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2023 ESPGHAN POSITION
PAPER ON COW MILK
ALLERGY (CMA)

YVAN VANDENPLAS MD, PhD

Wednesday, October 11

1pm EST



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Disclosures



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□ Y Vandenplas has participated as a clinical investigator, and/or advisory board member, and/or consultant, and/or speaker for:

▣ Abbott Nutrition, Alba Health, Arla, Ausnutria, Biogaia, By Heart, CHR Hansen, Danone, ELSE Nutrition, Friesland Campina, Nestle Health Science, Nestle Nutrition Institute, Nutricia, Mead Johnson Nutrition, Pileje, Sanulac, United Pharmaceuticals (Novalac), Yakult, Wyeth

□ **None pose any conflict of interest for this presentation**

The opinions reflected in this presentation are those of the speaker and independent of Nutricia North America



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Learning Objectives



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□ Following this presentation, participants will be able to:

▣ Better recognize the symptoms of CMA

▣ Summarize the updated ESPGHAN recommendations for diagnosing and managing of CMA

▣ Describe the role of hydrolyzed, amino acid, rice, and soy formulas for the management of CMA


▣ Detail the benefits of synbiotics, prebiotics, and lactose for formula fed infants



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An ESPGHAN position paper on the diagnosis, management and prevention of cow's milk allergy.


Vandenplas Y, Broekaert I, Domellöf M, Indrio F, Lapillonne A, Plenar C, Ribes-Koninckx C, Shamir R, Szajewska H, Thapar N, Thomassen RA, Verduci E, West C.
J Pediatr Gastroenterol Nutr. 2023 Jul 26. doi: 10.1097/MPG.0000000000003897.

Scan here to access the article








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What's New?

- Available evidence on the role of dietary practice in the prevention, diagnosis, and management of CMA
- The impact of CMA on nutrition, growth, cost, and QoL
- The roles of hydrolyzed rice formula, soy and vegetable infant feeds in the diagnostic and therapeutic approaches to CMA.





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What is CMA?

- CMA is defined as a **reproducible adverse reaction to one or more milk proteins** (usually caseins or whey beta-lactoglobulin) **mediated by IgE and / or non-IgE mechanisms.**³
- CMA prevalence is reported to be up to 3%² but is very variable depending on the country, region and the diagnostic method used ;
- e.g., challenge proven CMA was 0.6% in Europe.¹

Luckily most children outgrow their allergy to milk in early childhood - depending on the initial presentation (IgE or non-IgE-mediated) and severity of symptoms.^{2,4-8}

Abbreviations: CMA, Cow's milk protein allergy; IgE, immunoglobulin E.

1. Shamir R, et al. Allergy 2016.

2. Schreiner AB, et al. Allergy 2015.

3. Caron BG, et al. Current in Immunology 2013.




4. Shamir R, et al. Allergy 2016.

5. Schreiner AB, et al. Allergy 2015.

6. Shamir R, et al. Allergy 2016.

7. Caron BG, et al. Current in Immunology 2013.

8. Shamir R, et al. Allergy 2016.




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CMA - Symptoms Summary



Symptoms seen in order of importance in IgE and non-IgE-mediated CMA


	IgE	Non-IgE
Symptoms	Respiratory - wheeze, difficulty breathing Dermatological/Skin - pruritis, urticaria, acute angio-oedema Gastrointestinal/Digestive – less common (can see vomiting/diarrhea as late phase reaction) Circulatory - hypotension/tachycardia (in cases of anaphylaxis)	Gastrointestinal/Digestive - vomiting/diarrhea, blood/mucus in stool Dermatological/Skin - atopic dermatitis/eczema (mostly early onset) Respiratory – not common more prone to URTI/LRTI General: pain/arching after eating, chronic irritability/crying Circulatory – rare except hypotension in FPIES (20% have shock) ^{1,2}
Timing	Minutes - 1-2 hours	Hours to weeks
Age of onset	Can be any age (but mostly <1 year)	Can be any age (but mostly <6months)
Reproducible	Symptoms every time the food is consumed	

Abbreviations: CMPA, Cow's milk protein allergy; IgE, Immunoglobulin E; FPIES, Food protein-induced enterocolitis syndrome; URTI, Upper respiratory tract infection; LRTI, Lower respiratory tract infection.

1. Nowak-Węgrzyn A, et al. Allergy Asthma Proc. 2015.
2. Nowak-Węgrzyn A. J Allergy Clin Immunol. 2021.

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Managing Cow's Milk Protein Allergy with an Extensively Hydrolyzed Formula: Results from a Prospective, Non-Interventional Study in France (EVA Study)




Julie Lemale ^{1,*}, Jean-Luc Decline ², Catherine Dive-Pouletty ³, Chantal Touboul ⁴, Nadège Pichon ³ and Christophe Dupont ⁵

Number of symptoms at baseline	ITT (N=207)	PP (N=135)
0	14.5%	16.3%
1	26.1%	27.4%
2	29.0%	25.9%
3	23.2%	21.5%
4	5.8%	6.7%
5	1.4%	2.2%
6	0%	0%

Lemale J, et al. Nutrients. 2022;14(6):1203.

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Managing Cow's Milk Protein Allergy with an Extensively Hydrolyzed Formula: Results from a Prospective, Non-Interventional Study in France (EVA Study)




Julie Lemale ^{1,*}, Jean-Luc Decline ², Catherine Dive-Pouletty ³, Chantal Touboul ⁴, Nadège Pichon ³ and Christophe Dupont ⁵

Type of symptoms	ITT (N=207)	PP (N=135)
Crying	70.5%	71.1%
Regurgitation	64.2%	65.9%
Abnormal stools	64.3%	59.3%
Atopic eczema	31.9%	32.6%
Failure to thrive	20.3%	17.8%
Immediate reactions	14.5%	14.8%
Rectal bleeding	9.7%	11.1%
Respiratory symptoms	6.2%	5.9%
Urticaria	1.9%	3.1%

Lemale J, et al. Nutrients. 2022;14(6):1203.

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Milk allergy/intolerance and atopic dermatitis in infancy and childhood


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Novembre E. *Allergy* 2001;56(Suppl 67):105-8




Severe atopic eczema children : 1/3 rd have CMPA

CMPA children < 1 year: 40 – 50 % have atopic dermatitis

AD + CMPA: "many" develop tolerance to CMP in a "few" years

Persistent CMPA:





- more frequent history of familial atopic disease
- change in symptoms caused by CMP
- multiple food intolerance / allergic disease



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ESPGHAN POSITION STATEMENTS ON DIAGNOSIS AND MANAGEMENT OF COW MILK ALLERGY

DIAGNOSIS
MANAGEMENT


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Diagnosis

Diagnosis

□ IgE Allergy




- Skin Prick Test
- IgE specific RAST
- Negative predictive value
- Does not really help if "negative" (what is the case in most infants)



□ Non-IgE Allergy

- Aspecific symptoms
- No diagnostic tests
- There is no laboratory test that helps to diagnose non-IgE CMA

Incidence and natural history of challenge-proven cow's milk allergy in European children--EuroPrevall birth cohort.
Schoemaker *AAAllergy*. 2015 Aug;70(8):963-72
23.6% had no cow's milk-specific IgE in serum






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Diagnosis of CMA

Diagnosis


- Diagnostic Cow's Milk Elimination Diet
- Oral Food Challenge
- Specific IgE and Skin Prick Test
 - Total IgE does not generally contribute to dx of CMA
 - Elevated specific IgE and skin prick show sensitization to CMP, but do not confirm
- Atopy Patch Test
 - Insufficient evidence for diagnosis of CMA
- Component resolved diagnostics and basophil activation test
 - Insufficient evidence for diagnosis of CMA
- Endoscopic Evaluation
 - Insufficient evidence for diagnosis of CMA
- Biological Markers
 - Not indicated for diagnosis of CMA



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Awareness and Management Tools

Diagnosis




Bajero K, et al. Nutrients. 2022 May 14;14(10):2059.

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CoMSS™ Cow's Milk-related Symptom Score

Diagnosis



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The Cow's Milk-Related Symptom Score (CoMiSS™): A Useful Awareness Tool¹

Diagnosis

CoMiSS™ cannot be considered as a stand-alone CMA diagnostic tool, but that it was a useful awareness tool for CMPA as well as for monitoring symptom improvement.

- CoMiSS™ was developed as a clinical tool aimed at increasing health care professionals awareness of the presence and intensity of clinical manifestations possibly related to CM intake.
- Infants exhibiting symptoms possibly related to CM, present with a higher median CoMiSS™ score than healthy infants - 6 to 13 (from 16 studies) versus 3 to 4 (from 5 studies) respectively.
- In those with CMA, 11 studies found a CoMiSS™ score of ≥12 & predicted a favorable response to a CM-free diet; however, sensitivity and specificity varied.
- A decrease of CoMiSS™ score during a CM elimination diet was also predictive of seeing a reaction to the oral food challenge.

¹ Bajajrova K, et al. *Nutrients*. 2022 May 14;14(10):2059.



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The Cow's Milk Related Symptom Score: The 2022 Update¹

Diagnosis

CoMiSS™ raises awareness about symptoms that might be CM-related and it is not intended as a diagnostic tool.

- CoMiSS™ was originally developed in 2015 by a group of experts as a tool to increase the awareness among health care professionals of symptoms seen in infants that might relate to cow's milk allergy. 25 papers have since been published on the tool. The purpose of this consensus was to review and discuss the evidence. It included a panel of 10 experts, 7 of whom were part of the original group.
- The panel concluded:
 - the cut-offs should be lowered from ≥12 to ≥10.
 - sensitivity is more important than specificity (identifies potential cases) in an awareness tool.
 - a lower score <6 to indicate *not* CMA-related.
 - >1 week should be added to each symptom category to avoid scoring acute causes which are NOT often related to CMA.
 - the Brussels Infant and Toddlers Stool Scale (BITSS) is more valuable than Bristol Stool Scale.
 - There may be regional differences in CoMiSS™ in healthy infants as well as in those with CMA.

¹ Vandermolen Y, et al. *Nutrients*. 2022.



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Interpretation of the final score




Diagnosis

INTERPRETATION OF THE TOTAL SCORE

Total score ≥ 10: May be suggestive of cows milk-related symptoms and could potentially be CMA.

Total score < 6: Symptoms are not likely to be related to CMA. Look for other causes.

The CoMiSS® scoring form is not intended to be used as a diagnostic tool and should not replace an oral food challenge. CMA diagnosis should be confirmed by a 2 to 4 week elimination diet followed by an oral food challenge.



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CoMiss (Cow's Milk-related Symptom Score) – Awareness toll for CMA

Statement

The baseline Cow's Milk related Symptom Score (CoMiSS) and its reduction during an elimination diet may be indicative for CMA, but is not diagnostic.

Mean/
median

8.4/9

Votes

6: 7;
8 (2x);
9 (9x)

While CoMiSS might increase awareness and thus favor over-diagnosis, it might as well decrease over-diagnosis since symptoms in at least two organ systems are needed

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Diagnosis of CMA – Cow's Milk Elimination Diet

Diagnostic Cow's Milk Elimination Diet

- Allergy-focused clinical history – feeding history and personal and familial history of allergic disease.
- Physical exam

Non-IgE-mediated CMA

- Elimination diet typically requires 2-4 weeks before reintroduction
- Short term diagnostic elimination diet followed by reintroduction/OFC before embarking on a long-term elimination diet

IgE-mediated CMA

- Elimination diet typically requires 1-2 weeks before reintroduction

Statement

In IgE mediated allergy, the response to the diagnostic elimination diet is to be expected within 1 to 2 weeks.

8.8/9

8(2x); 9(11x)

Statement

In non-IgE mediated allergy, the response to the diagnostic elimination diet is to be expected within 2 to 4 weeks.

8.7/9

7:8:9(11x)

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Diagnostic Elimination Diet in Breastfed Infants

In the exclusively breastfed infant, CMA is rare.

Statement

In rare cases when CMA is suspected in an exclusively breastfed infant, diagnostic maternal CM free diet for 2-4 weeks whilst continuing to breastfeed may be considered. In order to confirm the diagnosis, CM should then be reintroduced in the maternal diet with monitoring of symptoms.

Mean/
median

8.8/9

Votes

8(3x); 9(10x)

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Formulas and the Elimination Diet

Diagnosis:
Elimination Diet

□ eHF

□ AAF

□ Rice

□ Soy

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Diagnostic Elimination Diet in Non-Breastfed Infants

Diagnosis:
Elimination Diet

• EHF is the first choice for CMA management.

• Preferable to use CM based eHFs

Statement	Mean/median	Votes
In formula fed infants, a CM derived extensively hydrolysed formula (eHF) is the first choice for a diagnostic elimination diet.	7.2/9	0 (2x); 7; 8(3x); 9(7)
Only CM derived eHFs tested in randomized clinical trials should be used.	8.6/9	7(2x);8; 9(10x)
There are insufficient comparative trials to make a recommendation whether to use whey versus casein hydrolysates.	8.8 / 9	8 (3x); 9 (10x)

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Diagnostic Elimination Diet in Non-Breastfed Infants

Diagnosis:
Elimination Diet

Subset of children where AAF may be indicated:

• Anaphylaxis

• Faltering Growth

• Multiple and Severe Complex GI Food Allergies

• Acute and chronic severe FPIEs

• EoE not responding to exclusion diet

• Symptom persistence on eHF

Statement	Mean/Median	Votes
In formula fed infants, amino acid-based formula (AAF) for a diagnostic elimination diet should be reserved for severe cases or patients with severe malnutrition.	8.5 / 9	7; 8 (4x); 9 (8x)

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AAF as first-line has gradually become the international trend

Diagnosis:
Elimination Diet

2009

Australia

AAF Save
medicare
resources

2016

Brazil¹

AAF as First-
line for
diagnosis

2019

Turkish³

AAF as First-
line
diagnosis

2017

2019

China

AAF as First-line
for diagnosis

¹ Fiocchi A, et al. World Allergy Organ J. 2018;11(1):2.

² Vandeplass Y, et al. Arch Dis Child. 2007;92(10):902-8.

³ Güler N, et al. Allergol Immunopathol (Madrid). 2020;48(2):202-10.

⁴ Guest JP, et al. Curr Med Res Opin. 2009;25(2):339-49.

⁵ Morais MBd, et al. Journal of Medical Economics. 2016; 1:21

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Plant-Based Formulas and Liquid Feedings for Infants and Toddlers.

Diagnosis:
Elimination Diet


Vandenplas Y, et al. Nutrients. 2021 Nov 11;13(11):4026


Worldwide, rice is the most cultivated crop.


Health care providers and parents are familiar with hydrolyzed rice-based infant formula for the treatment of CMA.

Hydrolyzed rice infant formulas are present in many European countries since more than 30 years, and occupy a significant market share

(2018 in France : 5% of all formulas for children aged 0–3 years)

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Comparison of Rice Drink to HRF


Diagnosis:
Elimination Diet


Per 100 kcal	Rice drink	HRF 1	HRF 2	HRF 3	Codex (Min-Max)
Calories (kcal/100 ml)	46	66	68	63	60-70
Protein (g)	0.9	2.7	2.5	2.2	1.8-3.0
Fat (g)	2.3	5.0	4.7	4.4	4.4-6.0
Carbohydrates (g)	18.2	11.0	11.9	12.2	9.0-14.0
Sugar (g)	11.8	1.4	0.8	1.0	-

Rice drink has lower calories, protein content and fat content than HRF.

Rice drink is not adapted to infants and should NOT be used instead of rice hydrolysate formula.

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Efficacy of HRF During CMA

Diagnosis:
Elimination
Diet

Author	Number	Groups	Results
Fiocchi et al.	18 infants : CMA and soy allergy	HRF	100% tolerance
Fiocchi et al.	100 children: CMA	Provocation test with HRF	All challenges negative
Reche et al.	92 infants: CMA	2 groups : 46 HRF 46 eHF	100% tolerance with HRF and 1 allergy to eHF
Vandenplas et al.	36 CMA	HRF	100% tolerance

Fiocchi A, et al. Clin Exp Allergy. 2003 Nov;33(11):1576-80.
Fiocchi A, et al. Clin Exp Allergy. 2006 Mar;36(3):311-6.
Reche M, et al. Pediatric Allergy Immunol. 2010 Jan;21(14 Pt 1):1577-85.
Vandenplas Y, et al. Eur J Pediatr. 2014 Sep;197(3):1209-16.

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Considerations of Arsenic in Rice Formula

Diagnosis:
Elimination
Diet

- Infants fed with cows' milk formulas ingest approximately 0.11mg/kg per day of inorganic arsenic, >3 times higher than the estimated intake from breast milk.
- For Reche et al., arsenic content in a HRF (Blemil Arroz) 6.4 x lower than levels found in "rice milk" (drink) in the UK by Meharg et al.
- Meyer et al. studied HRFs in Europe (assessing the powder) for content on total/inorganic arsenic:
 - For any HRF consumed at normal volume (600 ml) intake, exposure would be 0.16- 0.23 µg/kg body weight.
 - Well below average exposure in EFSA data by for infants [0.24- 0.43 µg/kg] and toddlers [0.32- 0.45 µg/kg per]
 - Also > 10 fold less than WHO guidelines

Arsenic levels in an average daily volume of HRF are 10-fold less than the WHO limits¹

Summary of rice formulas equating to an 8kg infant taking 600-800 ml per day.

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Reche M, et al. Pediatric Allergy Immunol. 2010;21:577-85.
Meyer J, et al. Rice Allergy Immunology. 2018.

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Soy

Diagnosis:
Elimination
Diet

- Soy infant formulas contain enzymatically hydrolyzed soy protein isolate
- ESPGHAN Committee on Nutrition & AAP
 - Recommended against the use of soy infant formula especially below the age of 6 months because of the risk of co-allergy

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Agostoni C, et al. J Pediatr Gastroenterol Nutr. 2009;49:112-26.
Bouillon-Buisset A, et al. Pediatrics. 2008;121:1058-64.

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Rice and Soy Statements

Diagnosis:
Elimination
Diet

Statement	Mean/ median	Votes
Although less studied than CM based eHFs, rice hydrolyzed rice formulas can be considered as an alternative for a diagnostic elimination diet.	7.4/8	1;5;6;7(2x); 8(2x);9(6x)
Soy infant formula should not be used as the first choice for the diagnostic elimination diet but can be considered in some cases for economic, cultural, and palatability reasons.	7.6/9	0;6;7(2x);8(2x); 9(7x)



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ORAL FOOD CHALLENGE



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Diagnosis:
OFC

Statement	Mean/ median	Votes
In clinical practice the open OFC is clinically more feasible and practical than DBPCFC and is sufficient to confirm the diagnosis of CMA and the development of oral tolerance.	8.7/9	7;8(2x); 9(10x)
In IgE-mediated CMA, the OFC test should be supervised by trained medical health care professionals	8.8/9	7;8(1x); 9(11x)

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Diagnosis:
OFC

Diagnosis of CMA

Elimination diet 1-4 weeks

Elimination diet 1-4 weeks
followed by reintroduction in breastfeeding
challenge in formula feeding

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Diagnosis:
OFC

Diagnosis of CMA

Elimination diet 1-4 weeks


Elimination diet 1-4 weeks
followed by reintroduction in breastfeeding
challenge in formula feeding


But many caregivers refuse the OFC


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WHAT IS NEW TO THE GUIDELINES?

DIAGNOSIS
MANAGEMENT

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Management

Management of Cow's Milk Allergy

What is NOT an option?

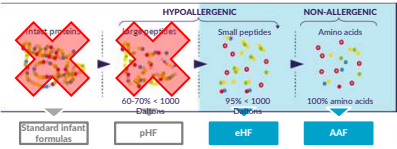


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Management


Specialized Formulas for the Management of CMA

- Various types of specialized formula exist to manage CMA
 - **Hypoallergenic formulas** are cow's milk protein-based formulas in which the protein has been hydrolysed. These can be either partially hydrolysed formulas (pHF) or extensively hydrolysed formulas (eHF) depending on the level of hydrolysis and thus allergenicity. **eHF provide effective management for 90% of infants with CMPA. pHF are not intended for the dietary management of diagnosed CMPA.**
 - **Non-allergenic or amino acid formulas (AAF)** are free amino acid-based, and are thus the least allergic option, commonly recommended for infants reacting to eHF i.e. 10% of infants with CMPA.



Standard infant formulas pHF eHF AAF

Koletko S et al. J Pediatr Gastroenterol Nutr. 2012;55(2):221-6.
Lombard MJ et al. Allergy. 2012;67(10):1199-205.
Muraro A et al. Allergy. 2014;69(8):1039-25.
Dupont C et al. British J Nutr. 2012; 107(2):151-155.



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Management

Current Guidelines and Future Strategies for the Management of Cow's Milk Allergy.

Vandenplas Y, Brough HA, Flocchi A, Migdady M, Munasir Z, Salvatore S, Thapar N, Venter C, Vieira MC, Meyer R. J Asthma Allergy. 2021 Oct 21;14:1243-1256

CM-based partial hydrolysates cannot be recommended in the management of CMA because of insufficient efficacy and possible reactions, since only about half of the infants with CMA will tolerate a partial hydrolysate.

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Management

Management of Cow's Milk Allergy

What is THE BEST option?



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Management

Prevention and management of CMA in non-exclusively breastfed infants.
Vandenplas Y Nutrients. 2017;9(7)

	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		

eHFs are the 1st-choice for most of CMA infants

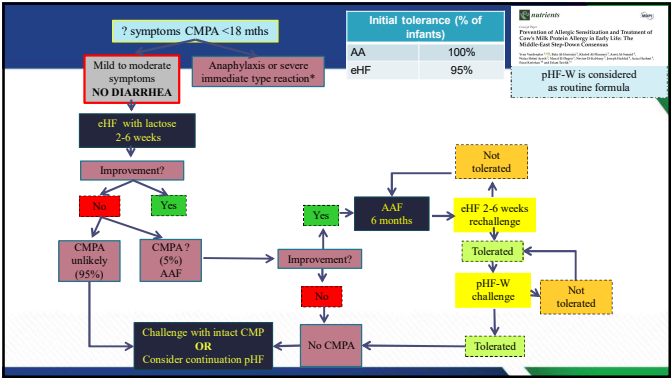
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Management

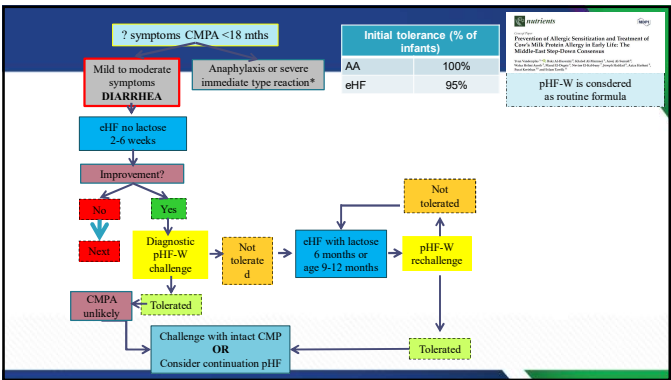
Statement	Mean/ median	votes
In formula fed infants, a CM derived eHF is the first choice for a therapeutic elimination diet.	7.8/9	0; 7(2); 8(3x); 9(7x)

Duration at least > 6 months
9-12 months
whatever of both is reached first

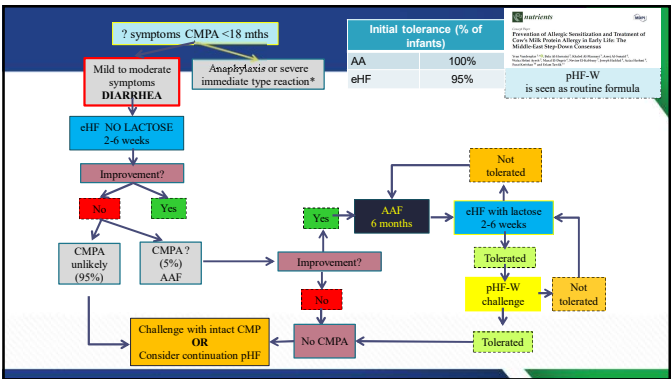
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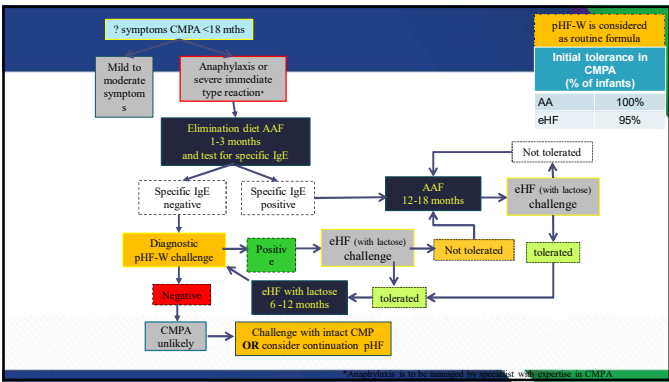
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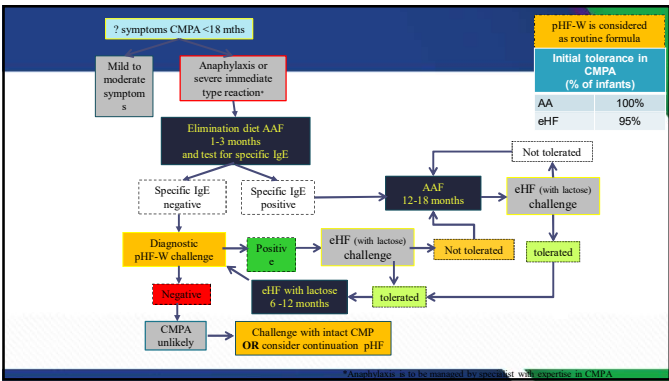
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Management		
Statement	Mean/ median	votes
Regarding the therapeutic elimination diet, AAF should be reserved for severe cases (faltering growth, anaphylaxis) or infants with an absent or partial response to eHF.	8.3/9	1,8; 9(11x)

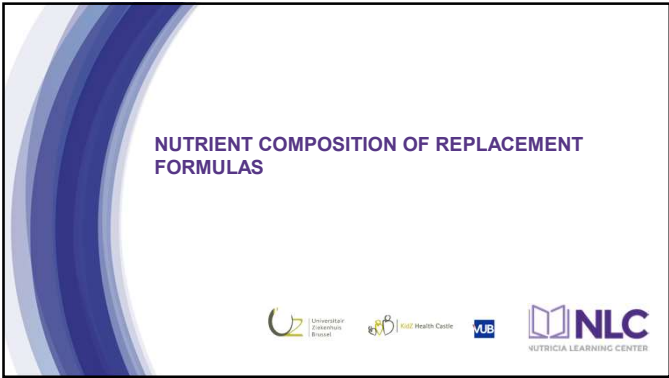
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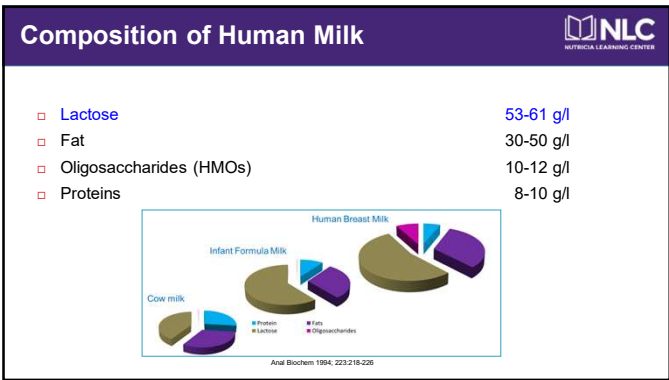
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Prebiotic Human Milk Oligosaccharides (HMOs)

- HMOs: 3rd most prevalent component in human milk
- Some biotechnologically produced structures identical to HMOs are added to some therapeutic formulas
- Further studies are needed to evaluate the efficacy and nutritional value of HMO supplemented formulas in comparison to those supplemented with non-human prebiotic

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What are Synbiotics?

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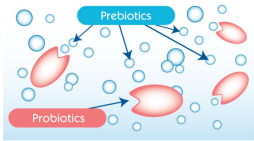
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Synbiotic blend

Prebiotic (food for beneficial bacteria)

+ **Probiotic** (live beneficial bacteria)

= **Synbiotic**



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Synbiotics


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Infants prescribed AAF with synbiotics had a significantly higher probability of achieving asymptomatic management without elimination diet, with a shorter clinical course of symptoms.¹

AAF with synbiotics was associated with fewer symptoms (-37%, p<0.001), infections (-35%, p<0.001), medication prescriptions (-49%, p<0.001) and healthcare contacts compared to AAF.¹

There are some data suggesting that AAF with synbiotics results in a faster recovery than the same AAF without synbiotics.¹

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Lactose


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Lactose is the main carbohydrate found in human milk and cow milk.


Benefits of lactose


1 Undigested lactose is fermented in the colon into short chain fatty acids and may confer a prebiotic benefit, promoting the proliferation of healthy bacteria.¹



2 Lactose can also help to increase calcium absorption.^{2,3}


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Lactose Impact on Formula-fed CMA Infants


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Microbiota in fecal samples from infants with CMPA who received an eHF with or without lactose

- Significant increase in bifidobacteria and lactic acid bacteria ($p<0.05$) reaching counts found in healthy controls
- Significant increase in Bacteroides/clostridia ($p<0.05$)

Lactose increases counts of commensal bacteria.

	healthy BF controls median	eHF with lactose median	eHF without lactose median
Bifidobacteria	9.08	7.66	6.85
Lactobacillus	9.2	9.1	8.5


Lactose decreases counts of pathogenic bacteria.

	healthy BF controls median	eHF with lactose median	eHF without lactose median
Bacteroides	7.04	8.15	9.2

Francavilla R, et al. Pediatr Allergy Immunol. 2012;23:420-7.

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Why is lactose preferable?


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Purified lactose may further improve palatability and help promote a healthy gut microbiome and calcium absorption.


	Lactose Containing Formula	Lactose-free Formula
Calcium (n=18)		
Intake (mg/d)	507 ± 105	500 ± 91
Percentage absorption (%)	66.5 ± 11.9	56.2 ± 15.3 ²
→ Total absorption (mg/d)	339 ± 88	279 ± 85 ³

^{2,3} Significantly different from lactose-containing formula (paired t test)
²p = 0.002, ³p = 0.006

Francavilla R, et al. Effect of lactose on gut microbiota and metabolism of infants with cow's milk allergy. Pediatr Allergy Immunol. 2012;23:420-427.
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Lactose and Taste


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Flavor, relative palatability and components of cow's milk hydrolyzed formulas and amino acid-based formula¹


- The overall judgement of palatability improved with increasing levels of lactose (Spearman's coeff. corr. 0.715; $p = 0.039$).

Palatability of hypoallergenic formulas for cow's milk allergy and healthcare professional recommendation²


- The aim of this study was to assess the palatability of four different eHFs suitable for CMA with HCPs
- Overall, whey-based lactose-containing EHF were ranked better than casein-based EHF

	Protein	Grams lactose
eHF W1	Whey	2.9 g/100 mL
eHF W2	Whey	3.8 g/100 mL
eHF C1	Casein	n/a
eHF C2	Casein	n/a

Percentage of HCPs ranking formula 1st (most liked)



eHF W1 eHF W2 eHF C1 eHF C2




Francavilla R, et al. 2012 Pediatrics. 2012;129:1211-1218. © 2012 Nestlé. All rights reserved. For personal use only. Not for redistribution.

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When to limit lactose?


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❑ Adverse reactions to lactose in CMA are not supported in the literature, and complete **avoidance of lactose in CMA is no longer warranted.**

❑ eHFs containing purified lactose are now available and have been found **safe and effective in the management of CMA.**

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TAKE HOME MESSAGE

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Breastfeeding provides the best nutrition for babies


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Breastfeeding protects against illness and infection in infants and children: a review of the evidence.



Oddy WH. Breastfeed Rev. 2001 Jul;9(2):11-8.


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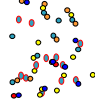
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Feeding a Child with CMA

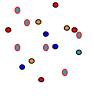
Milk intact proteins






Extensive hydrolysates with small peptides



Amino-acids RHF



- Casein and whey eHF : CM peptide remnants
- AAF and RHF: NO CM peptide remnants but also NO lactose

from Muraro et al. Allergy 69 (2014)

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Best practice for confirming CMA diagnosis upon suspicion

Breastfed baby

Continue breastfeeding; mother should be on a CM-free diet and calcium for 2-4 weeks

Formula-fed baby mild to moderate symptoms

May require extensively hydrolysed formula (eHF) or hydrolysed rice formula (rHF) for 2-4 weeks

Formula-fed baby severe symptoms (vomiting, diarrhoea)

Amino acid (based) formula (AAF) for 2-4 weeks

Long-term management

Eliminate all CM sources (refer to dietitian/nutritionist)

Good compliance

Not CMA

Reintroduction/challenge CM

Reintroduction/challenge CM

May not be CMA

Not CMA

Not CMA

Doubtful compliance

Refer patient to dietitian or nutritionist for reevaluation

No symptoms

Not CMA

Symptoms

CMA

Consider switching to other regimens to confirm

Consider breast milk or eHF/rHF/AAF (depending on tolerance) for 6 months or until 9 to 12 months of age

Monitor tolerance development

To confirm the diagnosis of CMA and avoid overdiagnosis, an oral food challenge test is recommended after a short diagnostic elimination diet

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References

Nwaru BL, et al. Allergy. 2014.

Flom DJ & Scherer SH. Nutrients. 2019.

Hill DJ & Hooking CS. Eu J Clin Nutr. 1995

Schoemaker AA, et al. Allergy. 2015.

Spergel JM. J. Allergy Clin Immunol. 2013.

Sampson H, et al. J Allergy Clin Immunol. 2019.

Canani RB, et al. Frontiers in Immunology. 2019.

Nowak-Węryzyn A, et al. Allergy Asthma Proc. 2015

Nowak-Węryzyn A (UpToDate). (Online). 2021.

Lemiale J, et al. Nutrients. 2022;14(6):1203.

Novembre E. Allergy 2001;56(Suppl 67):105-8.

Schoemaker AA. Allergy. 2015 Aug;70(8):963-72.

Bajero K, et al. Nutrients. 2022 May 14;14(10):2059.

Vandenplas Y, et al. Nutrients. 2022.

Fiocchi A, et al. World Allergy Organ J. 2018;11(1):2.

Vandenplas Y, et al. Arch Dis Child. 2007;92(10):902-8.

Guler N, et al. Allergol Immunopathol (Madr). 2020;48(2):202-10.

Guest JR, et al. Curr Med Res Opin. 2009;25(2):339-49.

Morais MB, et al. Journal of Medical Economics. 2016:1-21.

Vandenplas Y, et al. Nutrients. 2021 Nov 11;13(11):4026.

Fiocchi A, et al. Clin Exp Allergy. 2003 Nov;33(11):1576-80.

Fiocchi A, et al. Clin Exp Allergy. 2006 Mar;36(3):311-6.

Vandenplas Y, et al. Eur J Pediatr. 2014 Sep;173(9):1209-16.

Reche. Pediatr Allergy Immunol 2010;21:577-85.

Meyer et al. Ped Allergy Immunology 2018.

Miraglia del Giudice, et al. Ital J Pediatr. 2015;41:42.

Maslin, et al. J. Pediatr Allergy Immunol. 2018;29:857-62.

Agostoni C, et al. J Pediatr Gastroenterol Nutr. 2009;49:112-25.

Bhatia J, Greer F. Pediatrics 2008;121:1062-8.

Koletsko S et al. J Pediatr Gastroenterol Nutr. 2012;55(2):221-9.

Lombard MJ et al. Afr Fam Pract. 2012;54(3):199-201.

Muraro A et al. Allergy. 2014;69(8):1008-25.

Dupont C et al. British J Nutr. 2012; 107:325–338.

Vandenplas Y, et al. J Asthma Allergy. 2021 Oct 21;14:1243-1256.

Vandenplas Y Nutrients. 2017;9(7).

Vandenplas Y, et al. Nutrients. 2019 Jun 26;11(7):1444.

Vandenplas Y, et al. Asthma and Allergy 2021 (in press)

Anal Biochem 1994; 223:218-226.

Sorensen K, et al. Nutrients 2021;13:935.

Heine RG, et al. World Allergy Organ J. 2017;10.

Heyman MB. Pediatrics. 2006;118:1279-86.




Abrams SA, et al. Am J Clin Nutr. 2002;76:442-6.

Francaville R, et al. Pediatr Allergy Immunol. 2012;23:420-7.

Steven AA. Am J Clin Nutr 2002;76:442–6.

Oddy WH. Breastfeed Rev. 2001 Jul;9(2):11-8.

Muraro et al. Allergy 69 (2014)

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