

Thank you for joining! We'll begin shortly

## What's Under the Lid of Your Hypoallergenic Formula?

**Liz Bacon, MS, RD, LD** Medical Science Liaison September 9, 2025



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#### **Disclosures**

NLC NUTRICIA LEARNING CENTER

Liz Bacon, MS, RD, LD is an employee of Nutricia North America.

Host/Moderator:

Ellen Avery, MS, RD, LD is an employee of Nutricia North America.

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#### **Objectives**



- 1 List beneficial bioactive components in human milk
- 2 Review clinical relevance of prebiotics, nucleotides, and whey in formula
- Describe the importance of lactose in infant formula and benefits to the gut
- 4 Summarize the benefits of these components in formula for infants with food allergies

> Nutricia North America supports the use of human milk wherever possible.

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## Alphabet Soup Exclusive Breathering Human Milk Nursing Described by Milk Nursing Breastfeeding Human Milk Breast Milk Nursing Need Feedings Need Feedings

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Alphabet Soup	NUTRICA ALARMAN CHINTER
Human Milk Nursing Nursing Nursing Expressive Organization Breastfeeding Human Milk	Breast Milk/Human Milk Milk produced by the human mammary glands to feed infants and young children
Breast Milknessy Mod Feeding Ponor Human Milk	Breastfeeding The practice of feeding an infant or young child breastmilk directly from the breast

#### MINLC **Benefits of Breastfeeding** Victora CG, Bahl R, Barros AJ, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. Lancet. 2016;387:475-90. **Risk Reduction Higher Performance** Sudden infant death: 36% Intelligence tests: 3.4 IQ Necrotizing enterocolitis: 58% Otitis media: 43% Asthma: 9% Malocclusions: 68% Overweight/Obesity: 26% Type 2 Diabetes: 35%

## **Stages of Human Milk Consumption**



#### Colostrum

- · Rich in protein, fat-soluble vitamins, minerals, and
- immunoglobulins Passive immunity



#### **Transitional Milk**

- water-soluble vitamins
  Higher in kcals than



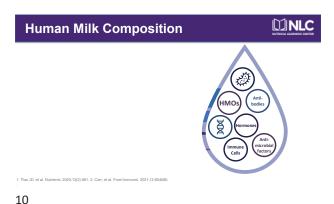
#### **Mature Milk**

- Fore milk: start of
- feed Hind milk: as breast
- empties

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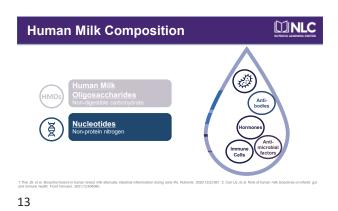
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#### **Human Milk Composition** Water (86-88%) Carbohydrates (lactose; 7%) Fat (4%) Protein (1%) Vitamins & Minerals (0.2%) z DA, et al. BMC Pediatr. 2014;14:216.



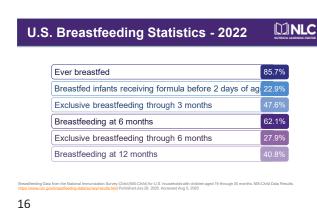


1.That JD, et al. Nations. 2020;12(2):581. Z. Carr LE, et al. Role of human mit bloachies on infants' gut and immunologoaccumides: health breefds, potential applications in refer formulae, and pharmacology. Nations. 4020;12:284



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KEEP IN MIND:
The majority of infants will receive some formula in the first 6 months of life.





History of Infant Formula

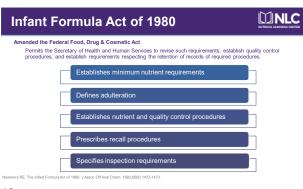
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Geinman RE, Greer FR, Pediatric Nutrition, 8th ed. Itasca, IL: American Academy of Pediatrics: 2020.

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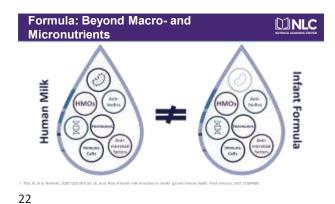


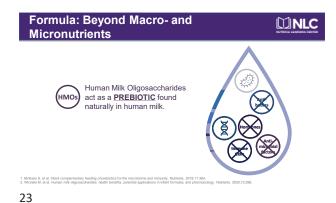
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Formula Ingredients	DI NLC NUTHICIA LEARNING CENTER	
GRAS or FDA-approved safe food additives	Examples:	
"Label claim" of an ingredient is the minimum among present at the end of shelf life	Taurine DHA/ARA Prebiotics/Probiotics	
Structure function label claims for infant formula ingredients	Lutein/Lycopene Lactoferrin	
"Truthful and not misleading"     "Competent and reliable scientific evidence"		
GRAS = generally recognized as safe; FDA = Food and Drug Administration.  Notinman RE, Gree FR. Pedidiric		

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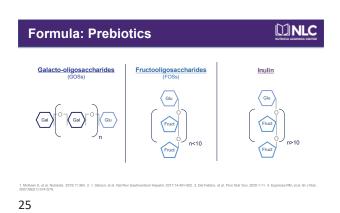
Infant formula is intended as an effective substitute for infant feeding.

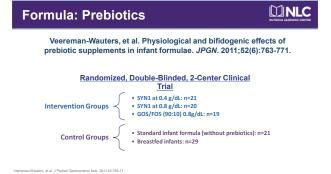




International Scientific
Association for Probiotics &
Prebiotics (ISAPP)
A prebiotic is 'a substrate that is selectively utilized by host microorganisms conferring a health benefit

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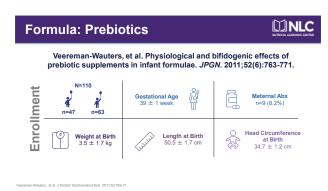


MINLC Formula: Prebiotics Veereman-Wauters, et al. Physiological and bifidogenic effects of prebiotic supplements in infant formulae. JPGN. 2011;52(6):763-771. Enrollment Day 14 Day 28 DOB
Sex
Gestational age
APGAR scores (1-10 minutes) Anthropometrics
 Fecal microbiota
 Parental records
 Formula intake
 Stool characteri Formula intakeStool characteristics Stool characteristicsCrying behaviorOccurrence of Mother antibiotic intake Perinatal data Crying behaviorOccurrence of regurgitation

Occurrent Mode of delivery
Anthropometrics at birth
Fecal microbiota (day 3) regurgitation

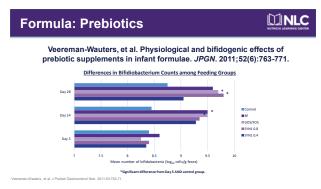
Occurrence of vomiting

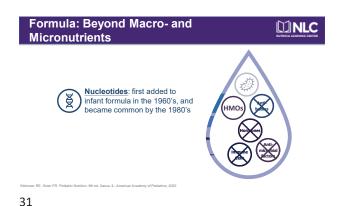
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Formula: Prebiotics			NUTRICIA LEARNING CENTER
		uters, et al. Physiological and bifidogenic effe ements in infant formulae. <i>JPGN</i> . 2011;52(6):70	
	Anthropometrics	No influence on growth during study period	
8	Food Intake	No difference between groups	
Day 28	Regurgitation & Vomiting	Little to no difference between groups	
Õ	Stool Frequency	No difference between groups Stool frequency decreased with time	
	Stool Consistency	Breastfed infants had the softest stools; control group had the hall infants on prebiotics had softer stools than the control group	ardest





The FDA does not set recommended levels of nucleotides for infant formula.

Nucleotides are not essential.
HOWEVER, during periods of rapid growth or disease, nucleotide synthesis may not be able to keep up with demand.

Gutierrez-Castrellon P, et al. Immune response to nucleotide-supplemented infant formulae: systematic review and meta-analysis. Br J Nutr. 2007;98(Supp1):S64-S67.

Databases

PubMed, Embase, LILACS, ARTEMISA, Cochrane Controlled Trial Register, Bandoller, and DARE

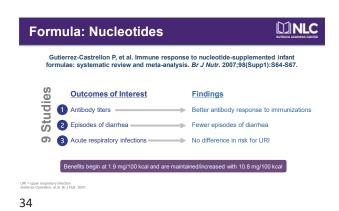
Inclusion Criteria

• RCT comparing Infant formula containing ribonucleotides with formulae without nucleotides or breastmik

• Healthy children under 2 years of age

Publication Quality

• Jadad and CONSORT guidelines



Wang L, et al. Effects of dietary nucleotide supplementation on growth in infants: a metaanalysis of randomized controlled trials. Eur J Nutr. 2019;58(3):1213-1221.

Databases

• PubMed, Web of Science, Cochrane Library, China National
Knowledge Infrastructure Database

Inclusion Criteria

• RCT focusing on effect of nucleotide supplementation on growth
• Healthy infants; no congenital or hereditary conditions
• Nucleotide supplementation was initiated within 1-month post-birth

Publication Quality

• PRISMA Guidelines
• Cochrane Collaboration Risk of Bias Tool

MINLC Formula: Nucleotides Wang L, et al. Effects of dietary nucleotide supplementation on growth in infants: a meta-analysis of randomized controlled trials. Eur J Nutr. 2019;58(3):1213-1221. **Outcomes of Interest Findings** 1 Weight & z-score -No effect of nucleotide supplementation 2 Rate of weight gain — Sig. increased rate [0.26 (95%CI: 0.06-0.47)] 3 Length & z-score = No effect of nucleotide supplementation 4 Rate of linear growth -Only 1 article identified 5 Head circumference & z-score = Sig. differences at 7-8 weeks [0.30 (95%Cl: 0.10-0.50)]\* 6 Rate of head circumference gain Sig. increased rate [0.34 (95%CI: 0.09-0.58)]

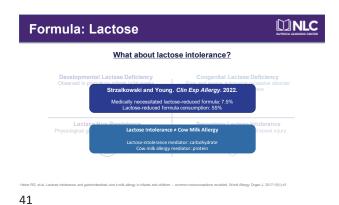
\*No effect on head circumference at week 16 and 20-28

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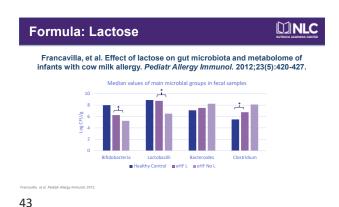
Wang, et al. Eur J Nutr. 2019.

Fo	rmula: Macronutrient Composition - F	Protein DINC
	Whey vs. Casein	
	Whey:Casein Ratio	
	∰ Human Milk 60:40  ☐ Cow Milk 20:80	
	Human milk proteins: composition and physiological significance. Needle Nutr Inst Workshop Series. 2019;90:93-101	
37		
Fo	rmula: Macronutrient Composition - F	Protein WINCA MANNING CONTEX
	Whey vs. Casein	
	Whey:Casein Ratio  Will Human Milk 60:40  COw Milk 20:80	Meyer, et al.  BMC Gastroenterol. 2015   Gastroesophageal Reflux  Gastric Emptyling
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	BM. Haman milk prateine: composition and physiological significance. Neatle Net rest Workshop Series. 2019;50:33-1 and degree of hydrolysis on gastric emplying in children. BMC Gastroenterol. 2015;15:137.	IO1. 2. Meyer, et al. Systematic review of the impact of feed
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	ormula: Macronutrient Compositi arbohydrate	on -
_ 0	<u>Lactose</u>	
	<ol> <li>Human milk contains ~7% carboh</li> <li>Primary carbohydrate in huma mil</li> <li>Lactose is a disaccharide</li> </ol>	
	Gal Glu	
Heyman ME	Committee on Nutrition, Ladose intelerance in Infants, children, and adolescents, Pediatrics. 2006;1118(3):127	9-1285.

What about lactose intolerance?			
Developmental Lactase Deficiency Observed in premature infants (<34 weeks gestation)	Congenital Lactase Deficiency Rare and severe autosomal recessive disorder presenting in newborns		
	MM		
Lactase Non-Persistence Physiological gradual decline of lactase activity	Secondary Lactose Intolerance May occur secondary to small bowel injury		
(Š)			

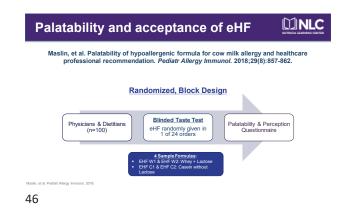


Formula: Lactose	MUTRICIA LEARNING CENTER		
Francavilla, et al. Effect of lactose on gut microbiota and metabolome of infants with cow milk allergy. <i>Pediatr Allergy Immunol.</i> 2012;23(5):420-427.			
Prospective Clinical Trial  Study Groups   • Control (n=12): healthy infants • Intervention (n=16): infants with CM  Intervention   • Phase 1: 2 eHF without lactose for 2 • Phase: 2: eHF with lactose for 2 mon			



How might these components in formula benefit infants with food allergies?

Palatability and acceptance of formula in CMA	DINLC
Sensory experiences that infants experience in the first m of life may correlate with food preferences in both childhoo adulthood	
Health professionals often observe selective/picky eating behaviors in children with a history of cow milk allergy      Hydrolysates and amino acid-based formulas are less palatable due to the hydrolysis process	
Warren CML et al. The US population-level burden of cont's milk allergy. World Allergy Organ J. 2022;15(4):100644.	



Palatability and acceptance of eHF

Maslin, et al. Palatability of hypoallergenic formula for cow milk allergy and healthcare professional recommendation. *Pediatr Allergy Immunol.* 2018;29(8):857-862.

Palatability Questionnaire Increase the chance of non-rejection

- Results in more content families
   Decreases wastage & healthcare costs
   Increases compliance
   Decreases witch to other formula

- Results in more content infants



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## Prebiotic Fibers and Bifidogenic Gut Colonization DINLC WE KNOW Supplementing Term Formula with GOS:FOS... 1 Stimulates the growth of bifidobacteria and lactobacilli in the intestine 2 Results in stool characteristics close to those found in human milk-fed

### Prebiotic Fibers and Bifidogenic Gut Colonization DINLC WE KNOW Supplementing Term Formula with GOS:FOS... 1 Stimulates the growth of bifidobacteria and lactobacilli in the intestine 2 Results in stool characteristics close to those found in human milk-fed Arslanoglu, et al. Early supplementation of prebiotic Asianogiu, et al. Early supperhentation of preblotic oligosaccharides protects formula-fed infants against infections during the first 6 months of life. *J Nutr.* 2007;137(11):2420-2424. 49 MINLC GOS/FOS: Developing infections and allergies Arsianogiu, et al. Early supplementation of prebiotic oligosaccharides protects formula-fed infants against infections during the first 6 months of life. *J Nutr.* 2007;137(11):2420-2424. Randomized, Double-Blinded, Controlled Study Healthy, term infants Parental history of atopic eczema, allergic rhinitis, or asthma Inclusion Control (n=104): 0.0 g/100 mL GOS/FOS **Study Groups** Intervention (n=102): 0.8 g/100 mL GOS/FOS

50

# GOS/FOS Decreases the incidence of infections during the first 6 months of life Arslanoglu, et al. Early supplementation of prebiotic oligosaccharides protects formula-fed infants against infections during the first 6 months of life. J Nutr. 2007;137(11):2420-2424.

rslanoglu, et al. J Nutr. 2007



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#### GOS/FOS Decreases the incidence of some allergic manifestations in the first 5 years

Arslanoglu, et al. Early neutral prebiotic oligosaccharide supplementation reduces the incidence of some allergic manifestations in the first 5 years of life. *J Biol Regul Homeost Agents*. 2013;26(3 Suppl):49-59.



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#### GOS/FOS Decreases the incidence of some allergic manifestations in the first 5 years

Arslanoglu, et al. Early neutral prebiotic oligosaccharide supplementation reduces the incidence of some allergic manifestations in the first 5 years of life. *J Biol Regul Homeost Agents*. 2013;26(3 Suppl):49-59.



Prevalence of persistence allergic manifestations at 5y in relation to the presence of atopic dermatitis at 6 months			
Allergic Manifestation at 5y	Odds Ratio		
Any persistent allergic manifestation	6.2 (1.9-20.3)		
Persistent atopic dermatitis	30.4 (3.4-272.8)		

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#### **In Summary**



Human milk provides infants with and without disease ideal nutrition and support growth and development.

Infant formulas are incorporating key elements of human milk - lactose, prebiotics, nucleotides, DHA/ARA - shown to support gut health and the immune system

Supporting infants with cow milk allergy:

- Incorporating whey and lactose into eHF may improve palatability
- Efforts to support the gut microbiome by consuming prebiotics appear to be beneficial

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