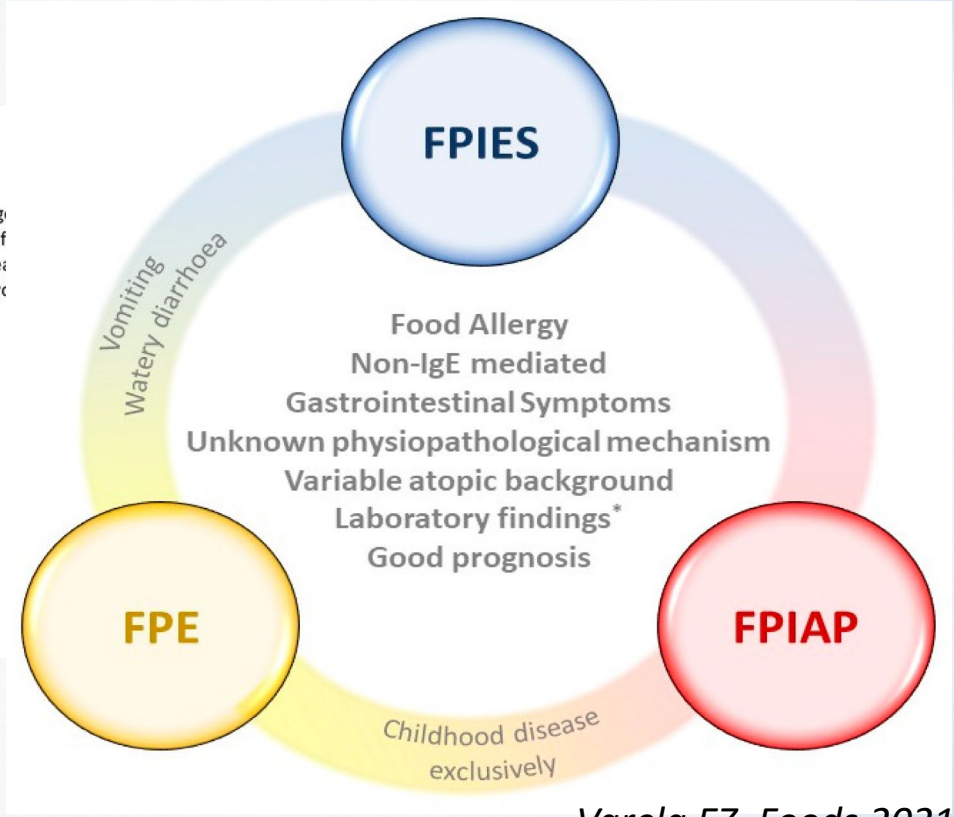




- Özgün semptom Φ
- Sistemik bulgular→
  - Kusma-regürjitasyon
  - İshal
  - Beslenme zorluğu
  - Rektal kanama
  - Ağlama krizleri
  - Büyüme geriliği
  - Uyku bozuklukları

Non-Ig E Aracılı İSPA

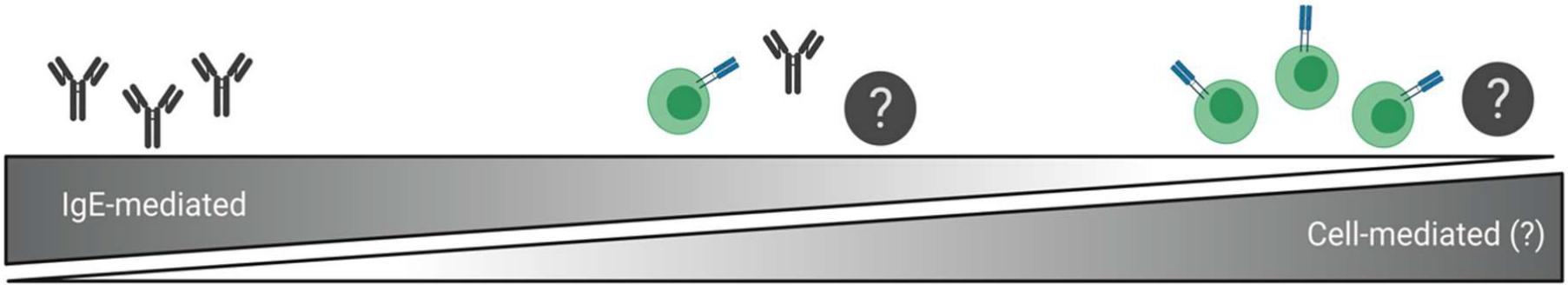




Varela EZ, Foods 2021

Gastrointestinal food allergies

IgE-mediated	Mixed IgE/non-IgE-mediated	Non-IgE-mediated
Immediate hypersensitivity/anaphylaxis OAS FDEIAn	Eosinophilic esophagitis Eosinophilic gastritis Eosinophilic colitis	FPIAP FPE, Celiac disease FPIES



BESİN ALERJİLERİNDE PÜF NOKTALARI

- Sıklığı giderek artmakta!
- Spesifik semptomu yok. Non-IgE aracılı ve mix tiplerinde klinik tiplerin fizyopatolojisi net değil.

İSPA → TANI

- **Ig E aracılı İSPA→**
  - Daha kolay
  - İS tüketimi ve semptom gelişme aralığı kısa
  - Gıda semptom ilişkisi kurmak kolay
- Laboratuvar→
  - Spesifik IgE
  - Deri prick test→Donanımlı ortam

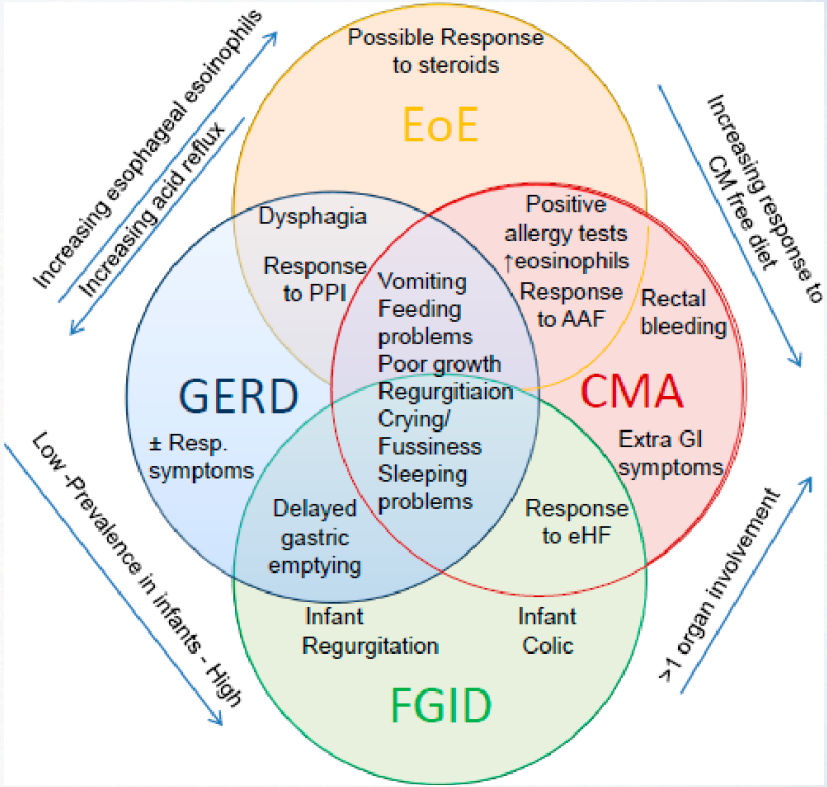
İSPA → TANI

- **Non-Ig E/ Mix aracılı İSPA→**
  - ZOR

- **FPİES→**
  - Klasik semptom ??!!
  - Diğer sebeplerin dışlanması
  - Olası gıda/İS eliminasyonu ile düzelme
- Tanı Doğrulaması→
  - Öykü şüpheli olduğu durumlarda
  - Oral Gıda challenge (OFC)
  - Yarar/Zarar ilişkisi ↑

İSPA → TANI

- **Ağlama/ Motilite bzk.→**
  - FGİDs ayırmak çok zor
  - Diğer sebeplerin dışlanması
  - Alerji odaklı öykü ve fizik bakı
  - Olası gıda/İS eliminasyonu ile düzelme
- Tanı Doğrulaması→
  - Gerekli !
  - Oral Gıda challenge (OFC)



nutrients

MDPI

Review

Cows' Milk Allergy-Associated Constipation: When to Look for It? A Narrative Review

Frances Connor [1,2], Silvia Salvatore [3], Enza D'Auria [4], Maria Elisabetta Baldassarre [5], Miriam Acunzo [4], Gaia Di Bella [3], Ilaria Farella [6], Simona Sestito [7] and Licia Pensabene [7,*]

1 Department of Gastroenterology, Hepatology and Liver Transplant, Queensland Children's Hospital, Brisbane 4101, Australia; adslbds0@tpg.com.au
2 Mayne Academy of Pediatrics, Faculty of Medicine, University of Queensland, Brisbane 4101, Australia
3 Department of Pediatrics, Ospedale "F. Del Ponte", University of Insubria, 21100 Varese, Italy; silvia.salvatore@uninsubria.it (S.S.); dibellagaia01@gmail.com (G.D.B.)
4 Department of Pediatrics, Vittore Buzzi Children's Hospital, University of Milan, 20154 Milan, Italy; enza.dauria@unimi.it (E.D.); miriam.acunzo@unimi.it (M.A.)
5 Department of Biomedical Science and Human Oncology, Neonatology and Neonatal Intensive Care Unit, "Aldo Moro" University of Bari, 70124 Bari, Italy; mariaelisabetta.baldassarre@uniba.it
6 Department of Biomedical Science and Human Oncology, Clinica Medica "A. Murri", "Aldo Moro" University of Bari, 70124 Bari, Italy; ilafarella@yahoo.com
7 Department of Medical and Surgical Sciences, Pediatric Unit, University "Magna Graecia" of Catanzaro, 88100 Catanzaro, Italy; sestitosimona@unicz.it
* Correspondence: pensabene@unicz.it; Tel.: +39-0-961883007; Fax: +39-0-961883489

Abstract: Constipation is a very common disorder, mostly functional in nature, that may persist for years in up to 35–52% of children. Food allergy prevalence, severity and persistence are increasing over time, and cows' milk protein is the commonest food allergen recognised to affect gastrointestinal motility in children. There is mounting evidence of the role of cows' milk (CM) allergy (CMA) in children with constipation. With this narrative review, we aim to provide clinicians with an updated and critical overview of food allergy-associated constipation. We searched Embase, Medline and the Cochrane Library, using keywords related to the topic. Only reviews and studies including children aged 0–17 years that were published in English were considered. Constipation has been reported in 4.6% of infants with CMA; the prevalence of food allergy underlying chronic constipation in children resistant to conventional treatment and presenting to tertiary clinics ranges between 28% and 78%. The identification of predisposing risk factors and of a specific phenotype of food allergy-induced constipation remains elusive. No allergic tests, radiological or motility investigations achieve sufficient sensitivity and specificity to screen children for CMA-related constipation. A 4-week cows' milk protein (CMP) elimination diet may be considered for children with chronic constipation resistant to conventional treatment and who lack alarm sign/symptoms of organic diseases. In subjects with ameliorated symptoms on CMP elimination, the diagnosis of CMA should be confirmed by a food challenge to avoid an unnecessary protracted diet.

Citation: Connor, F.; Salvatore, S.; D'Auria, E.; Baldassarre, M.E.; Acunzo, M.; Di Bella, G.; Farella, I.; Sestito, S.; Pensabene, L. Cows' Milk Allergy-Associated Constipation: When to Look for It? A Narrative Review. *Nutrients* **2022**, *14*, 1317. https://doi.org/10.3390/nu14061317

Academic Editors: Jon A. Vanderhoof and Margarida Castell Escuer

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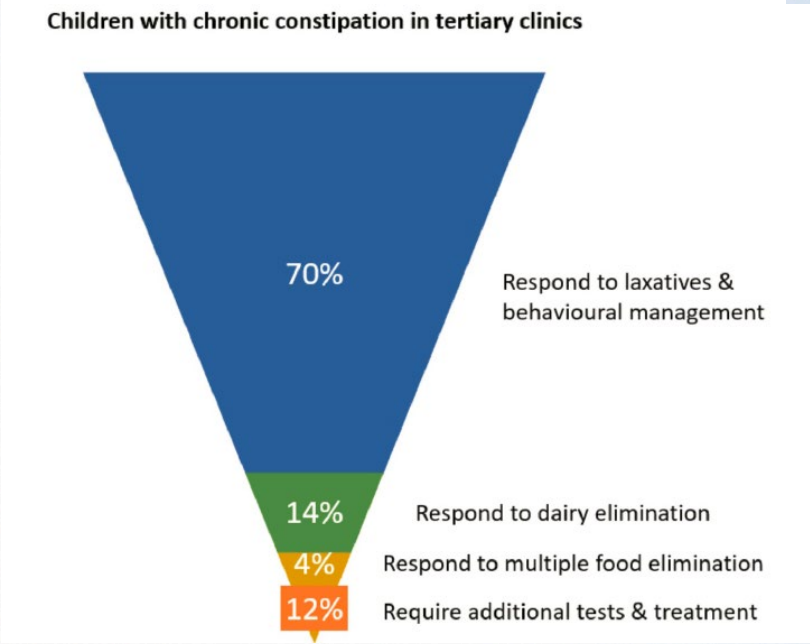


Nutrients, 2022

İSPA → TANI

- **Ağlama/ Motilite bzk.→**
  - FGİDs ayırmak çok zor
  - Diğer sebeplerin dışlanması
  - Alerji odaklı öykü ve fizik bakı
  - Olası gıda/İS eliminasyonu ile düzelme
- Tanı Doğrulaması→
  - Gerekli !
  - Oral Gıda challenge (OFC)

- **Tanı Doğrulama→**
  - Eliminasyon
    - IgE aracılı→ 2-4 hafta
    - Non-IgE/mix→ >6 hafta
  - OFC ile yakınmaların geri dönmesi
  - EoE→
    - Üst GİS endoskopi
    - Biyopsi

İSPA → TANI

- **Non-Ig E/ Mix aracılı İSPA→**
  - ZOR
- Laboratuvar
  - Fekal kalprotektin
  - Gıda sp IgG/G4
  - A1AT
  - Beta-defensin
  - TNF-ά
  - Fekal IgA
  - Eo-DN….
  - **YAMA TESTİ**

Fekal ve biyolojik markerlar tanıda önerilmemekte!

YT→tanıda önerilmemekte ancak çalışmalar sürdürülmeli

Calvani M, Nutrients, 2021

CoMiSS®: Cow's Milk-related Symptom Score

Last name: ..... First name: ..... Age: ..... Date: .....

PURPOSE

The CoMiSS® is a simple, fast and easy-to-use awareness tool for cow's milk-related symptoms. It increases awareness of the most common symptoms of cow's milk protein allergy (CMPA) that in turn can aid an earlier diagnosis. CoMiSS® can also be used to evaluate and quantify the evolution of symptoms during a therapeutic intervention.

INSTRUCTIONS

If there is a suspicion of cow's milk-related symptoms, rate the observed/reported symptoms by choosing the most appropriate score for each type of symptom. Once completed, add the scores together and put the total in the box at the bottom of the scoring form.

SYMPTOM	SCORE		
Crying*	0	≤ 1 hour/day	SCORE
	1	1 to 1.5 hours/day	
	2	1.5 to 2 hours/day	
	3	2 to 3 hours/day	
	4	3 to 4 hours/day	
	5	4 to 5 hours/day	
	6	≥ 5 hours/day	
Regurgitation	0	0 to 2 episodes/day	SCORE
	1	≥ 3 to ≤ 5 of small volume	
	2	> 5 episodes of >1 coffee spoon	
	3	> 5 episodes of ± half of the feeds in <half of the feeds	
	4	Continuous regurgitations of small volumes >30 min after each feed	
	5	Regurgitation of half to complete volume of a feed in at least half of the feeds	
	6	Regurgitation of the complete feed after each feeding	
Stools (Bristol scale)	4	Type 1 and 2 (hard stools)	SCORE
	0	Type 3 and 4 (normal stools)	
	2	Type 5 (soft stool)	
	4	Type 6 (liquid stool, if unrelated to infection)	
	6	Type 7 (watery stools)	
Skin symptoms	0 to 6	Atopic eczema — HEAD-NECK-TRUNK / ARMS-HANDS-LEGS-FEET	SCORE
		Absent 0 / 0	
		Mild 1 / 1	
		Moderate 2 / 2	
		Severe 3 / 3	
	0 or 6	Urticaria — NO 0 / YES 6	
Respiratory symptoms	0	No respiratory symptoms	SCORE
	1	Slight symptoms	
	2	Mild symptoms	
	3	Severe symptoms	

TOTAL SCORE

* Crying only considered if the child has been crying for 1 week or more, assessed by the parents, without any other obvious cause.

READING THE RESULT

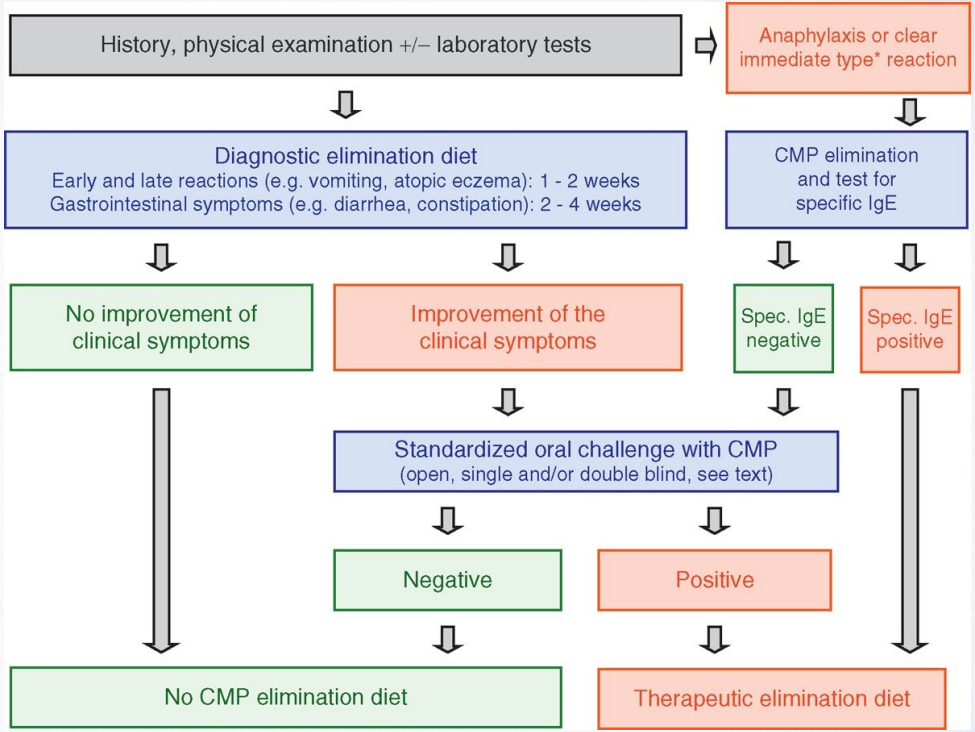
The scoring ranges from 0 to 33. Each symptom has a maximal score of 6, except respiratory symptoms where the maximal score is 3.
If final score ≥ 12, the symptoms are likely cow's milk related. This could potentially be CMPA.
If final score < 12, the symptoms are less likely related to cow's milk. Look for other causes.

CMPA diagnosis can only be confirmed by an elimination diet followed by an oral food challenge.

Vandenplas, Y., Dupont, C., Eigenmann, P., Host, A., Kuitunen, M., Ribes-Koninck, C., Shah, N., Shamir, R., Staiano, A., Szajewska, H. and Von Berg, A. (2015), A workshop report on the development of the Cow's Milk-related Symptom Score awareness tool for young children. Acta Paediatrica. doi: 10.1111/apa.12902

Vandenplas Y, Acta Pediatr, 2015

İSPA → TANI



Koletzko Z, JPGN, 2012

BESİN ALERJİLERİNDE PÜF NOKTALARI

- Sıklığı giderek artmakta!
- Spesifik semptomu yok. Non-IgE aracılı ve mix tiplerinde klinik tiplerin fizyopatolojisi net değil.
- Tanı halen eliminasyon diyeti ve OFC.

İSPA → ELİMİNASYON DİYETİ

- Görülme yaşı → Büyümenin en hızlı olduğu dönem
- İS eliminasyonu→ Fe, Ca, D vit, B12 alımı↓
- İnflamatuar süreç
  - Artmış sitokin yapımı
  - Artmış intestinal permeabilite
  - Artmış metabolik hız
  - GH direnci
  - Azalamış iştah

- **Sonuçları→**
  - **Malnutrisyon**
  - **Vitamin-mineral eksikliği**
  - **Beslenme sorunları**
  - **Atopik komorbidite**
  - **Ailede hayat kalitesi↓**

Vandenplas Y, JAA, 2021

BESİN ALERJİLERİNDE PÜF NOKTALARI

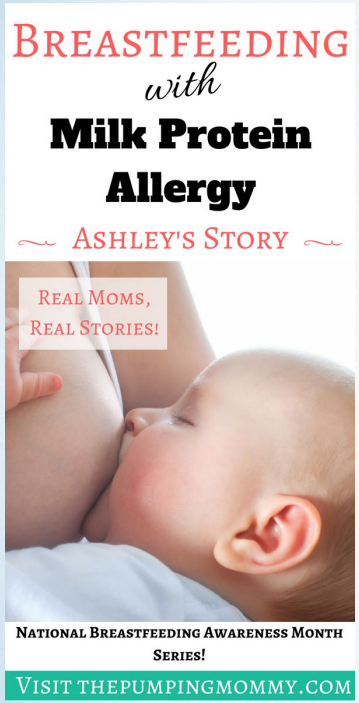
- Sıklığı giderek artmakta!
- Spesifik semptomu yok. Non-IgE aracılı ve mix tiplerinde klinik tiplerin fizyopatolojisi net değil.
- Tanı halen eliminasyon diyeti ve OFC.
- **Yeterli beslenme ve düzenli takip kritik öneme sahiptir!**

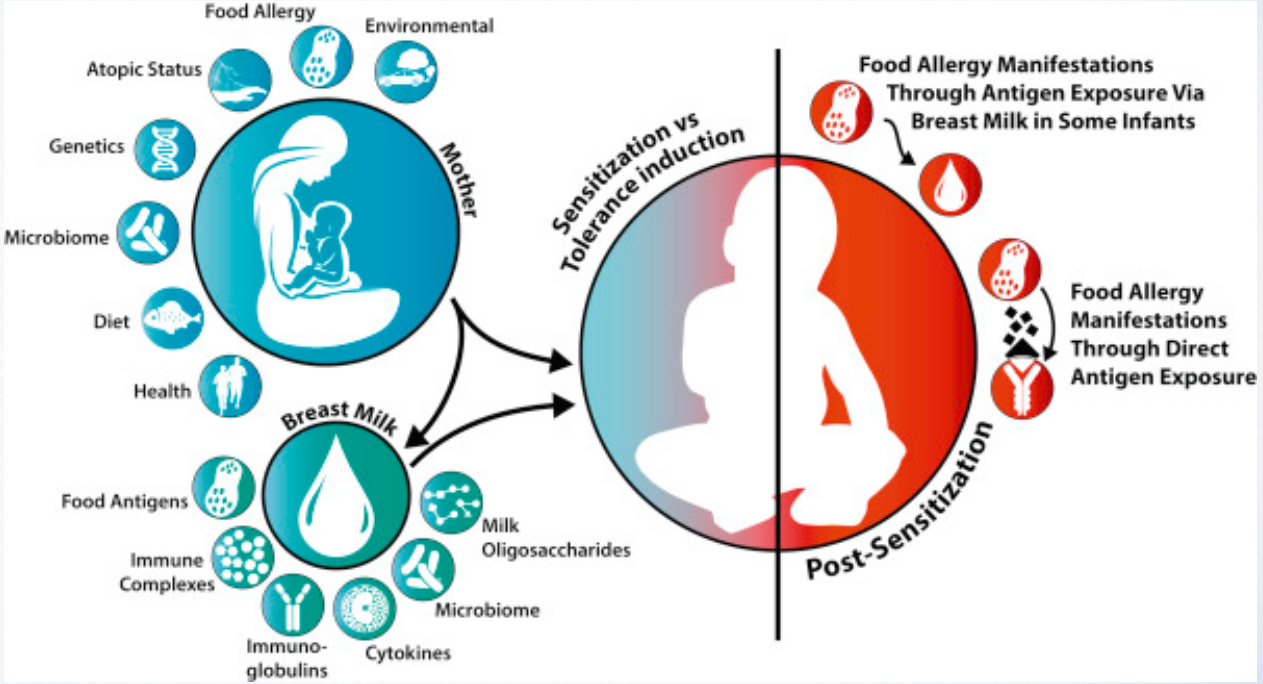
İSPA → BESLENME

1. Semptomların önlenmesi
   - İnek sütü alerjenlerinin eliminasyonu
   - Uygun büyüme ve gelişmeyi sağlayacak beslenme modeli

2. Oral toleransın sağlanması
   - İntestinal epitelin restorasyonu
   - İmmün sistemin restorasyonu
   - Sağlıklı mikrobiyota

İSPA yönetiminde tüm kılavuzlar ANNE SÜTÜNÜ ilk sırada önermektedir!





Jarvinen KM, Annals AAI, 2019

İSPA → BESLENME

Cow's milk allergy: towards an update of DRACMA guidelines

Table 2 Choosing the appropriate substitute formula in different presentations (original source: DRACMA guidelines [1])

Clinical presentation	1st choice	2nd choice
Anaphylaxis	AAF[a]	eHF[e, d]
Immediate gastrointestinal allergy	eHF[d, b]	AAF[f]/SF[g]
Food protein-induced enterocolitis syndrome (CMAES)	AAF	eHF[c]
Asthma and rhinitis	eHF[d, b]	AAF[f]/SF[g]
Acute urticaria or angioedema	eHF[d, b]	AAF[f]/SF[g]
Atopic dermatitis	eHF[d, b]	AAF[f]/SF[g]
Gastroesophageal reflux disease (GERD)	eHF[b]	AAF
Allergic eosinophilic oesophagitis	AAF	
Cow's milk protein-induced enteropathy	eHF[d, b]	AAF
Constipation	eHF[b]	AAF
Severe irritability (colic)	eHF[b]	AAF
CM protein-induced gastroenteritis and proctocolitis	eHF[b]	AAF
Milk-induced chronic pulmonary disease (Heiner's syndrome)[h]	AAF[f]	SF

WAOJ, 2016

Country/ region	Issuing scientific society	Guideline identification	DRACMA based?	Main characteristics	Ref.
Europe	ESPGHAN	ESPGHAN CMPA guidelines	No	Focus on non-IgE CMA	39
Europe	European Academy of Allergy and Clinical Immunology (EAACI)	EAACI food allergy guidelines	No	Not limited to CMA	40
United Kingdom	National Institute for Health and Care Excellence (NICE)	MAP (Milk Allergy in Primary Care)	No	Focus on non IgE-CMA in primary care	44
United Kingdom	NICE-derived	i-MAP (international MAP)	Partly	Focus on non IgE CMA in primary care	45
Italy	Italian Society of Pediatric Allergy	DRACMA	Yes	Italian translation	43
Turkey	Turkish Society of Pediatrics	Turkish Consensus	Partly	Focus on primary care	51
South America	World Allergy Organization (WAO)	DRACMA	Yes	Spanish translation	57

Table 3. Recommended therapeutic options according to different guidelines for different symptoms and signs of cow's milk allergy.

	Australia [29]		Dracma [10]		Espghan [3]	
	1st choice	2nd choice	1st choice	2nd choice	1st choice	2nd choice
GI syndromes	eHF soy (if >6 months)	AAF eHF	eHF	AAF	eHF	AAF
proctocolitis	eHF	AAF			eHF	AAF
Eos Eso	AAF		AAF		AAF	
Immediate FA	eHF soy (if >6 months)	AAF eHF	eHF	AAF/Soy	eHF	AAF
FPIES	eHF	AAF	eHF	AAF	eHF	AAF
Atopic eczema	eHF soy	AAF eHF	eHF	AAF/Soy	eHF	AAF
urticaria			eHF	AAF/Soy	eHF	AAF
Constipation			eHF	AAF		
Heiner syndrome			AAF	eHF		

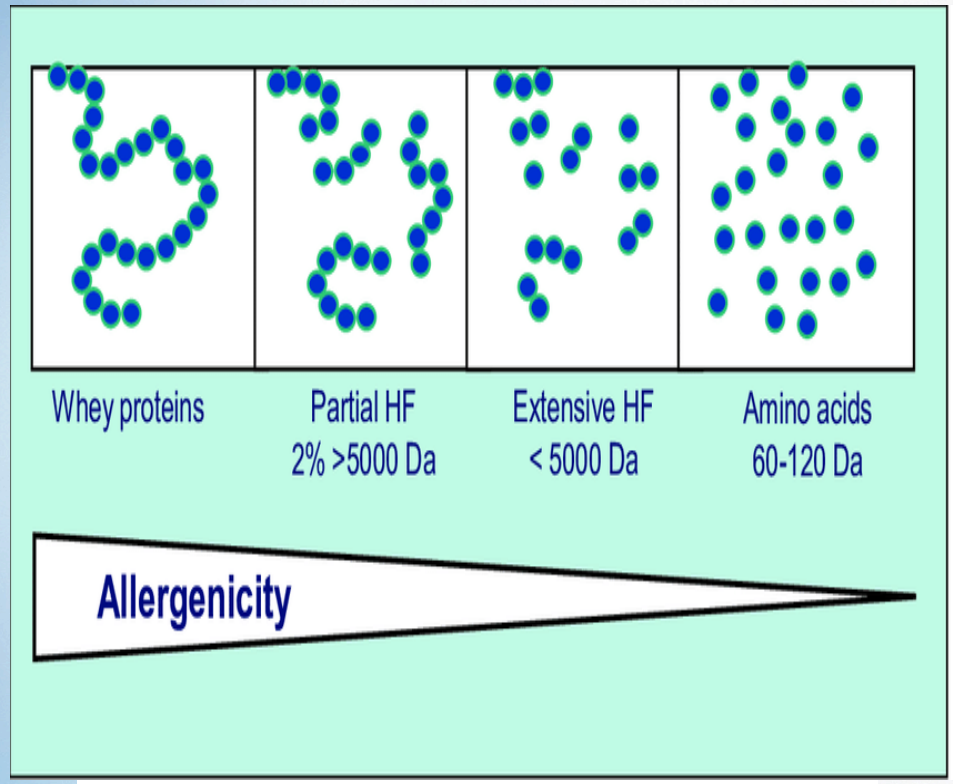
Fiocchi et al. World Allergy Organization Journal (2022) 15:100609
http://doi.org/10.1016/j.waojou.2021.100609

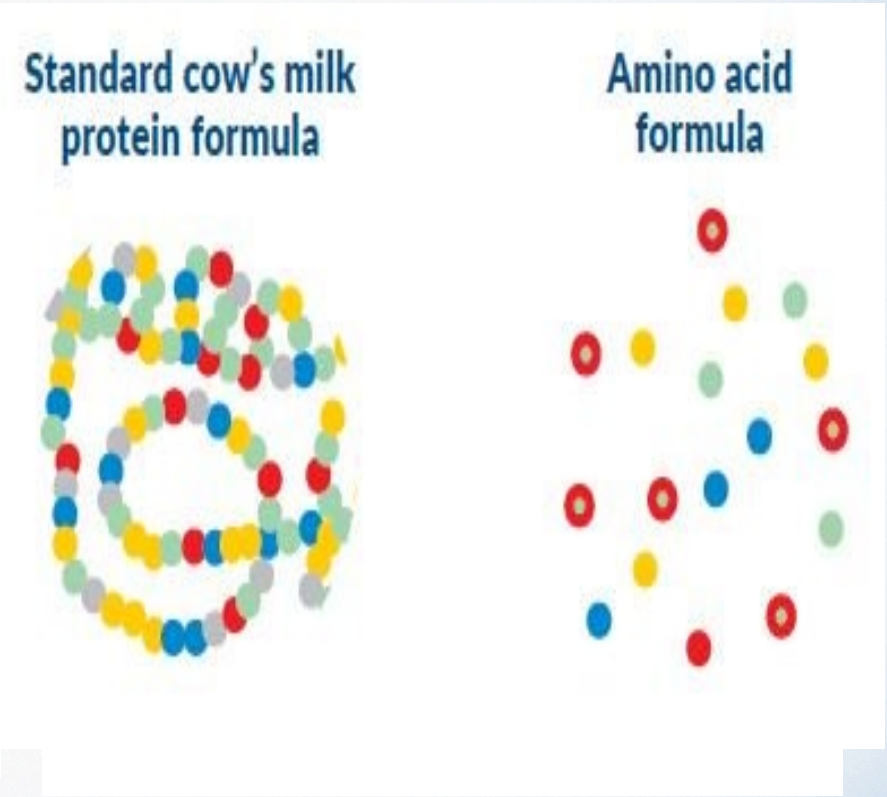
WORLD ALLERGY ORGANIZATION JOURNAL

World Allergy C
and Rationale fo
Allergy (DRACM
and definitions

Alessandro Fiocchi, MD[a]*, Antonio
Motohiro Ebisawa, MD, PhD[d] and
guideline group[†]

İSPA → BESLENME





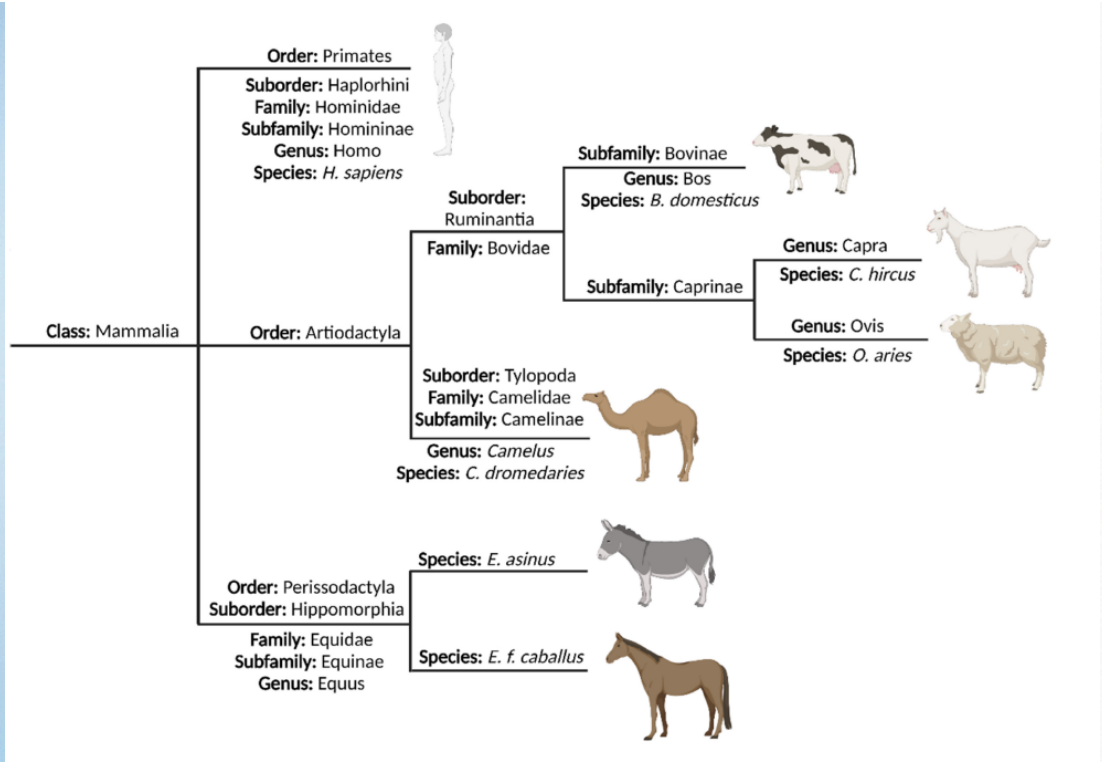
foods

MDPI

Review

Alternatives to Cow's Milk-Based Infant Formulas in the Prevention and Management of Cow's Milk Allergy

Natalia Zofia Maryniak, Ana Isabel Sancho, Egon Bech Hansen and Katrine Lindholm Bøgh *



- Antijenik benzerlik
- İçerik – gereksinim dengesizliği
- İS yerine kullanılmaz!
- Ancak; proteinleri formula teknolojisinde merak uyandırıcı

Marynlak NZ, Foods, 2022

foods

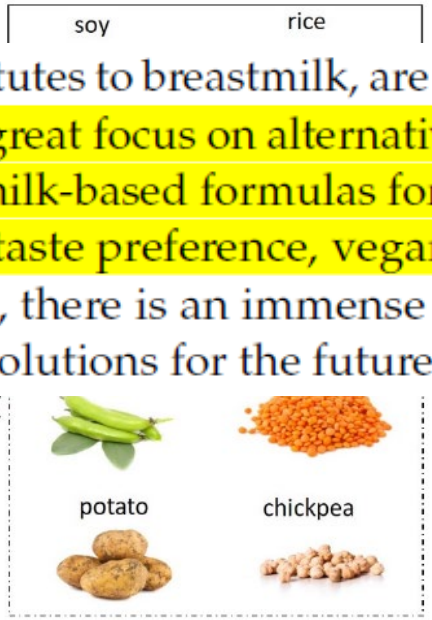
MDPI

Review

Alternatives to Cow's Milk-Based Infant Formulas in the Prevention and Management of Cow's Milk Allergy

Natalia Zofia Maryniak, Ana Isabel Sancho, Egon Bech Hansen and Katrine Lindholm Bøgh *

Infant formulas, as substitutes to breastmilk, are largely based on dairy proteins. Yet, in recent years, there has been a great focus on alternative protein sources of plant origin—not only as a substitute to cow's milk-based formulas for infants suffering from CMA or cow's milk intolerance but also for taste preference, vegan habits, environmental, climate, and ethical reasons [9,10]. Indeed, there is an immense focus on providing more sustainable and climate-friendly dietary solutions for the future [327–329].



Marynlak NZ, Foods, 2022

foods

MDPI

Review

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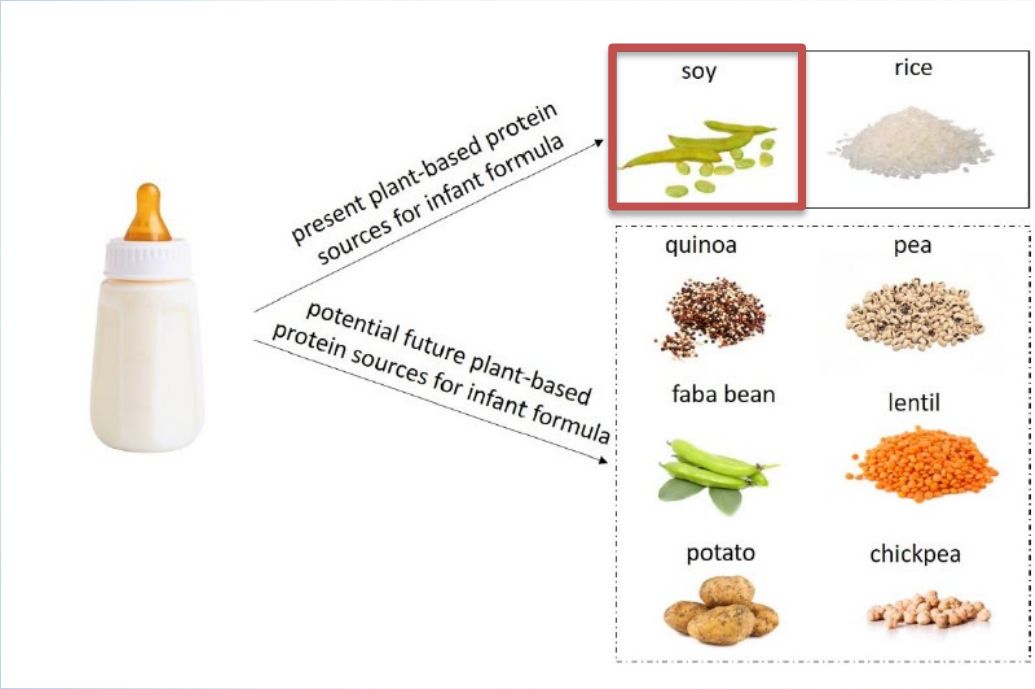
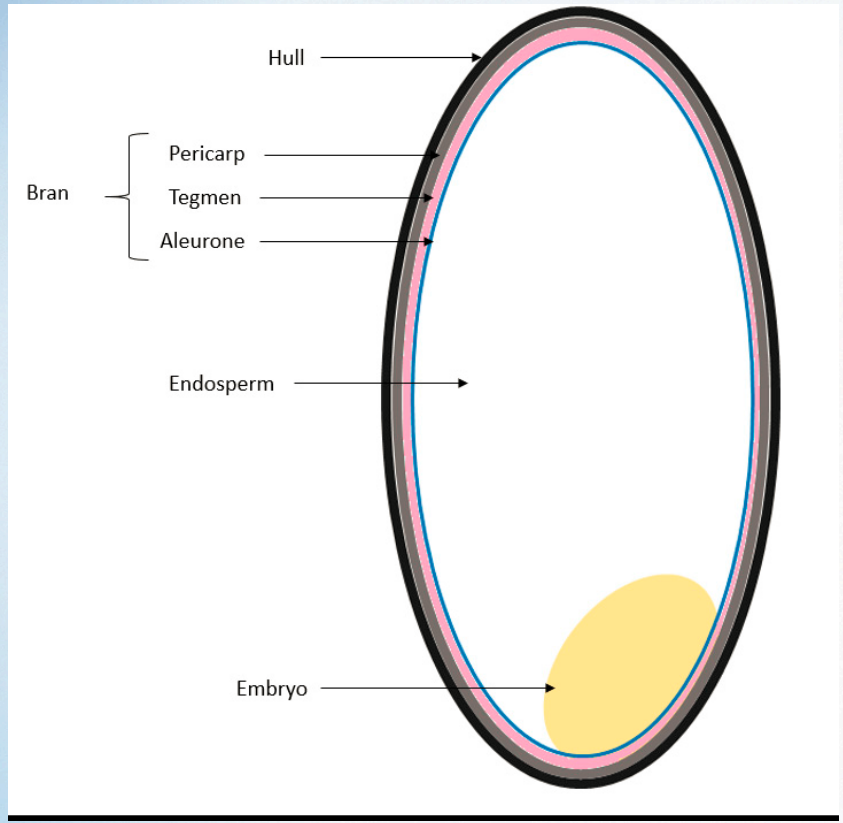
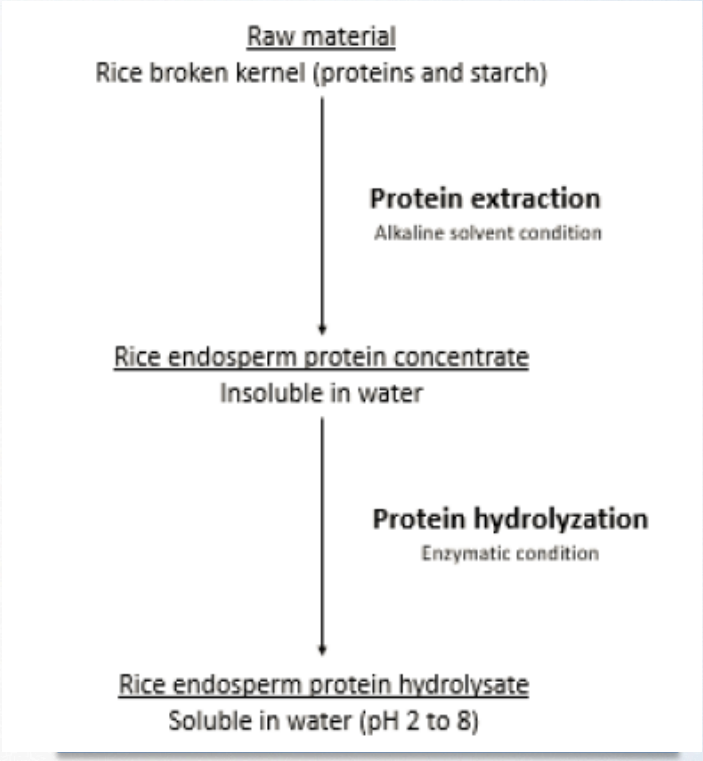


- **Soya**→1909……
- Soya alerjisi→
  - N popülasyonda %0.27
  - İSPA %10-14
  - Çoklu gada %12.9
- Soya→<6 ay önerilmez
- Soya ↔İSPA
  - eHF, AAF, HRHF bulunmayan koşullarda ikincil seçenek

Marynlak NZ, Foods, 2022

Veeeee PİRİNÇ PROTEİNİ





Dupont C, Nutrients 2020

HRPF→Hydrolysed Rice-protein based formula

- İçin … nli,
- Sad…
- Fito…
- GD…
- Ars…

(*AB'nir… …ştir*

(2006 , 201…

- İnor… ↓↓

(Pirin… …6)

FSMP→

- **İSPA**
- **Primer/sekonder laktoz intoleransı**
- **Kronik ishal**
- **Akut ishal sonrası refeeding**

Özel medikal amaçlar için kullanılan gıda ürünleri

↓

FSMP

Dupont C, Nutrients 2020

Table 3. Energy, protein, lipid, and carbohydrate content of HRPFs.

			Peptides Molecular	Addition of Free Amino-Acids					
Risola									
Blemil Expert Riz 1® [67]	71 kcal	1.7 g	10%: Free amino acids 20.8%: MW < 300 Da 29.9%: 300 Da < MW < 1000 Da 35.2%: 1000 Da < MW < 5000 Da	Yes	Yes	Yes	standard formulas	Lactose free	Corn Starch: 1.6 g Dextrin-maltose: 6.4 g
Blemil Arroz 2® Modilac Expert Riz 2® [67]	69 kcal	2 g		Yes	No	Yes			Corn Starch: 1.7 g Dextrin-maltose: 5.7 g
Novalac® 0–3 years [68]	68 kcal	1.8 g	95%: MW < 1000 Da	Yes	No	Yes			Corn Starch: 1.9g 40% rice syrup + 60% saccharose syrup: 6.7 g
Ross Formula [57]	68 kcal	1.9 g	Unknown	Yes	Yes	No			

HPRF ile beslenen sağlıklı bebeklerde büyüme normaldir!

Table 4. Healthy infants fed with HPRF had a normal growth.

Study	Patients	Type of Study	Intervention	Outcomes
Lasekan et al., 2006 [57]	65 healthy infants (without CMPA) Age: 0 to 16 weeks	Randomized double-blind trial	HRPF (Ross formula) or standard formula for 4 months	Height, weight, BMI, and cranial girth within normal limits No difference between groups
Girardet et al., 2010 [74]	78 healthy full-term infants Age: <1 month	Open multicenter prospective study	Lactose-containing HRPF (Modilac®) from the 1st month to the age of 4 to 6 months (after starting complementary feeding)	Average daily weight gain: 23.2 ± 4.3 g (PP population), with no difference with WHO standards [75] Height, weight, and BMI z-scores (intent to treat population): between 1.1 and −0.5 DS during the study period

HPRF ile beslenen İSPA.lı bebeklerde alerjik bulgular kontrol altına alınır!

Study					
Fiocchi et al., 2003 [77]	18 infants CMPA confirmed by a double-blind placebo-controlled food challenge (DBPCFC) Age: 1–9 years (average 5 years)	Clinical trial	1 test	HRPF (Risolac®)	HRPF: positive for 2/18 children Specific IgEs: CMP: positive in all children Soy: positive in 13/18 children Rice: positive in 7/18 children HRPF: permanently negative Double-blind placebo-controlled food challenge (DBPCFC) with HRPF: negative in all cases
Fiocchi et al., 2006 [69]	100 infants CMPA confirmed by DBPCFC Age: 3.2 ± 2.93 years	Prospective study	1 test	HRPF (Risolac®)	Skin Prick Test: Cow's milk and/or CMP fraction: positive in 87/99 children Rice: positive in 4/90 children HRPF: positive in 4/86 children Specific IgEs > 0.35 KU/L: Cow's milk and/or for a CMP fraction: in 92/95 children Rice: in 21/91 children HRP: in 4/91 children Rice specific IgEs: Rice: positive in 21/91 children (Pharmacia—Upjohn Diagnostic) and in 70/96 children (immunotransfer) HRPF: weakly positive in 6 children DBPCFC with HRPF was always negative.
Reche et al., 2010 [67]	92 infants CMPA IgE-mediated confirmed by a positive Oral Food Challenge (OFC) Age: average 4.3 months (1.1 to 10)	Prospective, open and randomized clinical trial	2 years	46 fed a HRPF (Blemil Arroz®/Modilac Expert Riz 1®) 46 fed a CMP-eHF	HRPF: well tolerated in all children CMP-eHF: 1 child developed allergy to this -CMP-eHF Evolution of number of children remaining allergic: similar in both groups.
Vandenplas et al., 2014 [68]	40 infants CMPA confirmed by OFC CMPA IgE-mediated or not Age: average 3.4 month (1 to 6)	Prospective trial	6 months	HRPF (Novalac Riz®)	Significant decrease of the allergy symptoms after 1 month Benefit confirmed after 3 and 6 months Clinical tolerance was assessed with the symptom-based score (SBS) [81], now published as the COMISS score [82,83]

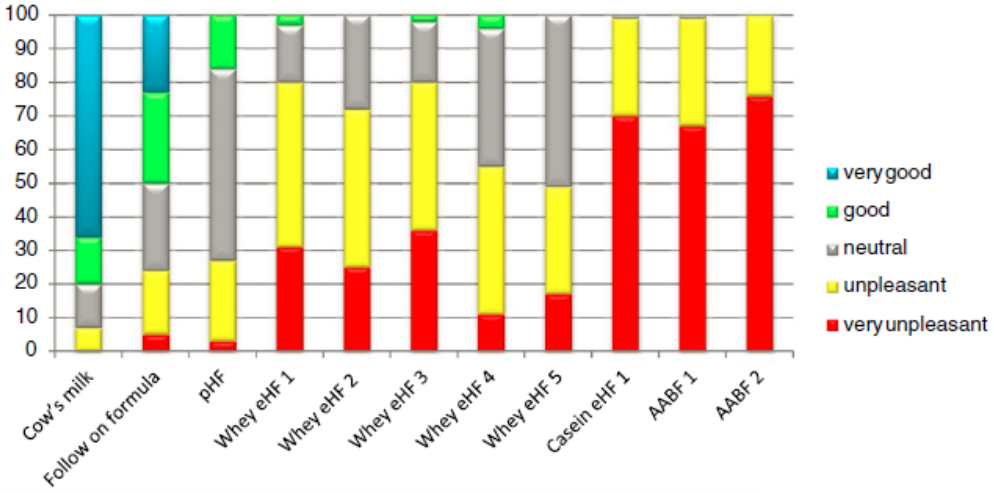
HPRF ile beslenen İPSA'lı bebeklerde büyüme normaldir!

Table 6. Growth and weight evolution and protein nutritional status in children affected with CPMA

D'Auria et al. 2003 [76]	16 infants CMPA + atopic dermatitis (DBPCFC or an open OFC or an open test) Age: 6–14 months	Observation	Weight: HRPF: −0.30 (−0.34) Soy formula: −0.21 (−0.14) Height: HRPF: −0.10 (−0.21) Soy formula: −0.12 (−0.23)	HRPF or soy formula	Soy formula: 0.11 (0.15). Height: HRPF: 0.07 (0.12) Soy formula: 0.27 (0.37). Protein nutritional status: Blood markers of protein homeostasis (albumin, pre-albumin, total plasma proteins, urea): similar in both groups
Savino et al., 2005 [66]	58 infants CMPA + atopic dermatitis 30 controls (without CMPA) Age: 1–24 months	Prospective, non-randomized, mono-centric, open		HRPF (Risolac®) Or a soy formula Or CMP-eHF Or free diet in control group	Weight; Weight z-score were similar in the 3 groups with CMPA during the first 2 years. Weight gain was smaller in the HRPF group (p 0.025) vs control group.
Agostoni et al., 2007 [87]	93 infants CMPA 32 controls Age: 6–12 months	Multi-center-forward, randomized, comparative, open	Weight: RHPF: −0.30 (−0.34) Control: −0.10 Height: RHPF: −0.21 Control: −0.12	soy formula (n-32), CMP-eHF (n-31) and HRPF (Risolac®) (n-30)	Weight: RHPF: −0.09 Control: 0.07 Height: RHPF: 0.11 Control: 0.27
Reche et al. 2010 [67]	92 infants CMPA (skin prick tests) Age: 1.5–9 months	Prospective open, randomized		CMP-eHF and HRPF	Weight: similar Height: similar
Vandenplas et al., 2014) [68]	42 infants Age: 3.4 ± 1.5 months		Weight: HRPF: −0.7 ± 1.0 Height: HRPF: −0.1 ± 1.0	HRPF	Weight: HRPF: −0.1 ± 0.9 Height: HRPF: −0.1 ± 1.1
Lasekan et al., 2006 [57]	65 infants Healthy infants (without CMPA) Age: 0 to 16 weeks	Randomized double-blind trial		HRPF (Ross formula) or standard formula for 4 months	Weight: similar Height: similar Protein nutritional status: Plasma protein concentrations, particularly for total plasma proteins, serum albumin, and pre-albumin/transthyretin: comparable in both groups

HPRF ile beslenen İPSA'lı bebeklerde oral tolerans diğer ürünler ile benzerdir!

Study	Patients	Type of Study	Intervention	Outcomes
Reche et al., 2010 [67]	92 infants CMPA IgE-mediated confirmed by a positive OFC Age: average 4.3 months (1.1 to 10)	Prospective, open and randomized clinical trial	46 fed a HRPF (Blemil Arroz®/Modilac Expert Riz 1®) 46 a CMP-eHF for 2 years	Percentage of children becoming tolerant: similar with the HRPF and the—CMP-eHF after 12, 18, and 24 months of feeding
Terraciano et al., 2010 [88]	72 infants CMPA Age: 14.1 ± 8.6 months	Prospective cohort	Fed with CMP-eHF or soya formula or HRPF For 26 months (median duration)	Time before tolerance was acquired (median duration of the disease): CMP-eHF group: 56 months (IC 95% not applicable) (average—ES: 40.2–4.8 months) Soy formula group: 28 months (IC 95% 11–37) (average—ES: 24.3–2.6) HRPF group: 20 months (IC 95% 10–33) (average—ES: 24.3–3.6) This beneficial effect was not observed in polysensitized children
Berni Canani et al., 2013 [86]	260 infants CMPA confirmed by DBPCFC with milk Age: 1 to 12 months	Multicenter retrospective observational study	71 fed with a CMP-eHF-Lactobacillus Rhamnosus GG (LGG) 55 with a CMP-eHF, 46 with a HRPF (Risolac®) 55 with a soy formula 33 with an amino-acids-based formula (AAF)	Percentage of patients having outgrown CMPA after 12 months: Similar with the CMP-eHF, the HRPF, soy formula and the AAF Significantly shorter in-CMP-eHF-LGG group (OR 4.8; 95% CI 2.2–10.5; p 0. 001)



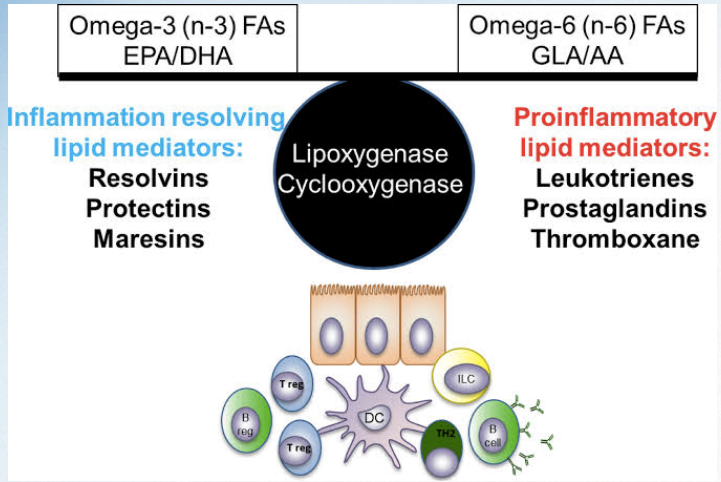
HRPF ve lezzet

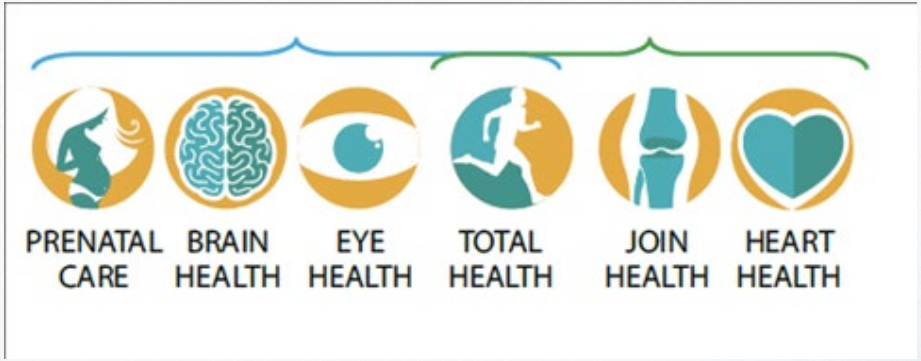
- Vandenplas ve ark.→
  - Beğenmeyen bebek %18.8
  - Ürün reddi 3/40
- Pedrosa ve ark.→
  - Erişkinlere tat denemesi
  - Lezzet HRPF ve Soya > eHP, AAP

Miraglia Del Giudice *et al. Italian Journal of Pediatrics* (2015) 41:42

EVOLVIA RP 1 & 2

	Evolvia RP1	Evolvia RP2
Protein	Hidrolize pirinç proteini 2,42 g/100 kcal	Hidrolize pirinç proteini 2.73 g/100 kcal
Yağ	25,5 g /100 g	24 g /100 g
DHA & ARA	125 mg /100 g & 125 mg/100 g	125 mg /100 g & 0
Prebiyotik	0,4 g/100 ml FOS & 0,4 g/100 ml inülin	0,2 g/100 ml FOS & 0,2 g/100 ml inülin
Probiyotik		*B. infantis IM1™ & L. rhamnosus*
Karbonhidrat	51,8 g/100 g	54,5 g/100 g
Enerji	496 kcal/100 g	494 kcal/100 g
MCT Oranı	6,6 g/100 g (25.9%)	4.6 g/100 g (19,2%)

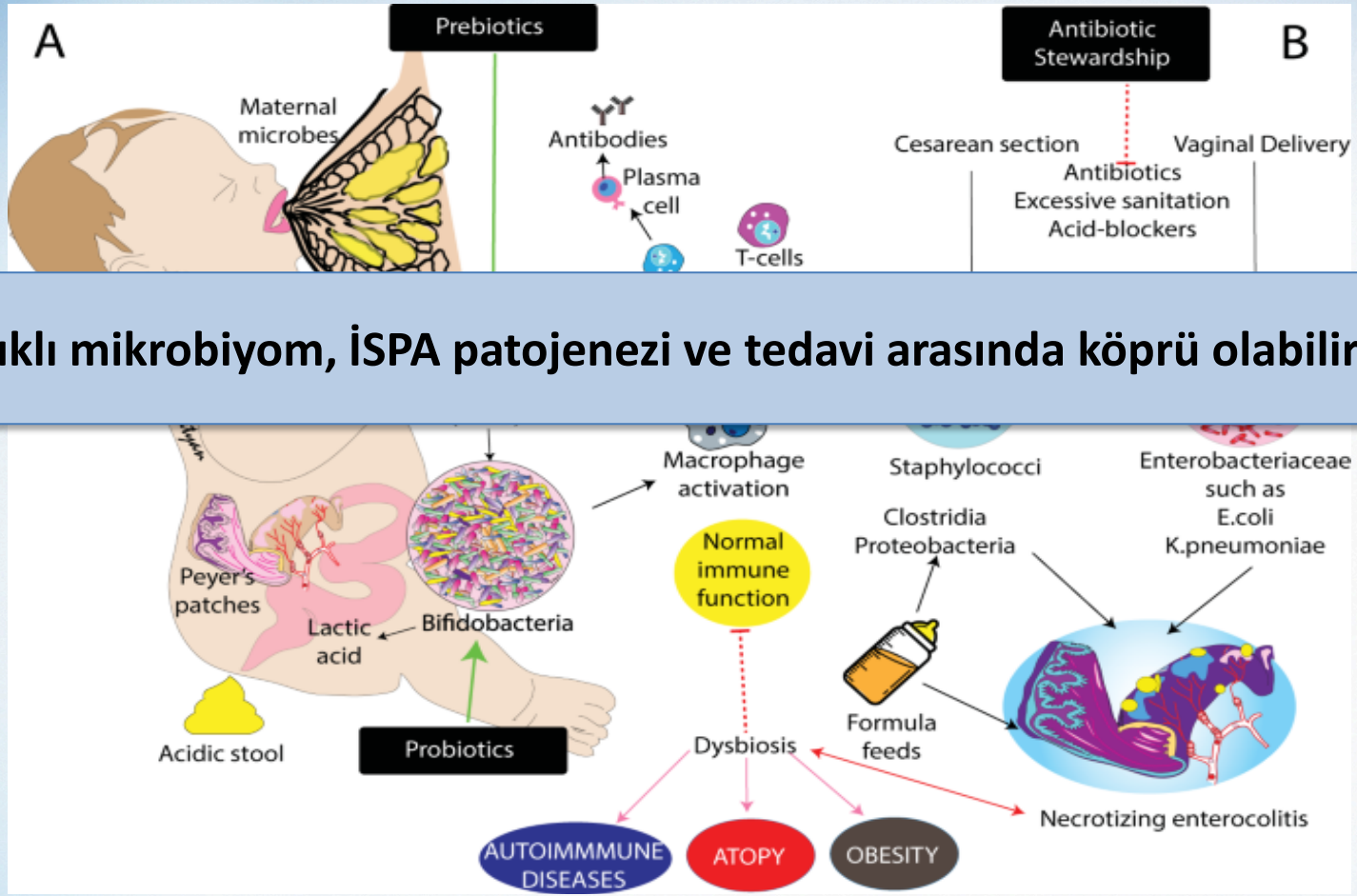

Omega-3 (n-3) FAs
EPA/DHA
Omega-6 (n-6) FAs
GLA/AA
Inflammation resolving lipid mediators:
Resolvins
Protectins
Maresins
Lipoxygenase
Cyclooxygenase
Proinflammatory lipid mediators:
Leukotrienes
Prostaglandins
Thromboxane
Treg
ILC
B reg
DC
TH2
Treg
B cell


PRENATAL CARE
BRAIN HEALTH
EYE HEALTH
TOTAL HEALTH
JOIN HEALTH
HEART HEALTH

EVOLVIA RP 1 & 2

	Evolvia RP1	Evolvia RP2
Protein	Hidrolize pirinç proteini 2,42 g/100 kcal	Hidrolize pirinç proteini 2.73 g/100 kcal
Yağ	25,5 g /100 g	24 g /100 g
DHA & ARA	125 mg /100 g & 125 mg/100 g	125 mg /100 g & 0
Prebiyotik	0,4 g/100 ml FOS & 0,4 g/100 ml inülin	0,2 g/100 ml FOS & 0,2 g/100 ml inülin
Probiyotik		*B. infantis IM1™ & L. rhamnosus*
Karbonhidrat	51,8 g/100 g	54,5 g/100 g
Enerji	496 kcal/100 g	494 kcal/100 g
MCT Oranı	6,6 g/100 g (25.9%)	4.6 g/100 g (19,2%)

Sağlıklı mikrobiyom, İSPA patojenezi ve tedavi arasında köprü olabilir mi?!



	DRACMA—2010	ESPGHAN—2012	EAACI—2014	BSACI—2014
Rice hydrolysed formula	Equivalent to CM eHF in countries where they are available	-Infants refusing or not tolerating a CM eHF or in vegan families	Further research is needed to compare these formulas with CM eHF	Rice milk should not be used under 4.5 years of age due to its natural inorganic arsenic content
Prebiotics and probiotics	More RCTs need to be conducted to elucidate whether probiotics are useful	No evidence that they have a role in treatment of CMA	Currently, probiotic supplements cannot be recommended for the management of food allergies	Evidence of preventative or therapeutic activity for food allergy is lacking

Pediatr Allergy Immunol 2007: 18: 599–606
DOI: 10.1111/j.1399-3038.2007.00566.x

PEDIATRIC ALLERGY AND IMMUNOLOGY

Growth of infants with IgE-mediated cow's milk allergy fed different formulas in the complementary feeding period

Carlo Agostoni[1], Alessandro Fiocchi[2], Enrica Riva[1], Luigi Terracciano[2], Teresita Sarratud[2], Alberto Martelli[2], Fabio Lodi[1], Enza D'Auria[1], GianVincenzo Zuccotti[3] and Marcello Giovannini[1]

[1]Department of Pediatrics, San Paolo Hospital, University of Milan, Milan, [2]Department of Child and Maternal Medicine, the Melloni Hospital, Milan, [3]Department of Pediatrics, L. Sacco Hospital, University of Milan, Milan, Italy

HASTA GRUBU	• 93 İSPA • 32 kontrol (AS), • Yaş: 6-12 ay
ÇALIŞMA TİPİ	• Çok merkezli, açık, randomize, prospektif
MÜDAHALE	• 32 Soya F • 31 e-İSHF • 30 HRPF
BAŞLANGIÇ TARTI VE BOY	• 4-6 ay (tamamlayıcı beslenmeye geçene kadar)
TARTI VE BOY	• Boy, tartı, BÇ, BMI z-skorları normal, • Günlük tartı alımı: 23.2 ± 4.3 g (WHO standartlarında)

Table 3. Standardized anthropometric parameters in the four groups of infants at 6, 9, and 12 months of age (mean values and 95% CI)

Months	Soy (n = 32)	CHy (n = 31)	RHy (n = 30)	BF (n = 32)	p-Value
Weight-for-age *z*-scores					
0	−0.13 (−0.39 to 0.13)	0.24 (−0.07 to 0.55)	0.28 (−0.06 to 0.63)	−0.03 (−0.38 to 0.31)	0.180
6	−0.45 (−0.71 to −0.19)	−0.44 (−0.74 to −0.13)	−0.41 (−0.76 to −0.06)	−0.36 (−0.63 to −0.09)	0.973
9	−0.60 (−0.82 to −0.38)	−0.45 (−0.77 to −0.12)	−0.28 (−0.68 to 0.12)	−0.43 (−0.71 to −0.15)	0.517
12	−0.61 (−0.90 to −0.33)	−0.27 (−0.59 to 0.04)	−0.23 (−0.61 to 0.14)	−0.47 (−0.79 to −0.15)	0.290
Length-for-age *z*-scores.					
0	−0.24 (−0.41 to −0.07)	0.19 (0.01–0.37)	0.01 (−0.38 to 0.40)	−0.11 (−0.39 to 0.17)	0.113
6	−0.55 (−0.81 to −0.29)	−0.40 (−0.69 to −0.10)	−0.73 (−1.00 to −0.46)	−0.49 (−0.75 to −0.24)	0.355
9	−0.49 (−0.74 to −0.23)	−0.33 (−0.59 to −0.06)	−0.58 (−0.94 to −0.21)	−0.48 (−0.77 to −0.20)	0.676
12	−0.43 (−0.73 to −0.13)	−0.16 (−0.51 to 0.19)	−0.49 (−0.79 to −0.18)	−0.48 (−0.79 to −0.17)	0.395
Weight-for-length *z*-scores.					
0	−0.20 (−0.47 to 0.06)	−0.37 (−0.65 to −0.09)	0.12 (−0.61 to 0.86)	−0.31 (−0.62 to −0.00)	0.375
6	−0.12 (−0.45 to 0.21)	−0.20 (−0.54 to 0.13)	0.04 (−0.34 to 0.42)	−0.01 (−0.29 to 0.25)	0.727
9	−0.18 (−0.47 to 0.09)	−0.25 (−0.59 to 0.08)	0.18 (−0.24 to 0.60)	−0.10 (−0.37 to 0.17)	0.260
12	−0.30 (−0.63 to 0.01)	−0.12 (−0.47 to 0.23)	0.24 (−0.15 to 0.65)	−0.11 (−0.46 to 0.23)	0.163

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

	Soy (n = 32)	CHy (n = 31)	RHy (n = 30)	BF (n = 32)	p-Value
Δ WA	−0.16 (−0.36 to 0.04)[a]	0.16 (−0.05 to 0.38)[b]	0.18 (−0.02 to 0.38)[b]	−0.10 (−0.28 to 0.07)	0.023
Δ 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)	0.548
Δ 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)	0.286

Different superscripts ([a, b]) indicate significant between-group comparisons at bivariate analysis.

Sabrınıza teşekkürler…..