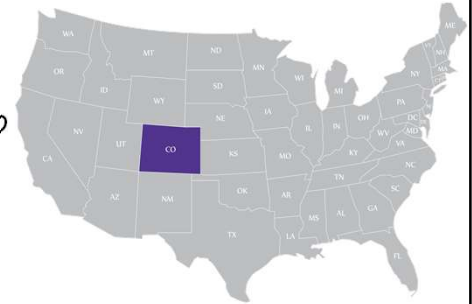


GUIDELINES IN FOOD ALLERGY: WHERE ARE WE IN 2022?



Carina Venter, PhD, RD
Associate Professor Allergy and Immunology
University of Colorado/Children's Hospital Colorado
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The opinions reflected in this presentation are those of the speaker and independent of Nutricia North America

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Learning Objectives

- 1) Identify recent food allergy guidelines available to clinicians for use in clinical practice
- 2) Summarize current updates in guidelines on the prevention, diagnosis, management, and treatment of food allergy

What is Cow Milk Allergy?

WHEEZING

POOR GROWTH

FEEDING REFUSAL

BACK ARCHING

REFLUX

COLIC

CONSTIPATION

ECZEMA

VOMITING

DIARRHEA

3

DRACMA GUIDELINES - What the update covers

- The diagnostic identification of the condition
- The choice of the replacement formula in case of cow's milk allergy (CMA) in infancy when the mother is not able to breastfeed, and
- The use of specific immunotherapy for cow's milk protein allergy.

DRACMA = World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy

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Summary of papers

- Fiocchi et al. World Allergy Organ J. 2022 Feb 1;15(1):100609 (From the DRACMA group)

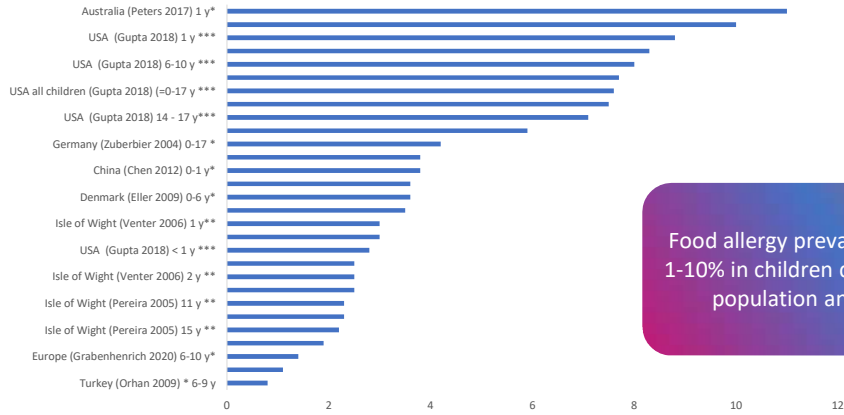
	Topic	Method of preparation
General		
1.	Overview and definitions	This paper
2.	CMA epidemiology and natural history	Narrative review
3.	CM allergens and immunologic mechanisms	Narrative review
4.	Clinical presentations: IgE-mediated	Narrative review
5.	Clinical presentations: non IgE-mediated	Narrative review
6.	Comparison among different guidelines	Systematic review
7.	DRACMA methodology	Synthesis of methods
CMA diagnosis		
8.	Diagnosis of CMA	Systematic review
9.	Recommendations on CMA diagnosis	Guideline
Treatment options		
10.	Breastfeeding a baby with CMA	Narrative review
11.	Substitutive formulae	Systematic review
12.	Recommendations on substitutive treatment	Guideline
13.	Oral immunotherapy for CMA	Systematic review
14.	Recommendations on CMA OIT	Guideline
15.	Other milks (goat's, ewe's, mare's, donkey's, camel's, and substitutes from non-animal source ^(*))	Narrative review
16.	Nutritional considerations in CMA infants	Narrative review
Conclusions		
17.	Which is the 1st choice formula case by case?	Synthesis of recommendations
18.	Unmet needs. Recommendations for research. Recommendation for the implementation of the DRACMA guidelines. Periodical update of DRACMA.	Synthesis of recommendations

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Prevalence

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What is the current prevalence and impact of food allergies in infants and children?



Food allergy prevalence range between 1-10% in children depending on the age, population and methods used.

*Oral food challenge
 **Sensitization plus clinical history or oral food challenge
 ***Parental report

References: 1. Peters et al. J Allergy Clin Immunol. 2017;140(1):145-153 e 148. 2-5. Gupta et al. Pediatrics. 2018; 142(6). 6. Zuberbier et al. Allergy. 2004;59(3):338-345. 7. Chen et al. Zhonghua Er Ke Za Zhi. 2012;50(1):5-9. 8. Eller et al. Allergy. 2009;64(7):1023-1029. 9. Venter et al. J Allergy Clin Immunol. 2006;117(5):1118-1124. 10. Gupta et al. Pediatrics. 2018; 142(6). 11-12. Pereira et al. J Allergy Clin Immunol. 2005;116(4):884-892. 13. Grabenhenrich et al. J Allergy & Clin Immunol. 2014;133(4):979-988. 14. Orhan et al. Clin Exp Allergy. 2009;39(7):1027-1035.

Cow's milk allergy represent about 10 – 50% of food allergies in children

Cow's milk allergy in children

Year	Country	Age (y)	Population (N)	Overall Food allergy prevalence (%)	Cow's milk (%)	Reference
2012	Philippines	14-16	11 434	-	-	Shek et al. ¹
2016	Singapore	0-3	1152	1.1-3.1	0.1-0.5	Tham et al. ²
2012	Hong Kong	0-14	7393	4.8	0.5	Ho et al. ³
2014	Korea	0-6	16 749	3.7	0.5	Park et al. ⁴
2015	Europe	0-2	12 049	-	0.5	Schoemaker et al. ⁵
2011	Chongqing, China	0-1	477	3.8	1.3	Chen et al. ⁶
2001	Japan	0-6	101 322	5.1	1.4	Noda et al. ⁷
				~10		
2015	Guangdong, China	1-7	2540	4	1.9	Zeng et al. ⁹
2008	UK	0-3	969	6	2	Venter et al. ¹⁰
2018	USA	0-18	38 408	7.6	2.0	Gupta et al. ¹¹

Kim et al. Int Arch Allergy Immunol. 2020;181(2):103-110.

References: 1. Shek et al. J Allergy Clin Immunol. 2010;126:324-331. e1-7. 2. Tham et al. J Allergy Clin Immunol. 2018 Mar-Apr;5(2):466-475.e1. 3. Ho et al. Asian Pac J Allergy Immunol. 2012;30:275-284. 4. Park et al. Allergy Asthma Immunol Res. 2014;6:131-136. 5. Schoemaker et al. Allergy. 2015;70(8):963-72. 6. Chen et al. Pediatr Allergy Immunol. 2011;22:356-360. 7. Noda et al. Jpn J Food Allergy. 2010;10:5-9. 8. Ebisawa et al. Allergol Int. 2009;58:475-483. 9. Zeng et al. World J Pediatr. 2015;11:219-225. 10. Venter et al. Allergy. 2008;63(3):354-359. 11. Gupta et al. Pediatrics. 2018;142(6).

Allergenicity

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DRACMA

Proteins in
cow's milk

Milk fraction	Protein family	Protein	Human (mg/ml)	Cow (mg/ml)	Allergen name	Impact	
Caseins	Caseins	α -s1-casein	0	11.6	Bos d 9	major	
		α -s2-casein	0	3.0	Bos d 10	minor	
		β -casein	2.2	9.6	Bos d 11	major	
		κ -casein	0.4	3.6	Bos d 12	minor	
		γ -casein	0	1.6	Bos d 8		
Whey proteins	Lipocalins	β -lactoglobulin (BLG)	0	3.0	Bos d 5	major	
	Lysozymes	α -lactalbumin (ALA)	2.2	1.2	Bos d 4	major	
	Transferrins	lactoferrin	6.0	0.1-0.2	-	(evtl.minor)	
	Albumins	serum albumin	0.4	0.4	Bos d 6	minor	
	Immunoglobulins	immunoglobulins		0.8	0.6	Bos d 7	minor
			other	0.8	0.6		

Table 2. Compositions of human and cow's milk, modified after Crittenden et al.¹¹⁹ and Villa et al.⁸¹ ^aAccording to the official WHO/IUIS nomenclature⁸⁰ allergens are abbreviated by the first letters of the genus in Latin, followed by the first letters of the species and a number, which represents the chronological order of their discovery. ^bBo. d.: abbreviations of Bos domesticus.

Jensen et al. World Allergy Organization Journal. 2022;15:100668
<http://doi.org/10.1016/j.waojou.2022.100668> (From the DRACMA group)

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DRACMA

The effect of processing on milk allergenicity

The diagram illustrates the milk processing flow. At the top, a Dairy Cow provides Cow's Milk to a Milk Processing Plant. The plant produces Dairy Products and Formula/Breastfeeding. Below this, the 3D structure of whey proteins in Raw Milk is shown. Processing steps include Acidic Treatment (at 35-50°C, pH 4.2-4.6, skim milk/cream separation), Pasteurization (Heating 62-68°C and cooling), and Homogenization (evaporation, condensation, drying ± hydrolysis for formula). These steps significantly impair the 3D-structure of whey proteins, their homo- and heteromeric aggregation state, and the composition of all hydrophilic and lipophilic milk constituents, thereby changing the immunogenicity and allergenicity of milk.


Fig. 1 Milk processing changes the 3D structure of whey proteins. Top: Cow's milk is an essential food and needs to be distributed to the people around the world. Therefore, milk processing aims at a) avoiding zoonotic infections of the consumer, and b) making milk products transportable and expanding their shelf life time. Milk processing plants are equipped to fulfill these needs and deliver safe products suited for all tastes and demands, from milk, to infant formula, and many more. Bottom: The major whey proteins are beta-lactoglobulin (50%-65% of all whey proteins) (colored dark red) and alpha-lactalbumin (10-12%) (colored orange). Derived from the dairy cow, these proteins are conformationally intact, and emulsified together with lipophilic compounds and vitamins in raw farm milk. Several processing steps in a dairy plant significantly impair the 3D-structure of whey proteins, their homo- and heteromeric aggregation state, the composition of all hydrophilic and lipophilic milk constituents, and thereby change the immunogenicity and allergenicity of milk

Jensen et al. World Allergy Organization Journal. 2022;15:100668
<http://doi.org/10.1016/j.waojou.2022.100668> (From the DRACMA group)

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Guidelines

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Review of guidelines

Strózyk et al. World Allergy Organization Journal. 2022;15:100613
<http://doi.org/10.1016/j.waojou.2021.100613> (FROM the DRACMA group)

Endorsed society of guidelines (country, year)	AGREE II domain scores						Overall score
	1 scope and purpose	2 stakeholder involvement	3 rigor of development	4 clarity of presentation	5 applicability	6 editorial independence	
NICE (United Kingdom, 2019) ¹⁶	98%	100%	100%	100%	100%	100%	100%
BSACI (United Kingdom, 2014) ¹⁷	100%	74%	91%	100%	82%	100%	100%
WAO (international, 2010) ²	100%	100%	97%	100%	89%	58%	100%
AAAAI and I-FPIES (international, 2017) ¹³	89%	56%	90%	100%	67%	100%	100%
EWGPAG (Italy, 2010) ⁸	89%	83%	32%	94%	68%	75%	78%
Spanish on non-IgE-mediated CMA (SEGHPN, AEPAP, SEPEAP, and SEICAP) (Spain, 2019) ¹⁵	100%	70%	44%	100%	47%	75%	72%
GPIFN and MAP (international, 2019) ¹⁰	70%	85%	28%	81%	69%	100%	50%
ISPGHAN (India, 2020) ¹²	72%	24%	14%	89%	58%	100%	67%
Spanish on IgE-mediated CMA (SEICAP) (Spain, 2015) ⁶	74%	9%	15%	83%	81%	72%	61%
ESPGHAN (Europe, 2012) ¹¹	69%	22%	20%	81%	63%	75%	61%
CNSFP (France, 2018) ⁹	59%	17%	13%	81%	53%	56%	44%
Finnish guidelines (the Finnish Allergy Programme) (Finland, 2012) ¹⁴	22%	15%	4%	50%	14%	53%	17%
Median	82%	63%	30%	92%	68%	75%	70%
q1	70%	21%	15%	81%	57%	69%	58%

The majority of the included CMA guidelines published from 2010 to 2020 were of good or very good quality. However, the weakest domain was the rigor of development, mostly due to the poorly described strengths and limitations of the body of evidence and the procedure for updating the guidelines.

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Treatment



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What is the most standardized/accepted way of establishing tolerance to cow's milk protein?

1. Oral immunotherapy using cow's milk
2. Introducing baked milk containing foods
3. Epicutaneous immunotherapy
4. Prebiotics
5. Probiotics

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How can patients with CMA acquire oral tolerance?

Development of tolerance of milk protein can be determined by using three approaches:

- 1) Using **Oral Immunotherapy**, Epicutaneous Immunotherapy or Sublingual Immunotherapy.
- 2) **Introducing baked milk** containing foods e.g. muffins or pizza at set time points in a child's diet during supervised oral food challenges (OFC) or using a ladder approach to introduce foods such as biscuits/cookies, cakes, muffins, waffles in a sequential and individualized manner at home.

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DRACMA

Treatment

- After a careful review of the summarized evidence and thorough discussions the WAO guideline panel suggests:
 - a) using oral immunotherapy with unheated cow's milk in those individuals with confirmed IgE-mediated CMA who value the ability to consume controlled quantities of milk more than avoiding the large adverse effects of therapy,
 - b) not using oral immunotherapy with unheated cow's milk in those who value avoiding large adverse effects of therapy more than the ability to consume controlled quantities of milk,
 - c) using omalizumab in those starting oral immunotherapy with unheated cow's milk,
 - d) not using oral immunotherapy with baked cow's milk in those who do not tolerate both unheated and baked milk, and
 - e) not using epicutaneous immunotherapy outside of a research setting.

The recommendations are labeled "conditional" due to the low certainty about the health effects based on the available evidence.

Brozek et al. World Allergy Organization Journal, Volume 15, Issue 4, April 2022, 100646
(From the DRACMA group)

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GA²LEN

Treatment

- The GA²LEN Task Force **suggests** offering **oral immunotherapy**, with standardized, evidence-based products and protocols, to selected children (e.g., aged 4+ years) with clinically diagnosed, persistent, severe, IgE-mediated **hen's egg or cow's milk allergy** to increase the amount of allergen tolerated while on therapy.

Muraro A et al. World Allergy Organ J. 2022;15(9):100687.
<https://authors.elsevier.com/sd/article/S1939455122000631>

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Management

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To best manage cow's milk allergy, the most appropriate options is

1. Strict avoidance of cow's milk and cow's milk containing foods at all times
2. An individualized avoidance approach
3. Delay introduction of baked milk as far as possible
4. Use a milk ladder approach in all individuals with cow's milk allergy
5. Use small amount of goat's milk as tolerated

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GA²LEN

Avoidance of the food allergen

- The GA²LEN Task Force **suggests** that people with a documented food allergy **avoid the offending food** unless their **individual** circumstances and risks allow for some consumption, as advised by their healthcare professional.
- The GA²LEN Task Force **suggests** that most breastfeeding mothers whose infants have a food allergy do not need to avoid the offending food themselves, though in rare cases this might be considered.

Muraro A et al. World Allergy Organ J. 2022;15(9):100687.
<https://authors.elsevier.com/sd/article/S1939455122000631>

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DRACMA

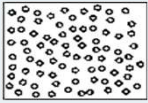


Maternal elimination during breast feeding – past guidelines

- Maternal cow's milk elimination diet was recommended in 8 guidelines.
- Six of the included guidelines recommended against a maternal elimination diet if the infant was asymptomatic on breastfeeding alone; in an additional one, it was recommended against elimination diet in case of mild symptoms.
- Supplementation of the maternal elimination diet with calcium was recommended in 7 guidelines including four guidelines that also recommended supplementation of vitamin D.

Strózyk et al. World Allergy Organization Journal (2022) 15:100613
<http://doi.org/10.1016/j.waojou.2021.100613>

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Defining the term "Hypoallergenic"

Formula type: (protein source)	Amino acid- based (AAF)	Extensively hydrolyzed (eHF)
Protein Source	100% free amino acids	Cow milk
Peptide size, kilodaltons	N/A (free AAs ~0.12 ¹) 	Most <1.5 ² Up to 5% >3.5 ³ 
Allergenicity	Least  Most	
Hypoallergenic? ²	<input checked="" type="checkbox"/> YES	<input checked="" type="checkbox"/> YES

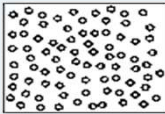




"Hypoallergenic"

- North America: ≥90% of patients with CMA tolerate (with 95% CI)²
- Europe: Formulas labeled "HA" are partially hydrolyzed and should not be used for CMA⁴
- North America & Europe: Extensively hydrolyzed/amino acid-based formulas are recommended for CMA⁵

1. <https://www.seas.upenn.edu/~cis535/Fall2004/HW/GCB535HW6b.pdf>, July 3, 2018. 2. American Academy of Pediatrics Committee on Nutrition. Pediatrics. 2000;106:346-9. 3. Lowe, et al. Expert Rev Clin Immunol. 2013;9:31-41. 4. Bahna. Ann Allergy Asthma Immunol. 2008;101:453-9. 5. Host, et al. Arch Dis Child. 1999;81:80-4. Illustration courtesy of Nutricia Medical and Scientific Affairs, North America.

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Only 2 formula types are hypoallergenic

Formula type: (protein source)	Amino acid- based (AAF)	Extensively hydrolyzed (eHF)	Partially hydrolyzed (pHF)	Regular (Intact protein)
Protein source	100% free amino acids	Cow milk	Cow milk	Cow milk
Peptide size, kilodaltons	N/A (free AAs ~0.12 ¹) 	Most <1.5 ² Up to 5% >3.5 ³ 	Dairy: Most <5 ³ and up to 18% >6 ³ 	Dairy: 14-67 ³ Soy: 20-225 ⁴ 
Allergenicity	Least  Most			
Hypoallergenic? ²	<input checked="" type="checkbox"/> YES	<input checked="" type="checkbox"/> YES	<input type="checkbox"/> NOT HYPOALLERGENIC	<input type="checkbox"/> NOT HYPOALLERGENIC

1. <https://www.seas.upenn.edu/~cis535/Fall2004/HW/GCB535HW6b.pdf>, July 3, 2018. 2. American Academy of Pediatrics Committee on Nutrition. Pediatrics. 2000;106:346-9. 3. Lowe, et al. Expert Rev Clin Immunol. 2013;9:31-41. 4. Hongsprabhas, et al. Joint ACS AGFD-ACS ICST Symposium; 2014. Illustration courtesy of Nutricia Medical and Scientific Affairs, North America.

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What do the guidelines recommend regarding formula choice for specific presentations of food allergies?

Clinical Presentation	DRACMA ¹	BSACI Guidelines ²	NIAID US Guidelines ³	ESPGHAN ⁴
Anaphylaxis	AAF	AAF	No specific recommendation	AAF
Acute urticaria or angioedema	EHF	EHF	No specific recommendation	EHF
Atopic eczema/dermatitis	EHF	EHF	No specific recommendation	EHF
Eosinophilic esophagitis (EoE)	AAF	AAF	The NIAID guidelines acknowledge that trials in EoE have shown symptom relief and endoscopic improvement in almost all children on AAF/elemental diet, though no specific recommendation on formula choice is made.	AAF (as specified by current ESPGHAN guidelines on EoE)
Gastroesophageal reflux disease	EHF	EHF	No specific recommendation	EHF
Cow's milk protein-induced enteropathy	EHF	EHF unless severe in which case AAF	No specific recommendation	EHF but AAF if complicated by faltering growth
Food protein-induced enterocolitis syndrome (FPIES)	EHF	AAF	Hypoallergenic formulas are recommended	EHF
Proctocolitis	EHF	EHF	No specific recommendation	EHF
Breastfeeding with ongoing symptoms (already on maternal elimination diet) or requiring a top-up formula	No recommendation	AAF	No specific recommendation	With severe symptoms that are complicated by growth faltering, a hypoallergenic formula up to 2 weeks may be warranted. In many countries, AAF is used for diagnostic elimination in extremely sick exclusively breast-fed infants. Although this is not evidence based, it is aimed at stabilizing symptoms.

AAF, amino-acid formula; EHF, Extensively hydrolyzed formula; ESPGHAN, European Society for Paediatric Gastroenterology, Hepatology and Nutrition.
 References: 1. Fiocchi et al. J Allergy Clin Immunol. 2010;126(6):1119-28 e12. 2. Luyt et al. Clin Exp Allergy. 2014;44(5):642-72. 3. Boyce et al. J Allergy Clin Immunol. 2010 Dec;126(6):1105-18. 4. Koletzko et al. J Pediatr Gastroenterol Nutr. 2012;55(2):221-229.

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Partially hydrolyzed formula (pHF)

- 0/10 patients with IgE-mediated CMA tolerate pHF
- Reactions occurred to consumption of 15 – 120 ml
- Only NICE guidelines mentioned pHF and recommended against it

- Egan et al. Pediatr Allergy Immunol. 2017 Jun;28(4):401-405.

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GA²LEN

Infant formula choice

- The GA²LEN Task Force **suggests** that most infants (0-1 year) with cow's milk allergy who need a breast milk alternative use a **documented hypoallergenic extensively hydrolyzed cow's milk formula**, or an **amino-acid based formula** if better tolerated or more appropriate.
- The GA²LEN Task Force **suggests** against partially hydrolyzed cow's milk formula, mammalian milks and, for infants under 6 months, soy-based formula.

Muraro A et al. World Allergy Organ J. 2022;15(9):100687.
<https://authors.elsevier.com/sd/article/S1939455122000631>

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DRACMA

Probiotics – summary of current guidelines

- Either no evidence/controversy for use of pre-/probiotics in infant formula for management of cow's milk allergy
- Many current guidelines made no recommendation on the use of pre-/probiotics in infant formula

Strózyk et al. World Allergy Organization Journal (2022) 15:100613
<http://doi.org/10.1016/j.waojou.2021.100613>

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Probiotics

- The GA²LEN Task Force makes no recommendation for or against any **prebiotics, probiotics or synbiotics** that have been evaluated so far for managing food allergy, whether used as a supplement or added to infant formula.

Muraro A et al. World Allergy Organ J. 2022;15(9):100687.
<https://authors.elsevier.com/sd/article/S1939455122000631>

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Plant-Based Based Infant Formula

	Rice-based formula	Soy based formula
Hydrolyzed	Extensively and partially	None
Tolerance	well tolerated in the majority of infants with IgE-mediated cow's milk allergy; can be a concern in non-IgE-mediated cow's milk allergy (FPIES to rice)	Well-tolerated in the majority of infants with IgE-mediated cow's milk allergy; can be a concern in non-IgE-mediated cow's milk allergy
	Enriched with lysine, threonine, tryptophan, carnitine and taurine, iron and zinc.	Enriched with methionine, taurine and carnitine, iron, zinc, calcium, phosphorus.
Taste	Well tolerated	Well-tolerated
Other concerns	Arsenic content is within safe limits	Potential hormonal effects on the reproductive system, due to the isoflavones
		Not recommended for first 6 months of life
		BUT growth, bone health and metabolic, reproductive, endocrine, allergy outcomes and neurological function do not differ between children fed soy formulas, cow's milk formulas and breast milk.

Rice-based formula was recommended as the management of choice in selected infants according to 3 guidelines and, in 1 additional set of guidelines, hydrolyzed rice formula was recommended as an alternative if the infant refuses or does not respond to EHF.

Mentioned by 10 guidelines usually recommended/suggested in children > 6 months

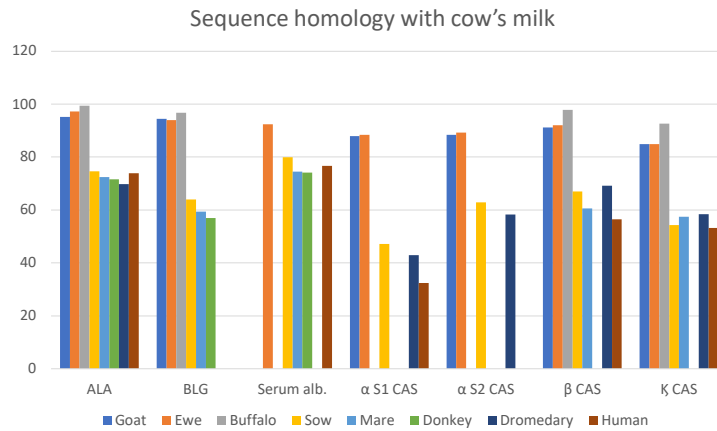
Vandenplas et al. Br J Nutr. 2014;111:1340-60; Agostoni et al. Crit Rev Food Sci Nutr. 2016;56:65-9; Meyer et al. Pediatr Allergy Immunol. 2018;29:561-3; Meyer et al. Clin Transl Allergy. 2016;6:25; Stróżyk et al. Clin Exp Allergy. 2020;50:766-79; Koletzko et al. J Pediatr Gastroenterol Nutr. 2012;55:221-9; Muraro et al. Allergy. 2014;69:1008-25.

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Other Mammalian Milks



- The use of other mammalian milks is not recommended for the management of cow's milk allergy due to a high level of **cross-reactivity** and nutritional concerns.
- **The greatest level of cross-reaction is seen between cow's, sheep/ewe's and goat's milk.**
- Less similarity is seen between these milk and the milk from pig, horse and donkey, camels and dromedaries.



Fiocchi et al. *Pediatr Allergy Immunol.* 2010;21 Suppl 21:1-125.

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DRACMA

Other Mammalian Milks


Use of other mammalian milks was not recommended in children with CMA according to 7 guidelines; however, in 1 of these, an exception was made for equine milk with modified fat content, which could be used as an alternative.

- The use of other mammalian milks is not recommended for the management of cow's milk allergy due to a high level of cross-reactivity and **nutritional concerns**.
- The calcium content of mare's and donkey's milk is lower than cow's milk.
Folate and vitamin B12 content of buffalo, sheep and **goat's** milk is lower than cow's milk and not available for other milks.

Proximates	Promimate composition of human, cow, buffalo, goat, and sheep milks (per 100 g of milk)*														
	Human	Cow		Goat		Buffalo		Sheep		Mare		Donkey		Dromedary/Camel	
	Average	Average	Range	Average	Range	Average	Range	Average	Range	Average	Range	Average	Range	Average	Range
Energy (kJ)	291	262	247-274	270	243-289	412	296-495	420	388-451	199	171-295	156	135-215	234	185-332
Energy (kcal)	70	62	59-66	66	58-74	99	71-118	100	93-108	48	41-71	37	32-51	56	44-79
Total protein (g)	1	3.3	3.2-3.4	3.4	2.9-3.8	4	2.7-4.6	5.6	5.4-6.0	2.0 ^c	1.4-3.2	1.6 ^c	1.4-1.8	3.1 ^d	2.4-4.2
Total fat (g)	4.4	3.3	3.1-3.3	3.9	3.3-4.5	7.5	5.3-9.0	6.4	5.8-7.0	1.6 ^{b,e}	0.5-4.2	0.7 ^b	0.3-1.8	N/A	2.0-6.0
Lactose (g)	6.9	4.7	4.5-5.1	4.4	4.2-4.5	4.4	3.2-4.9	5.1	4.5-5.4	6.6b	5.6-7.2	6.4 ^b	5.9-6.9	4.3 ^a	3.5-4.9

* Values for human milk (mature, fluid) are from USDA (USDA, 2009), food code 01107. The values for cow, goat and sheep milks were calculated using values where available in the following food composition tables: USDA, cow - food code 01211 "Milk, whole, 3.25 percent milk fat, without added vitamin A and vitamin D"; goat - 01106 "Milk, goat, fluid, with added vitamin D"; sheep - food code 01109 "Milk, sheep, fluid" (USDA, 2009); FSA (2002): cow - food code 10-316 "Whole milk, pasteurized, average (average of summer and winter milk)"; goat - 12-328 "Goats milk, pasteurized"; sheep - food code 12-329 "Sheep milk, raw" (FSA, 2002); Danish Food Composition Databank: cow - food code 0156 "Milk, whole, conventional (not organic), 3.5 percent fat"; goat - 0516 "Goat milk" (NFI, 2009); New Zealand food composition tables: cow - food code F1028 "Whole milk, pasteurized, average (average of summer and winter milk)"; goat - 12-328 "Goats milk, pasteurized"; sheep - food code F52 "Sheep's milk, raw" (Espersen et al., 2009); Columbian food composition table: cow - food code G101 "Milk, whole, crude (leche, entera, cruda)"; goat - G086 "Goat milk, whole, crude (leche de cabra, entera cruda)" (FAO/LATINFOODS, 2009). Argentinian food composition table: sheep - food code G087 "milk, of sheep, whole, fresh (leche, de oveja, entera, fresca)" (FAO/LATINFOODS, 2009). The number of data points varied.
 Values for buffalo milk were obtained from Medhammar et al., 2011.
 Values for Energy kJ for mare, donkey, and dromedary camel were obtained from Medhammar et al., 2011. Blank spaces indicate that no data were available.
 The table includes the results of the statistical analysis for buffalo, yak, mare, donkey, dromedary camel and reindeer milks; the other milks did not have enough data points to include them in this analysis. Values in a row with different superscripts are significantly different (P < 0.05).

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Other Plant-Based Beverages


- Plant-based “milk” are used for medical conditions, cultural dietary preferences and a health-related perceptions.
- Plant-based milks are often **nutritionally inadequate**, particularly in children < 1 year of age.
- The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) Nutrition Committee:
 - “In young children beyond the first year of life requiring a dairy-free diet, commercial formula may be a preferable alternative to cow’s milk, when such formula constitutes a substantial source of otherwise absent or reduced nutrients (egg, protein, calcium, vitamin D) in the child’s restricted diet.”
 - inadequate nutritional intake can adversely affect a child’s nutritional status, growth, and development
 - plant-based products should provide a comparable nutritional content to conventional cow’s milk
 - growth studies and bone mineralization studies of young children fed plant-based milks are needed.

Five guidelines recommended against use of soy plant-based beverage in infants with CMA. According to 3 guidelines, use of rice plant-based beverage is not advised in children under 4.5 years of age. Two guidelines, recommend against any plant-based beverages.

Inappropriate use can lead to poor growth, severe growth deficiency disorders in rare cases kwashiorkor/marasmus, electrolyte disorders, kidney stones, and severe nutrient deficiencies including iron deficiency anemia, rickets, and scurvy.

Merritt et al. *Pediatr Gastroenterol Nutr.* 2020;71(2):276-281.

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Plant-Based Beverages

- Alternative beverages include soy, coconut, almond, rice, oat, hazelnut, cashew, walnut, pea, sesame, hemp, tigernut, quinoa
- Availability of these formulas also differ internationally but the majority can be ordered online
- It is important to be aware of the cost of alternative milks, and compare their nutrient composition against that of cow milk, particularly in terms of protein, energy, calcium, vitamin B12, Vitamin D and iodine
- Fat content is also important in children under the age of 2 years

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Factors to consider that may indicate a toddler is ready to transition to a plant-based beverage are:

Child is:

1. At least one year of age and eats a varied solid food diet with a variety of foods from each food group;
2. Gets at least 2/3 of their energy from the varied solid food diet and consumes no more than 16 fluid ounces/500 ml of milk substitute per day
3. Eats age-appropriate textures; AND gets enough protein and fat and micronutrients in the diet from the solid foods and the available milk substitute
4. No feeding difficulties that may reduce food variety, no known micronutrient deficiencies and no religious/cultural dietary requirements that reduces the variety of foods consumed
5. All of the above

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Plant-Based Milk – Buying Guide

- For toddlers who are eating well, children and adults, a suitable plant-based alternative is recommended.
- These milks should ideally only be used in children under 2 years of age following a dietary assessment.
- It should also not be used as a main drink in children under 1 year of age.

Factors to consider that may indicate a toddler is ready to transition to a plant-based beverage are:

- Child is at least one year of age
- Eats a varied solid food diet with a variety of foods from each food group;
- Gets at least 2/3 of their energy from the varied solid food diet;
- Consumes no more than 16 fluid ounces/500 ml of milk substitute per day (this includes breast milk, formula, and other dairy substitutes like yogurt);
- Eats age-appropriate textures; AND
- Gets enough protein and fat and micronutrients in the diet from the solid foods and the available milk substitute
- No feeding difficulties that may reduce food variety
- No known micronutrient deficiencies
- No religious/cultural dietary requirements that reduces the variety of foods consumed

Durban et al. Immunol Allergy Clin North Am. 2021;41(2):233-270.
Groetch and Venter. Journal of Food Allergy. 2020;2:11.

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Summary

DRACMA guidelines are still being developed

Take home points from current guidelines

We need to understand the effect of processing/heating on allergenicity better

Oral immunotherapy should be used in suitable cases

The verdict on pre-/probiotics is still out

INDIVIDUALIZED avoidance of the food allergen(s) should be advised

Use a hypoallergenic formula (not partially hydrolyzed formula)

Avoid other mammalian milks

Use the help of an RD when choosing plant-based milks in children (> 1 year of age)