HUMAN MILK BANKING:
THE RIGHT TO ACCESSIBILITY TO EVERY NEWBORN

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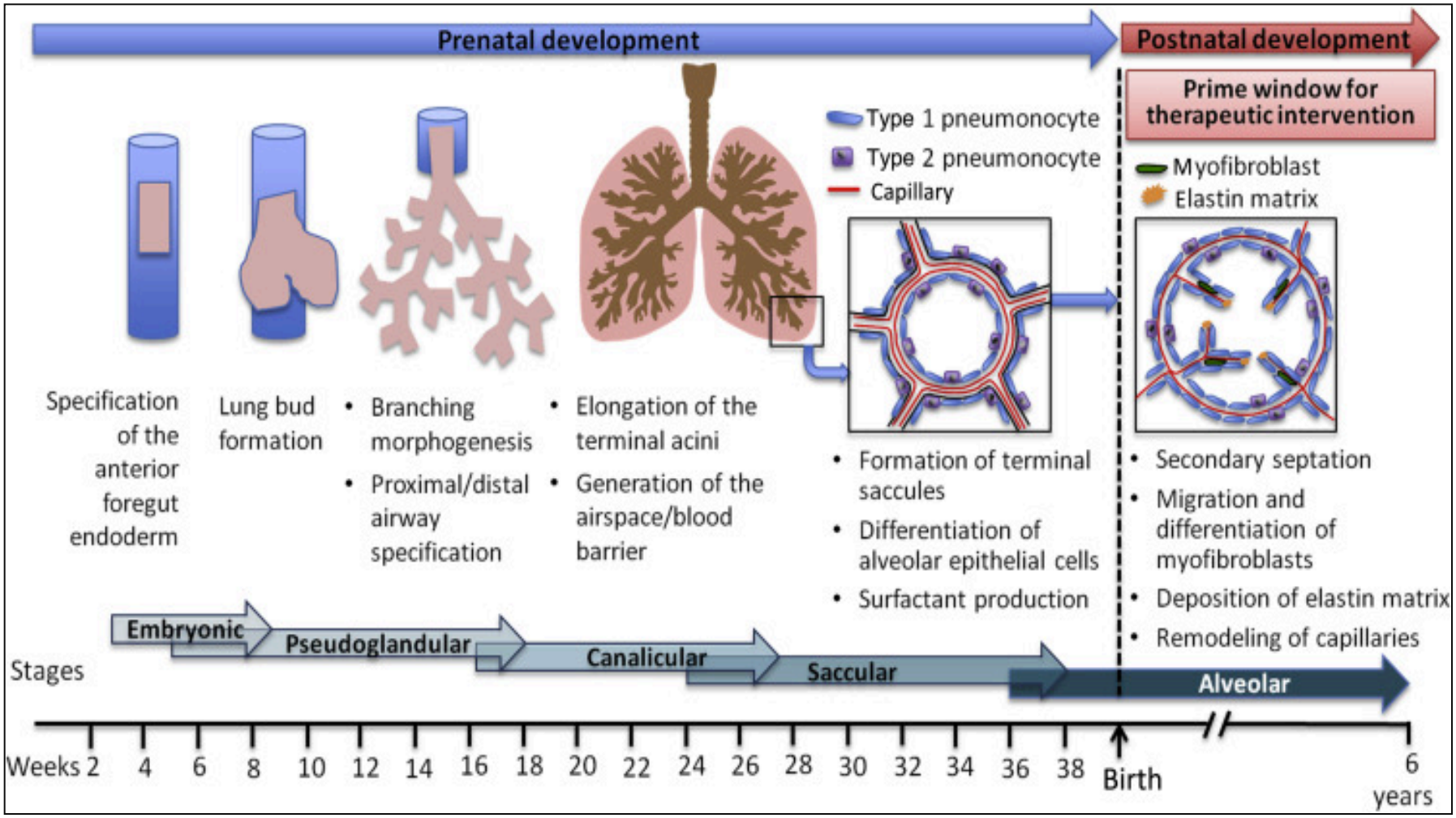
Outline

- The key role of human milk (HM) in shaping the health
- The vital importance for preterm infants
- Emerging bioactive compounds in HM
- Donor human milk (DHM): the second best option
- Clinical benefits deriving from the use of DHM
- Human milk banking in Europe, some practical and organizational points

Nutrition is a key factor for normal development of all fetal (and neonatal) organs and their function.

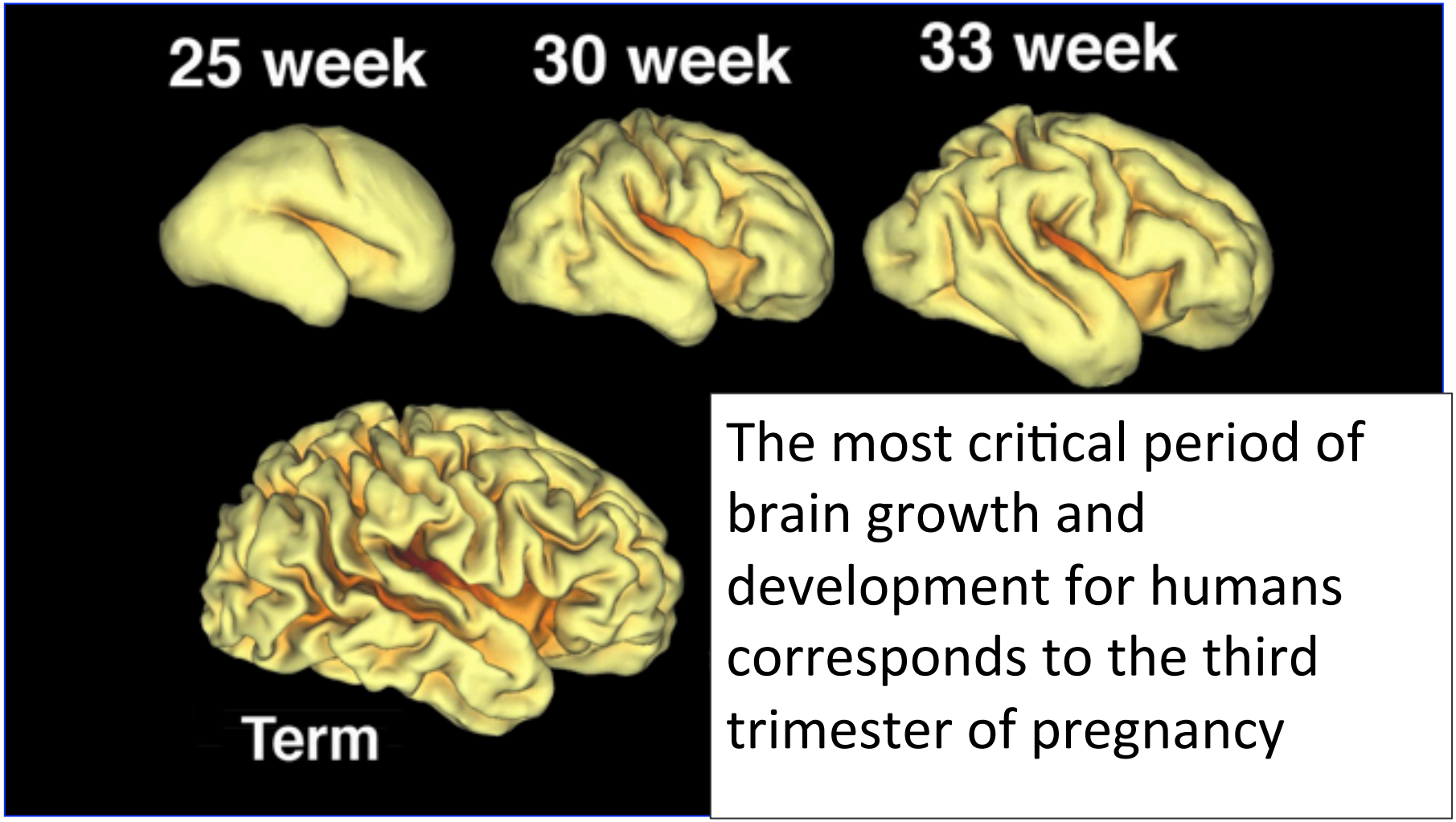
Critical (Vulnerable) Window

Impact of Nutrition- Lung



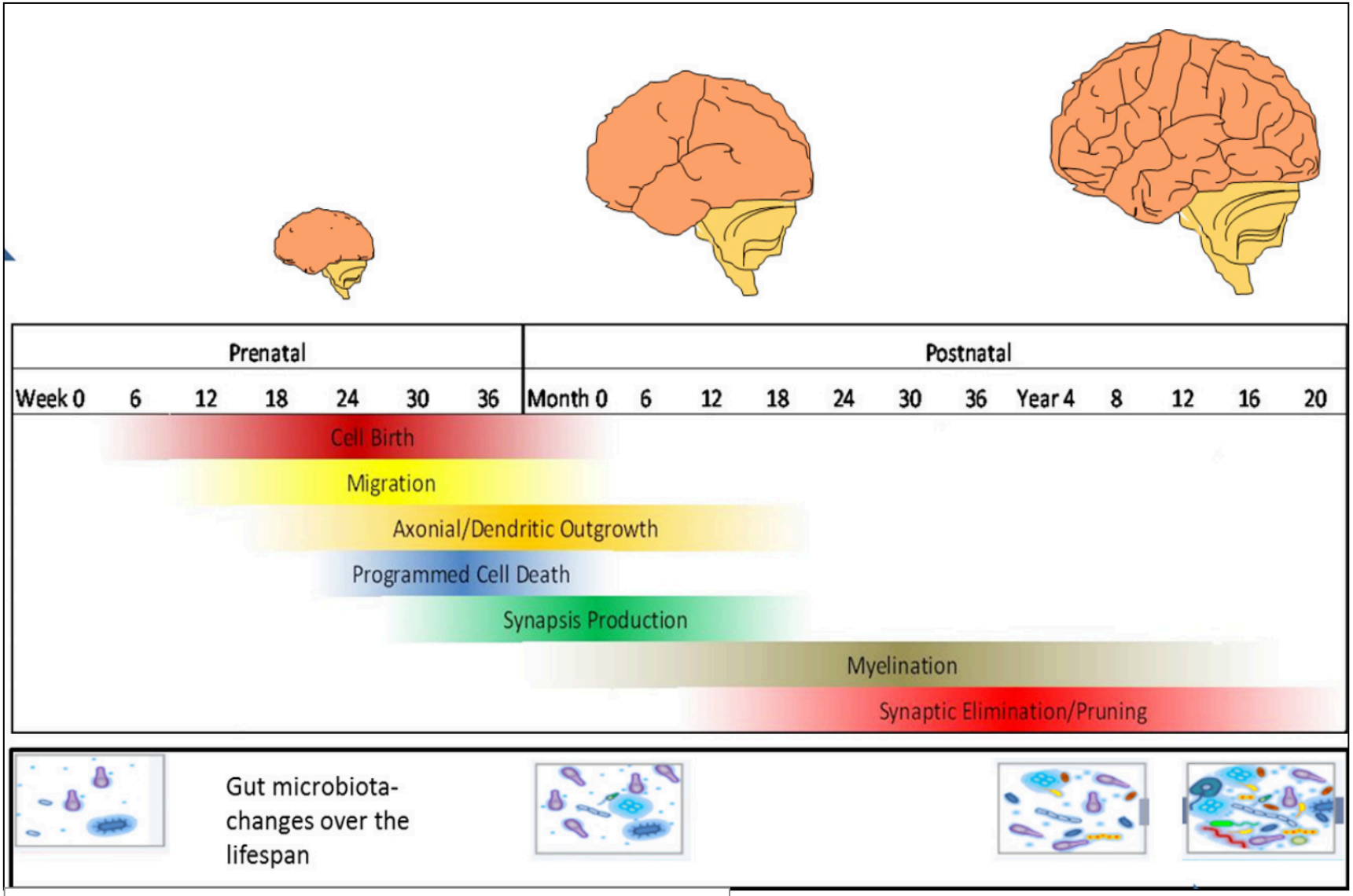
Normal lung development occurs in distinct stages, all can be affected by impaired availibility of oxygen and other nutrients.

Brain



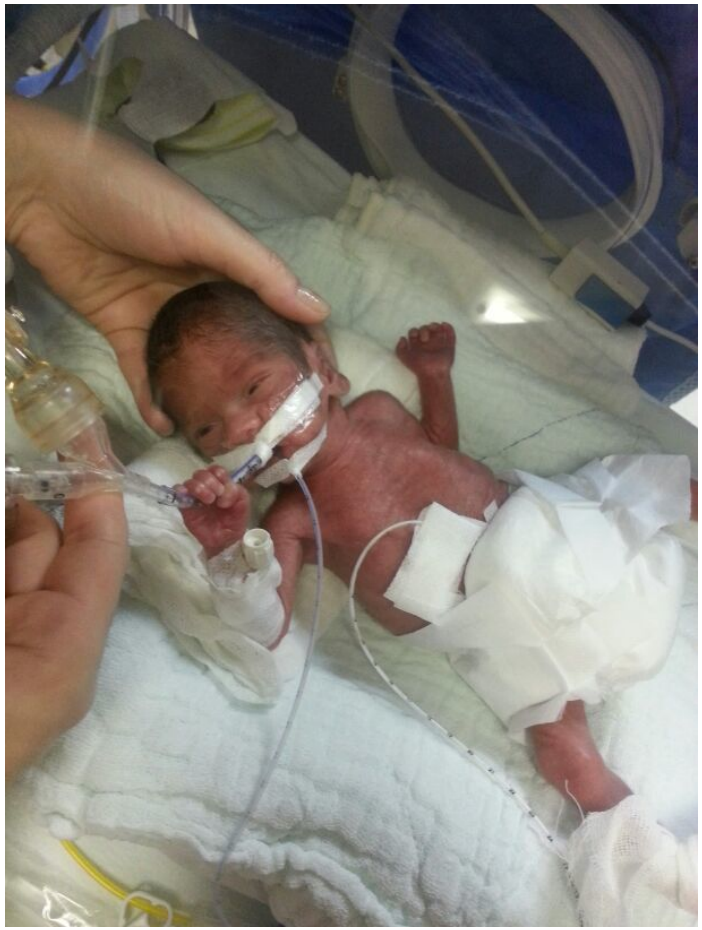
The most critical period of brain growth and development for humans corresponds to the third trimester of pregnancy

Gut Microbiota



O'Mahony S. Neuroscience 2017

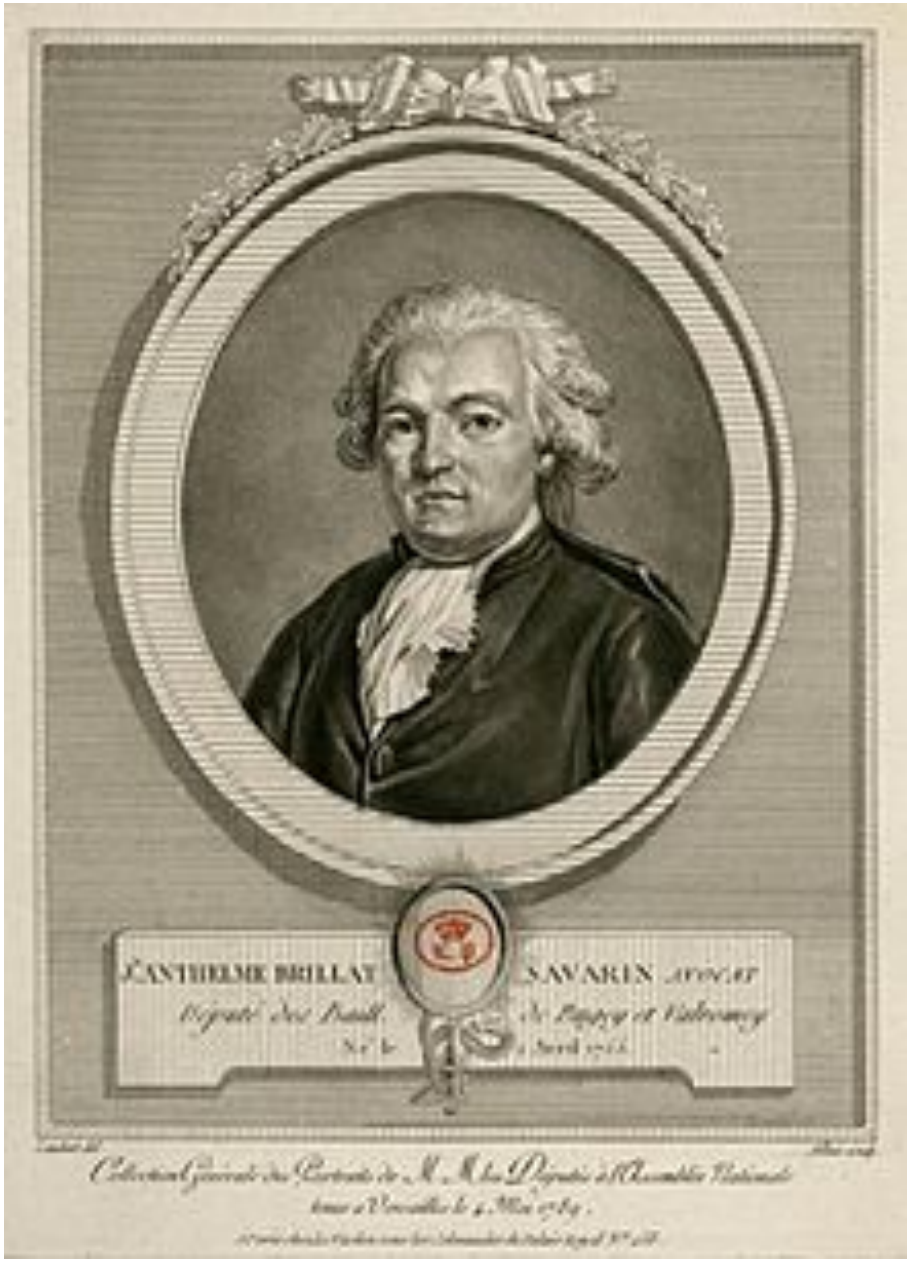
High Level of Responsibility
All under our hands…



- For preterm infants these developmental processes take place in the neonatal intensive care unit (NICU) environment.

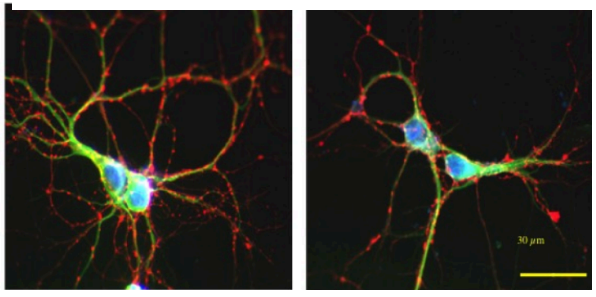
Tell me what you eat and I will tell you what you are !

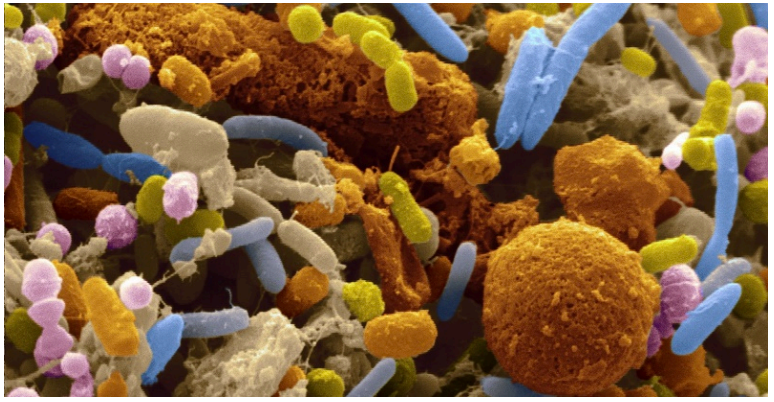
Jean Anthelme Brillat-Savarin
1755-1826



Nutrition is fundamental for..

- growth
- development and maturation of the tissues and organs
- “programming”
- development of a balanced microbiota





Nutritional Goals

- Ensure a growth similar to the IU growth rate

- Ensure a body composition similar to that of the fetus of the same gestational age
- Prevent postnatal growth failure
- Minimize the risk of NEC
- Ensure a satisfactory neurocognitive development
- Promote the development of a balanced intestinal microbiota
- Improve the health outcomes at the short- and long-term

Arslanoglu S. Enteral Nutrition of Preterm Infants. Textbook of Neonatology 2017

Recipe=HM

- Dual action
  - Source of nutrients
  - A myriad of bioactive components
- The most potent immunonutrient
- A synbiotic
- Chronobiotic
- Proven clinical benefits

HUMAN MILK

- Human milk is an admirable biological fluid that has evolved through millions of years
- Sustains life in a pathogen rich and nutrient-poor extrauterine environment
- Crucial for nutrition and immuno-protection and….

PROVEN HEALTH BENEFITS OF HUMAN MILK- Term Infants

Prevention against

- Infection
- Obesity
- Diabetes
- Guluten enteropathy, IBD
- Leukemia
- SIDS
- Allergy

Improves NC Outcome

Decreases Mortality

PROVEN HEALTH BENEFITS OF HUMAN MILK- Preterm Infants

- **Prevention against NICU Challenges**
  - Sepsis*
  - NEC
  - BPD
  - ROP
- **At intermediate and long-term effect**
  - Improves neurocognitive outcome
  - Prevention against CV disease risk factors
- **Decreases mortality***

ORIGINAL ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS

Does Breastmilk Influence the Development of Bronchopulmonary Dysplasia?

Juliane Spiegler, MD[1], Michael Preuß, PhD[2], Corinna Gebauer, MD[3], Meike Bendiks, MD[1], Egbert Herting, PhD[1], and Wolfgang Göpel, MD[1], on behalf of the German Neonatal Network (GNN)*

ASN 2014 ANNUAL MEETING SYMPOSIUM SUMMARY

It's Alive: Microbes and Cells in Human Milk and Their Potential Benefits to Mother and Infant[1–3]

Lars Bode,[4]* Mark McGuire,[5] Juan M. Rodriguez,[6] Donna T. Geddes,[7] Foteini Hassiotou,[7] Peter E. Hartmann,[7] and Michelle K. McGuire[8]

[4]Department of Pediatrics, University of California, San Diego, La Jolla, CA; [5]Department of Animal and Veterinary Sciences, University of Idaho, Moscow, ID; [6]Department of Nutrition, Food Science, and Food Technology, Complutense University of Madrid, Madrid, Spain; [7]School of Chemistry and Biochemistry, Faculty of Science, University of Western Australia, Crawley, WA, Australia; and [8]School of Biological Sciences, Washington State University, Pullman, WA

ABSTRACT

Human milk is the optimal source of nutrition for the nursing infant. Classically, the nutrients (water, protein, lipid, carbohydrate, vitamins, and minerals) were studied as the critical components of milk serving the growth needs of the infant for optimum growth. However, human milk contains factors other than the classically defined nutrients for which researchers are investigating potential roles in infant and maternal health, development, and well-being. The symposium addressed some of the exciting factors being studied, including microbes and maternal cells found within milk. Drs. Michelle McGuire and Juan M. Rodriguez addressed the presence of a bacterial community in human milk produced by healthy and mastitic mothers, potential sources of those bacteria, and the impact of milk-derived bacteria on the nursing infant. Drs. Donna Geddes, Peter Hartmann, and Foteini Hassiotou discussed the potential importance of maternal cells. For years, immune cells were known to be present in human milk, but recent evidence suggests that their impact is as much on the infant as on the health of the lactating mammary gland. Finally, the existence of highly plastic stem cells in human milk opens doors for previously unforeseen developmental "training" of the nursing infant. *Adv Nutr* 5: 571–573, 2014.

Introduction

Human milk is "alive" and contains cells of both bacterial and host origin. Typically, the presence of bacteria in milk was considered an indication of infection. However, this notion may need revision because culture-dependent and -independent techniques more recently revealed that human milk produced by healthy women contains a diverse microbial community including >200 phylotypes. A core milk microbiome with a limited number of operational taxonomic units represents ~50% of the relative abundance. The other 50% of bacteria in human milk appears to be very person-alized, suggesting that their community structure can be modified by the mother's environmental exposure. How these bacteria reach the mammary gland and are incorporated into the milk remains unclear. Combined results of various studies suggest that some bacteria present in the maternal gastrointestinal tract could reach the mammary gland during late pregnancy and lactation through a mechanism involving intestinal immune cells. Thus, modulation of the maternal gastrointestinal microbiota during pregnancy and lactation could have a direct effect on infant health via their incorporation into milk. Conversely, some factors may cause a mammary dysbiosis, leading to infectious mastitis, a condition that represents 1 of the primary medical causes for early undesired weaning. Thus, altering human milk microbiota may offer novel ways to improve the health of the breast-fed infant and potentially the breastfeeding mother. The symposium presentations by Drs. Michelle McGuire and Juan M. Rodriguez focused on bacterial cells and shared emerging research data from metagenomic, transcriptomic, and metabolomic studies focused on the role of human milk bacteria in health and disease. Dr. Donna Geddes' symposium presentation focused on maternal immune cells because their numbers and composition rapidly respond to infections in the mammary gland and other maternal infections but also to infant infections. Although the maternal response to infant infection is not fully understood, it was

*This article is a summary of the symposium "It's Alive: Microbes and Cells in Human Milk and Their Potential Benefits to Mother and Infant" held 29 April 2014 at the ASN Scientific Sessions and Annual Meeting at Experimental Biology 2014 in San Diego, CA. The symposium was sponsored by the American Society for Nutrition (ASN), and the ASN Lactation Research Interest Section, and was supported by a nonrestricted educational grant from Medela.
†The organizer has indicated that attendees at the symposium will be submitted for publication in an upcoming issue of Advances in Nutrition.
‡Author disclosures: L. Bode, M. McGuire, J. M. Rodriguez, D. T. Geddes, F. Hassiotou, P. E. Hartmann, and M. K. McGuire, no conflicts of interest.
*To whom correspondence should be addressed. E-mail: lbode@ucsd.edu.

Advances in Nutrition An International Review Journal

Cochrane Library
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Formula versus donor breast milk for feeding preterm or low birth weight infants (Review)

Quigley M, McGuire W

Quigley M, McGuire W.
Formula versus donor breast milk for feeding preterm or low birth weight infants.
Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD002971.
DOI: 10.1002/14651858.CD002971.pub3.

www.cochranelibrary.com

Formula versus donor breast milk for feeding preterm or low birth weight infants (Review)

WILEY

Human Milk Feeding as a Protective Factor for Retinopathy of Prematurity: A Meta-analysis

Jianjun Zhou, MD*, Vivek V. Shukla, MD†, Danny John, MBA, MPH†, Chao Chen, MD, PhD*

abstract

OBJECTIVE: Studies have suggested that human milk feeding decreases the incidence of retinopathy of prematurity (ROP); however, conflicting results have been reported.

OBJECTIVE: The aim of this meta-analysis was to pool currently available data on incidence of ROP in infants fed human milk versus formula.

DATA SOURCES: Medline, PubMed, and EBSCO were searched for articles published through February 2015.

STUDY SELECTION: Longitudinal studies comparing the incidence of ROP in infants who were fed human milk and formula were selected. Studies involving donor milk were not included.

DATA EXTRACTION: Two independent reviewers conducted the searches and extracted data. Meta-analysis used odds ratios (ORs), and subgroup analyses were performed.

RESULTS: Five studies with 2208 preterm infants were included. Searches including various proportions of human milk versus formula, any-stage ROP, and severe ROP were defined to pool data for analyses. For any-stage ROP, the ORs (95% confidence intervals [CIs]) were as follows: exclusive human milk versus any formula, 0.29 (0.12 to 0.72); mainly human milk versus mainly formula, 0.51 (0.26 to 1.03); any human milk versus exclusive formula, 0.54 (0.15 to 1.96); and exclusive human milk versus exclusive formula, 0.25 (0.13 to 0.49). For severe ROP, they were 0.11 (0.04 to 0.30), 0.16 (0.06 to 0.43), 0.42 (0.08 to 2.18), and 0.10 (0.04 to 0.29), respectively.

LIMITATIONS: Prospective randomized studies being impossible because of ethical issues, we chose observational studies for analysis. A few studies involving subgroup analyses presented high heterogeneity.

CONCLUSIONS: Based on current limited evidence, in very preterm newborns, human milk feeding potentially plays a protective role in preventing any-stage ROP and severe ROP.

*Children's Hospital of Fudan University, Shanghai, China; †The Hospital for Sick Children, Toronto, Ontario, and ‡Hospital Spon Asscos Education Initiative, Manchester, United Kingdom

Drs Zhou and Chen conceptualized the study; Drs Zhou, Shukla, and Chen planned the study; Drs Zhou and Shukla searched for articles and drafted the manuscript; Dr Chen supervised the progress of the study; Drs Zhou and Shukla and Mr John collected data; Mr John performed the meta-analysis and critically appraised the manuscript; and all authors revised the manuscript and consented to the final manuscript as submitted.

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Address correspondence to Chao Chen, Division of Neonatology, Children's Hospital of Fudan University, 399 Wanyuan Road, Minhang District, Shanghai, China 201102. E-mail: chen0108@163.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

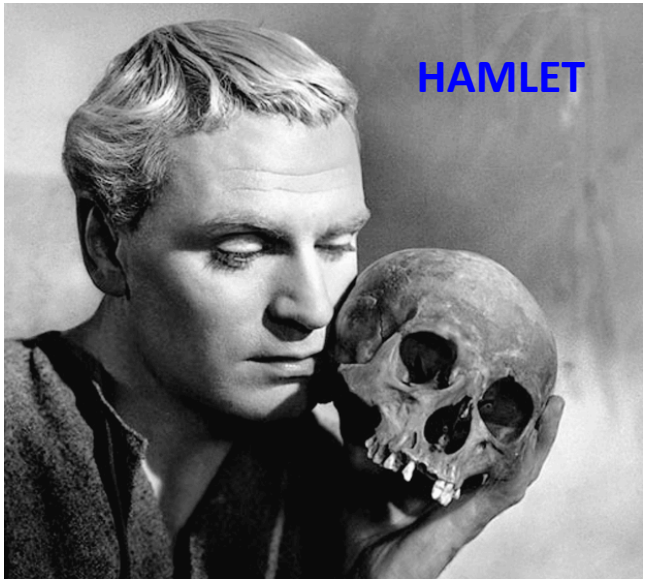
REVIEW ARTICLE

Every Drop is Gold

HM is a life-saving, disease preventing immuno-potent nutrient.

Therapeutic nutrient

HM- A Myriad of Bioactive Compounds



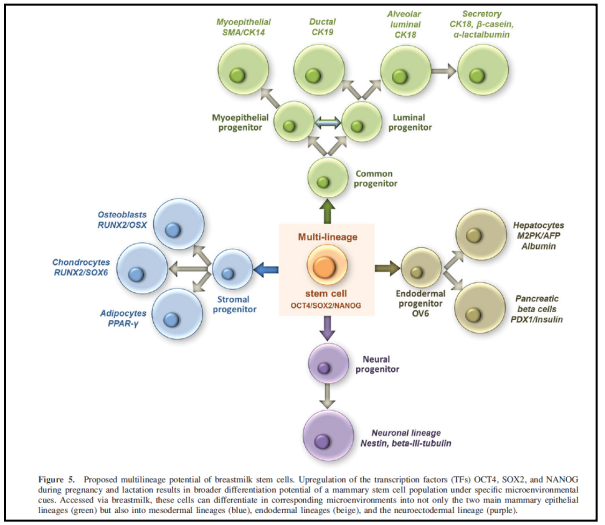
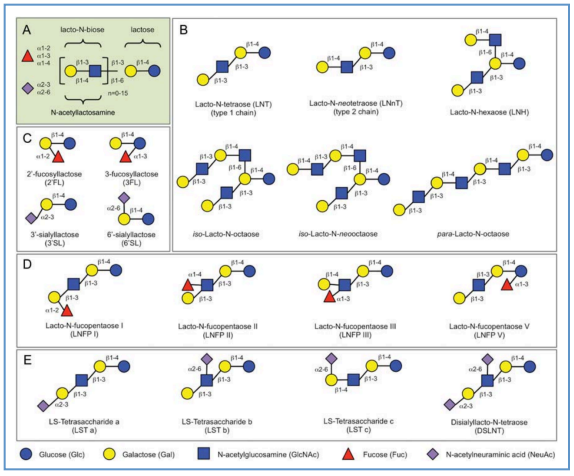
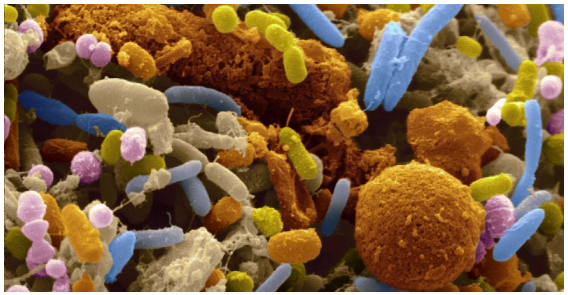
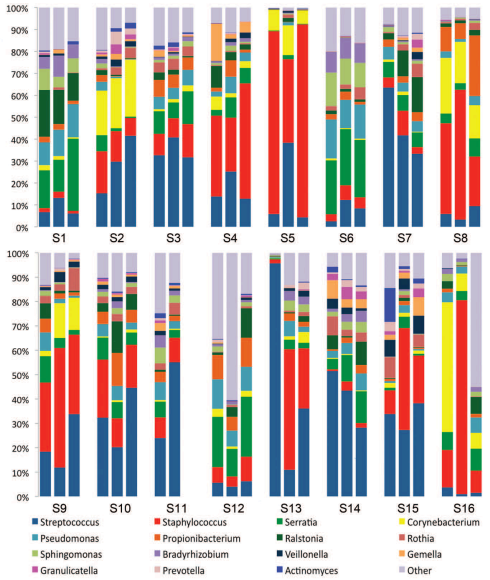


Figure 5. Proposed multilineage potential of breastmilk stem cells. Upregulation of the transcription factors (TFs) OCT4, SOX2, and NANOG during pregnancy and lactation results in broader differentiation potential of a mammary stem cell population under specific microenvironmental cues. Accessed via breastmilk, these cells can differentiate in corresponding microenvironments into not only the two main mammary epithelial lineages (green) but also into mesodermal lineages (blue), endodermal lineages (beige), and the neuroectodermal lineage (purple).

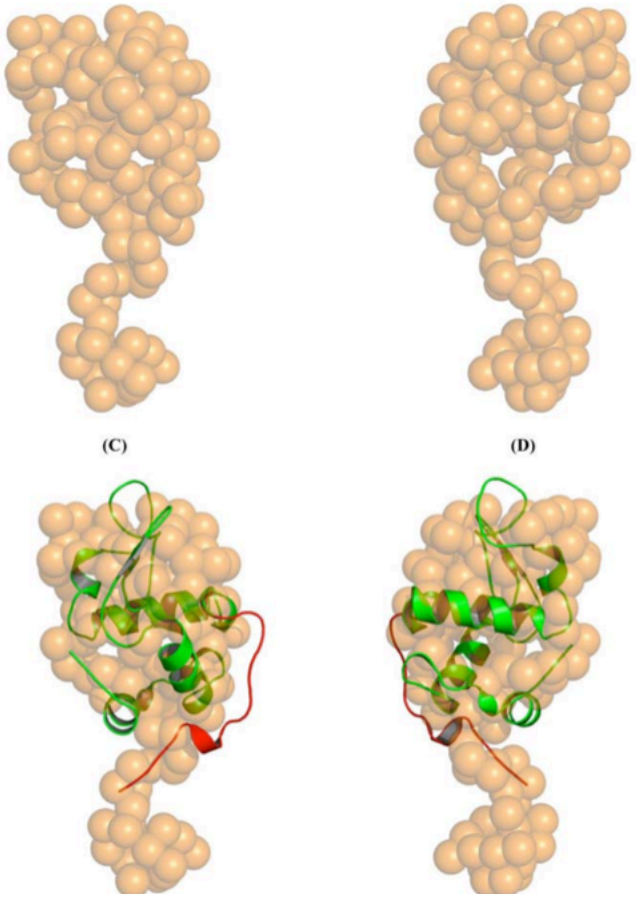




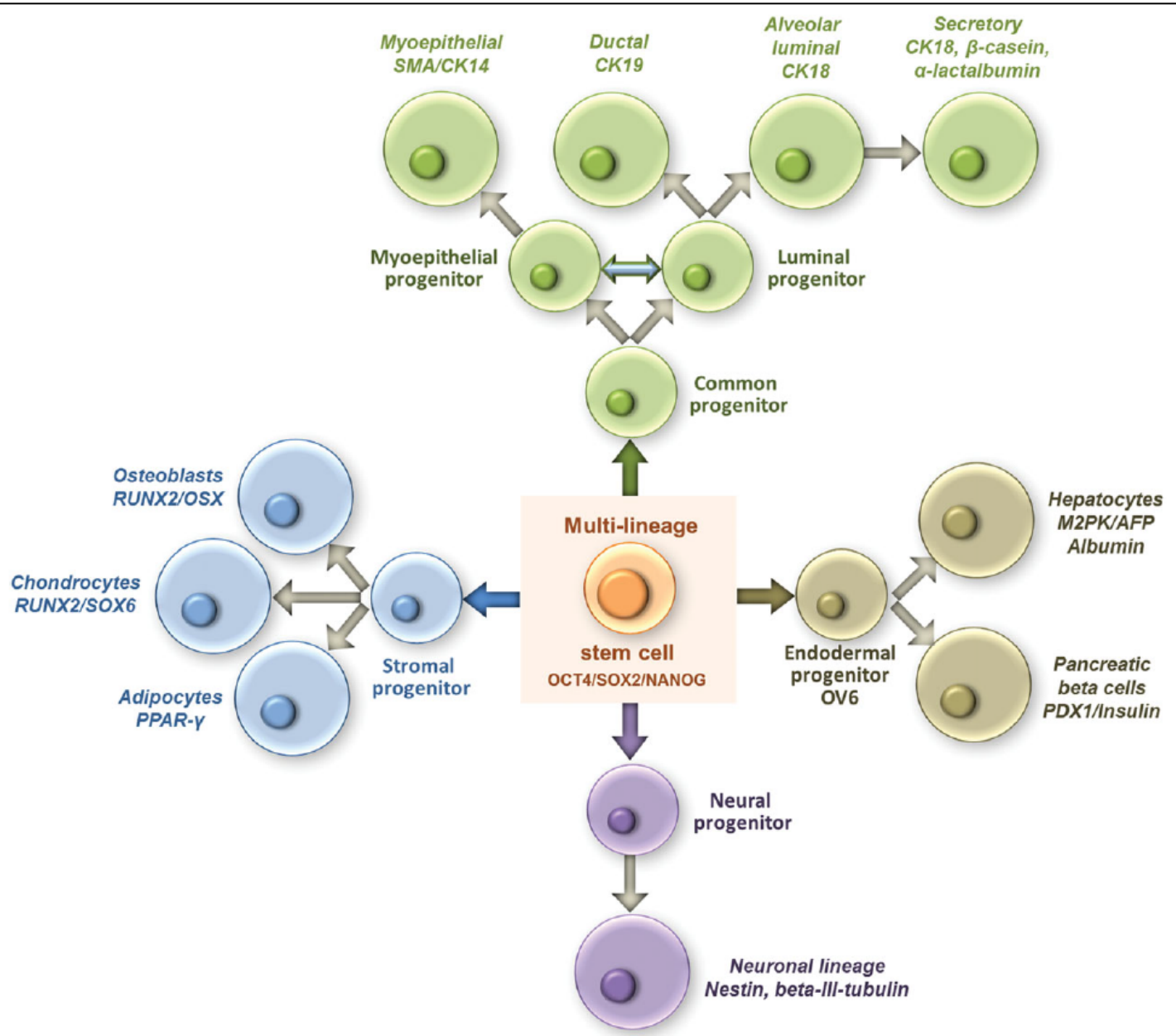


HAMLET (human alpha-lactalbumin made lethal to tumor cells)

A vast antitumoral activity



Ho C S, J; Rydström, A; Trulsson, M; Bålfors, J; Storm, P; Puthia, M; Nadeem, A; Svanborg, C (Oct 2012). "HAMLET: functional properties and therapeutic potential.". *Future oncology (London, England)* **8** (10): 1301–13.



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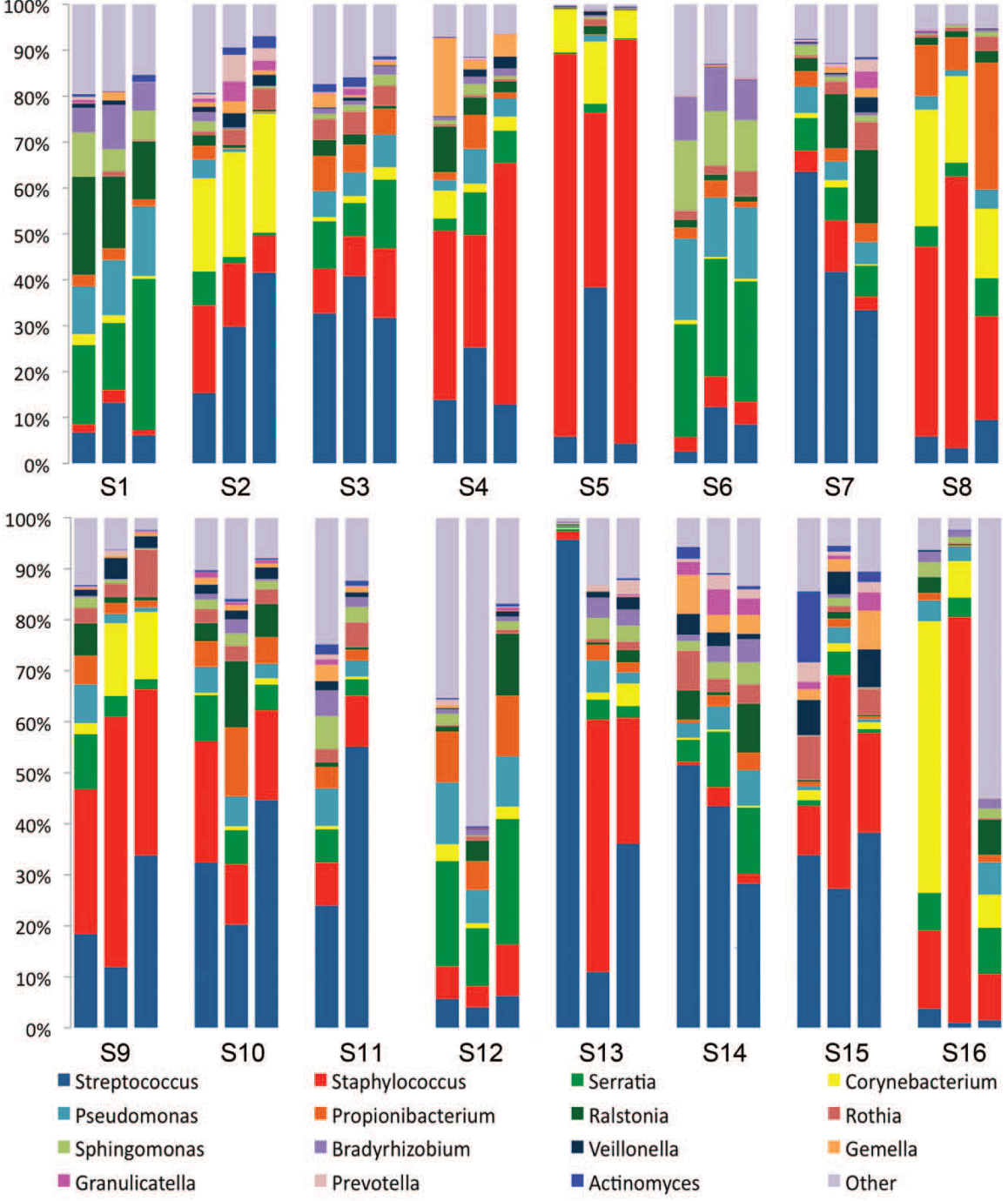
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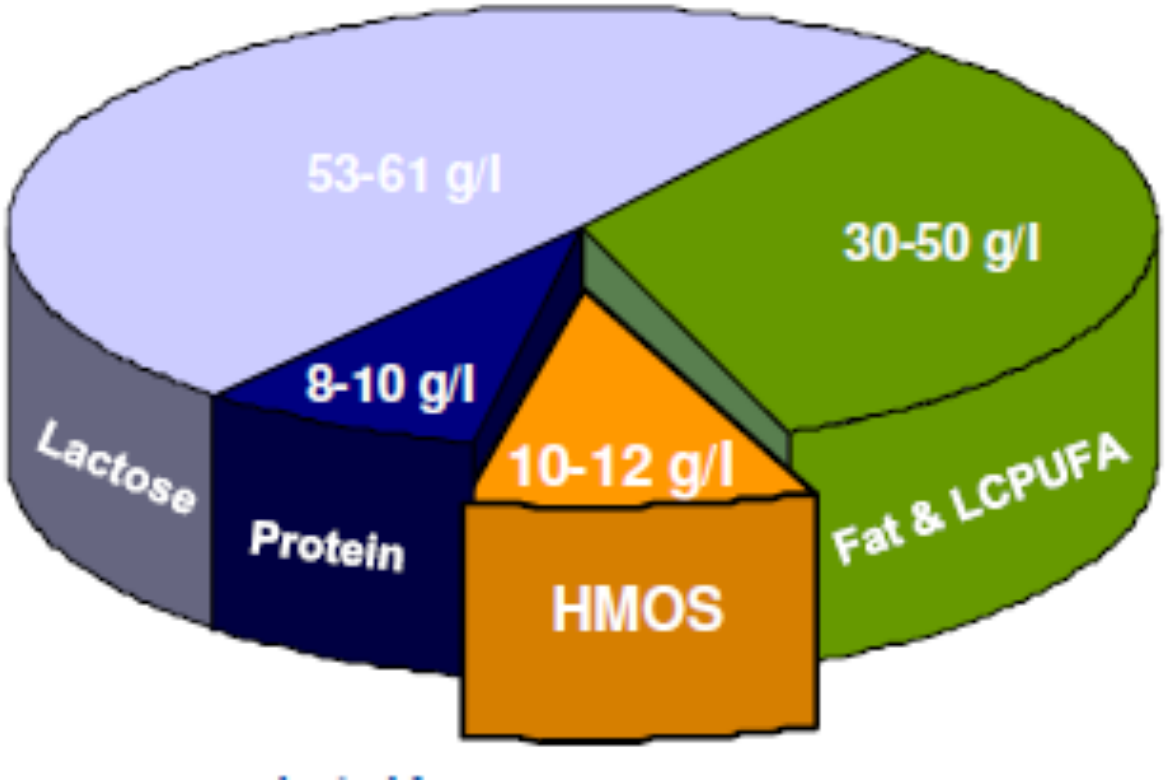
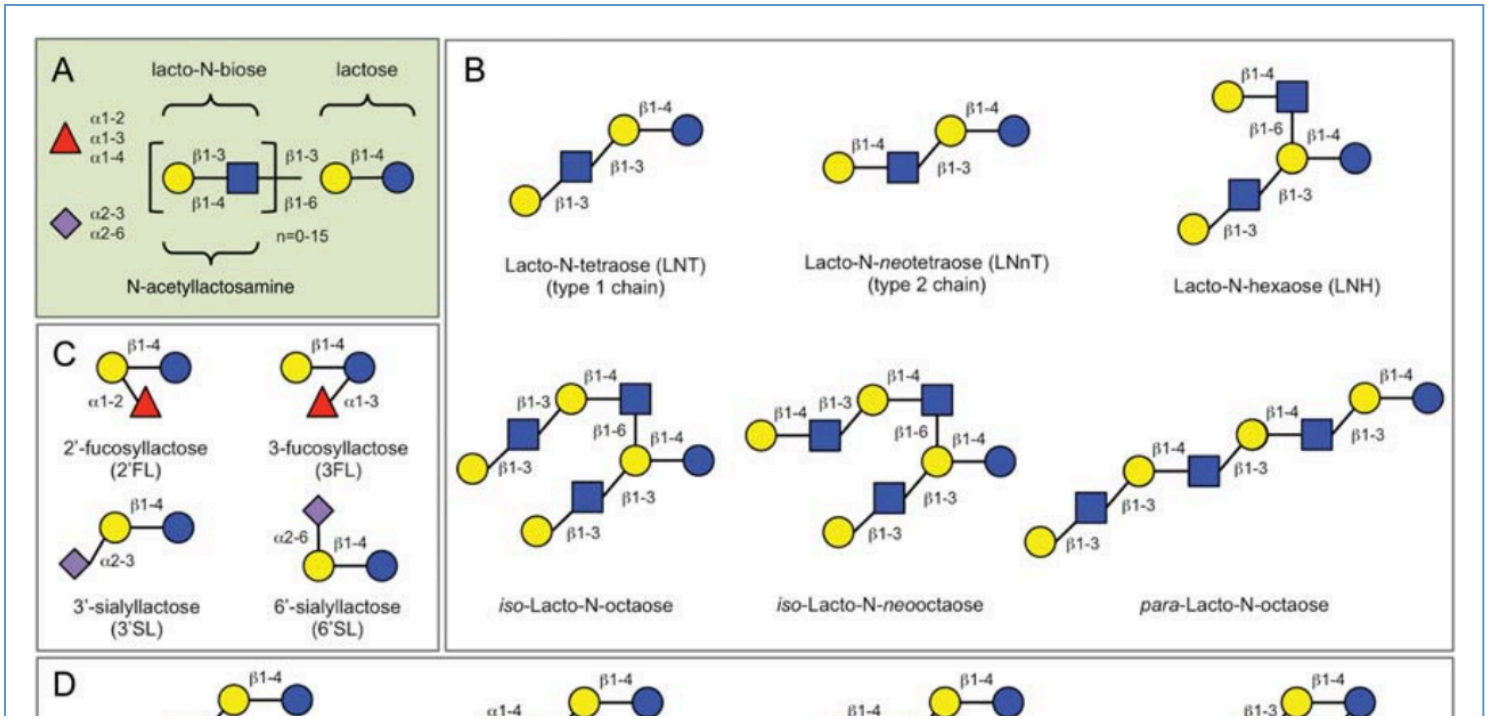
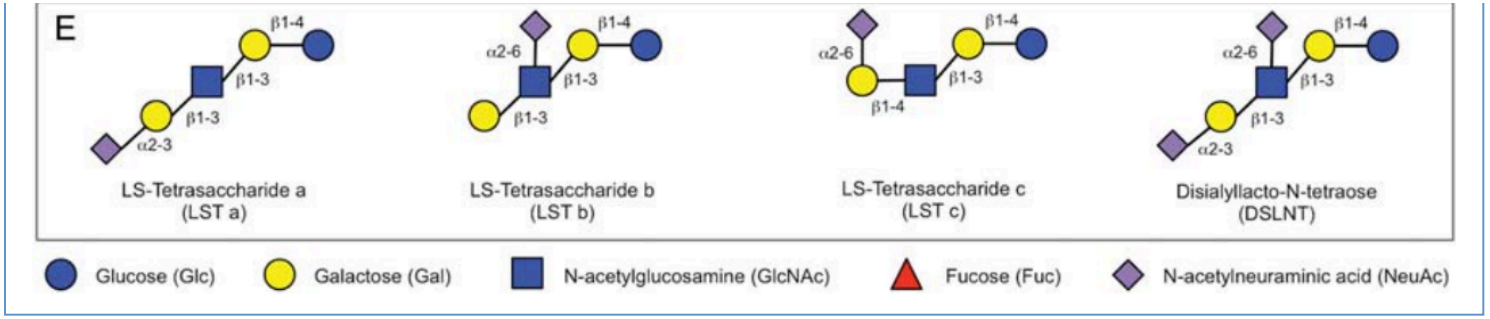
S9
S10
S11
S12
S13
S14
S15
S16
Streptococcus
Staphylococcus
Serratia
Corynebacterium
Pseudomonas
Propionibacterium
Ralstonia
Rothia
Sphingomonas
Bradyrhizobium
Veillonella
Gemella
Granulicatella
Prevotella
Actinomyces
Other

Prebiotics


53-61 g/l
30-50 g/l
8-10 g/l
10-12 g/l
Lactose
Protein
HMOS
Fat & LCPUFA

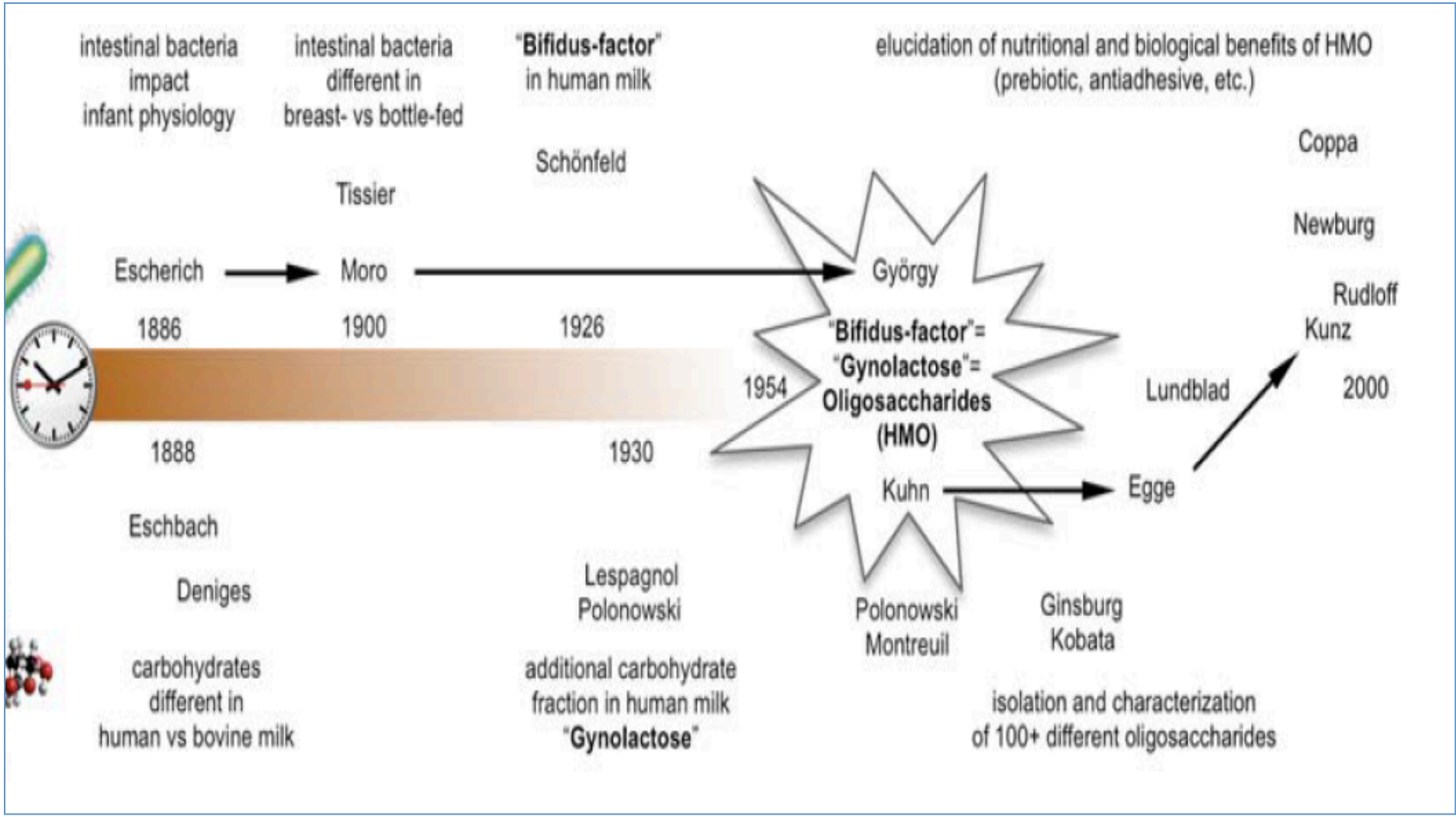


Composed of the five monosaccharides glucose (Glc), galactose (Gal), N-acetylglucosamine (GlcNAc), fucose (Fuc) and sialic acid (Sia), with N-acetylneuraminic acid (Neu5Ac) as the predominant.



Bode L. Human milk oligosaccharides: every baby needs a sugar mama. Glycobiology. 2012 Sep;22(9):1147-62.

Timeline with Key Events in HMO Discovery



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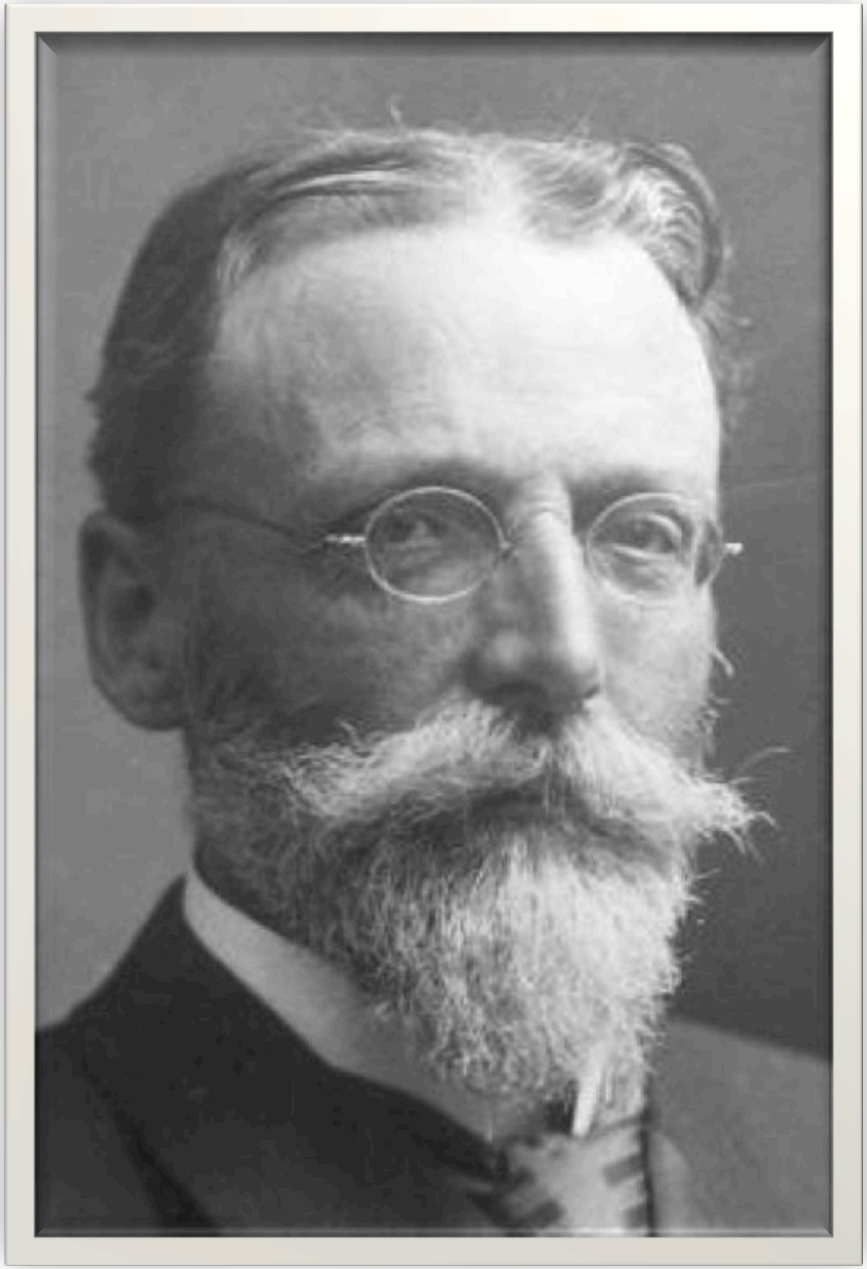


DIE

DARMBAKTERIEN

DES SÄUGLINGS

UND IHRE

BEZIEHUNGEN ZUR PHYSIOLOGIE DER VERDAUUNG

VON

Dr. THEODOR ESCHERICH,
ORDENTLICHEM ASSISTENTEN DER MED. KLINIK IN WÜRZBURG.

MIT 8 TAFELN UND 3 IN DEN TEXT GEDRUCKTEN HOLZSCHNITTEN.

STUTTGART.
VERLAG VON FERDINAND ENKE.
1886.

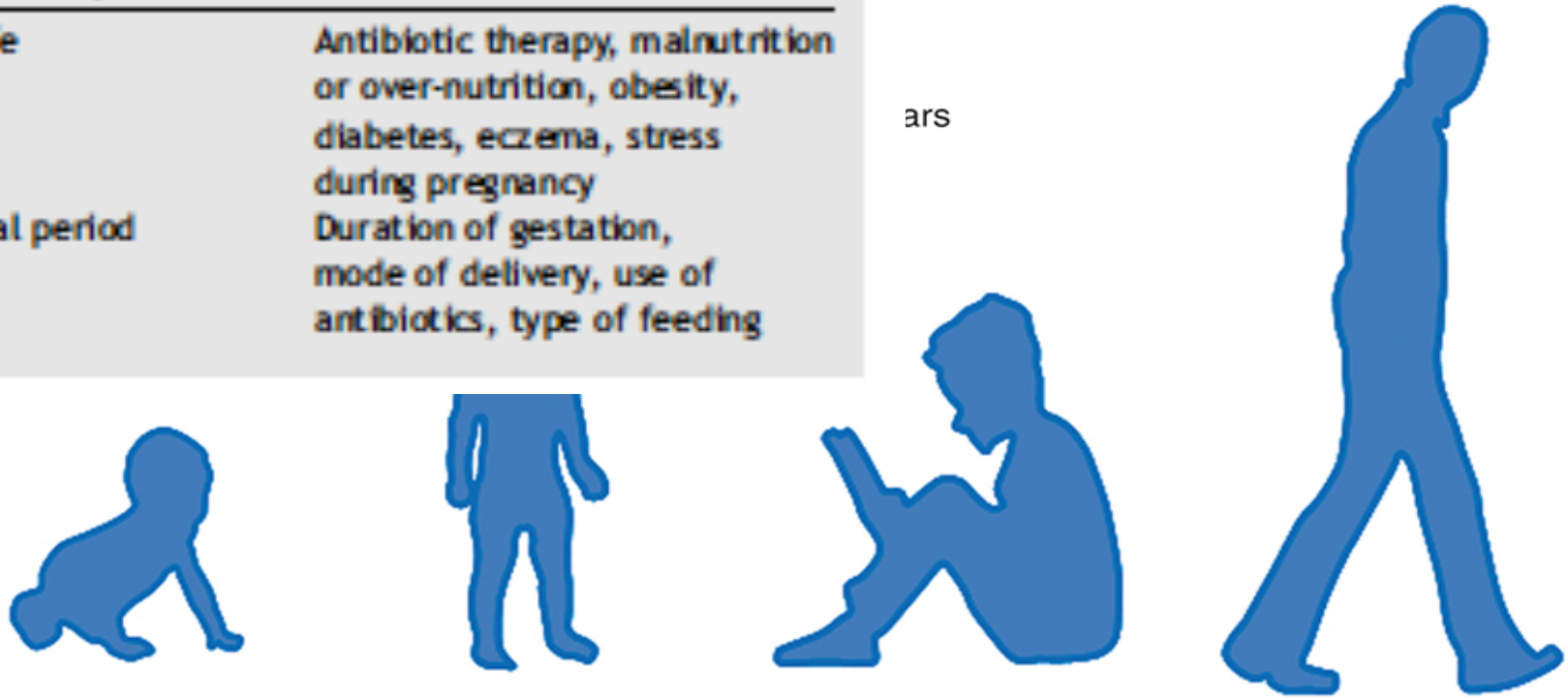
Table 1 Factors influencing gut microbiota during development.

Development phase	Factor
Fetal life	Antibiotic therapy, malnutrition or over-nutrition, obesity, diabetes, eczema, stress during pregnancy
Postnatal period	Duration of gestation, mode of delivery, use of antibiotics, type of feeding

gramming

ars

Intestinal microbial symbiosis



Infancy

- Breast or formula feeding

Toddlerhood

- Solid food weaning

Childhood

Teens

0–1 year | 1–6 years | 6–13 years | 13–19 years

a

Mother/infant microbiota interaction

b

Gut microbiota and host child communication: energy storage and metabolism, immune function, barrier integrity, autonomic nervous system, processes of the host (epithelial cell proliferation, intestinal motility)

Food–host microbiome interaction

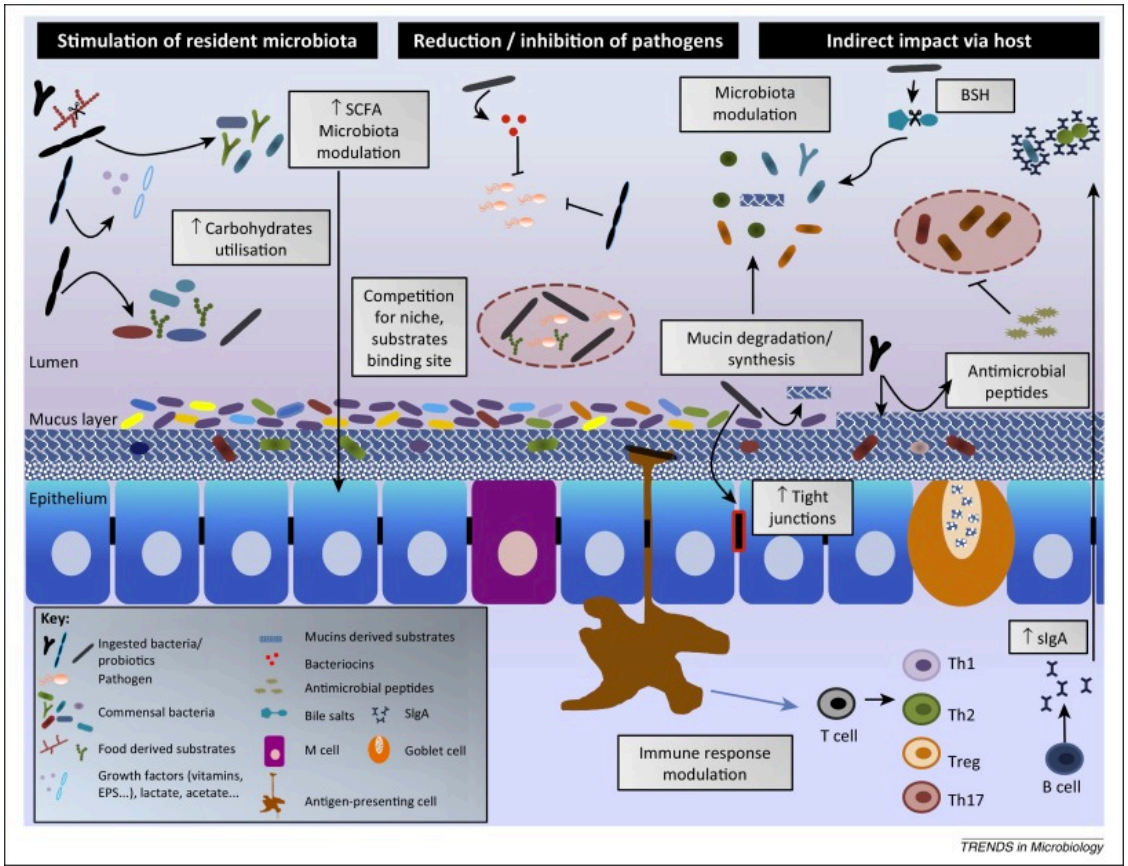
Praveen et al. Microbiome (2015) 3:41
DOI 10.1186/s40168-015-0104-7

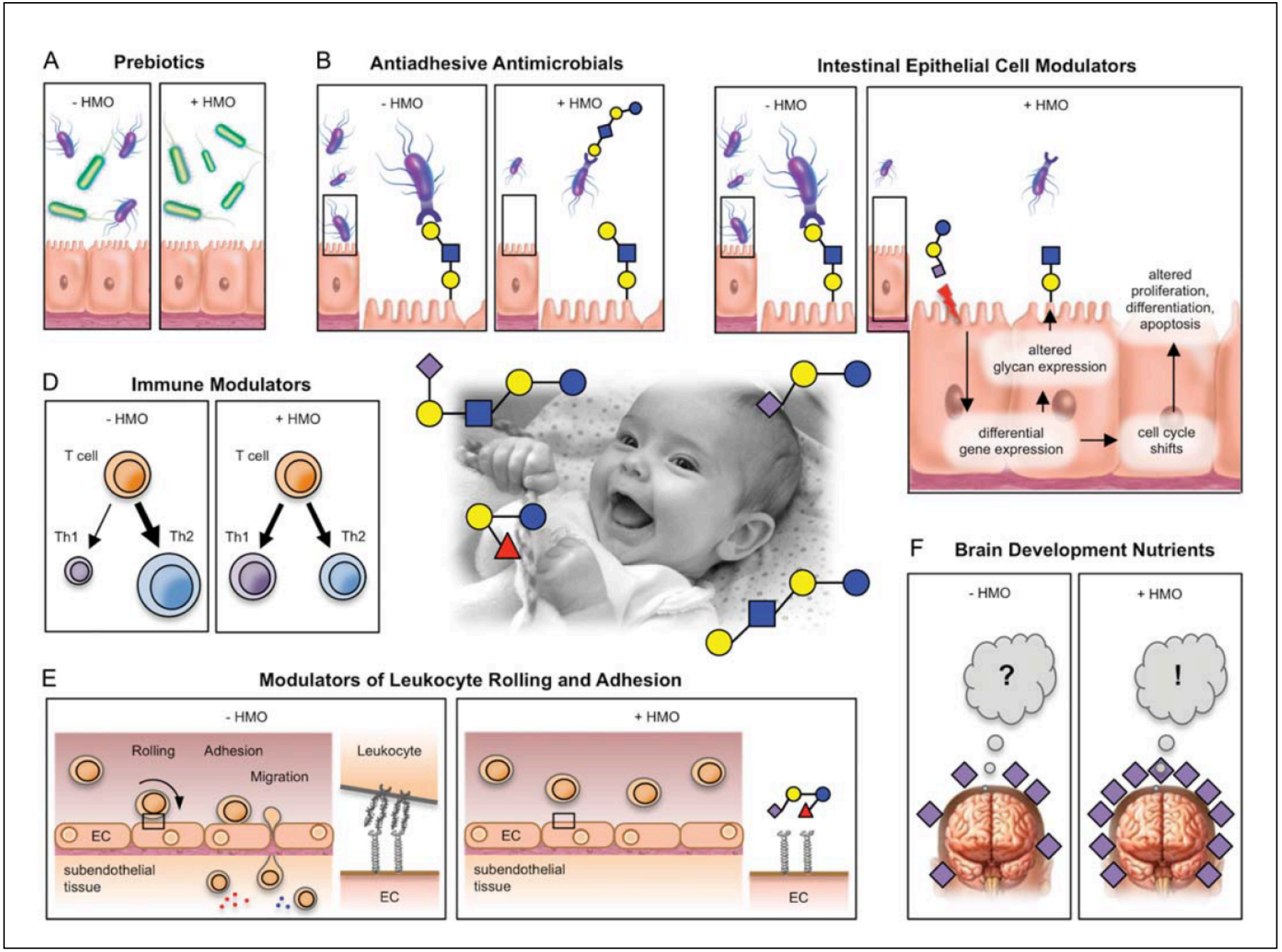
Microbiome

RESEARCH Open Access

The role of breast-feeding in infant immune system: a systems perspective on the intestinal microbiome

Paurush Praveen[1*], Ferenc Jordan[1], Corrado Priami[1,2] and Melissa J. Morine[1,2]





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CONSENSUS STATEMENT

OPEN

EXPERT CONSENSUS DOCUMENT

The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics

Glenn R. Gibson[1], Robert Hutkins[2], Mary Ellen Sanders[3], Susan L. Prescott[4], Raylene A. Reimer[5], Seppo J. Salminen[6], Karen Scott[7], Catherine Stanton[8], Kelly S. Swanson[9], Patrice D. Cani[10], Kristin Verbeke[11] and Gregor Reid[12]

Abstract | In December 2016, a panel of experts in microbiology, nutrition and clinical research was convened by the International Scientific Association for Probiotics and Prebiotics to review the definition and scope of prebiotics. Consistent with the original embodiment of prebiotics, but aware of the latest scientific and clinical developments, the panel updated the definition of a prebiotic: a substrate that is selectively utilized by host microorganisms conferring a health benefit. This definition expands the concept of prebiotics to possibly include non-carbohydrate substances, applications to body sites other than the gastrointestinal tract, and diverse categories other than food. The requirement for selective microbiota-mediated mechanisms was retained. Beneficial health effects must be documented for a substance to be considered a prebiotic. The consensus definition applies also to prebiotics for use by animals, in which microbiota-focused strategies to maintain health and prevent disease is as relevant as for humans. Ultimately, the goal of this Consensus Statement is to engender appropriate use of the term 'prebiotic' by relevant stakeholders so that consistency and clarity can be achieved in research reports, product marketing and regulatory oversight of the category. To this end, we have reviewed several aspects of prebiotic science including its development, health benefits and legislation.

Improving human health through modulation of the microbiome is an evolving strategy that is part of a comprehensive, holistic approach to lifestyle wellness[1]. The rich, diverse microbial ecosystems inhabiting mucosal and cutaneous surfaces provide targets for approaches to maintain or improve health or to treat disease. The ability to shift the composition and metabolic signatures of these microbial populations is now possible, via dietary or non-dietary interventions[2,3].

Over 20 years ago, a class of compounds, termed prebiotics, were recognized for their ability to manipulate host microbiota to the benefit of the host[4]. At that time fructans (fructooligosaccharides (FOS) and inulin) and galactans (galactooligosaccharides or GOS) fit that category, with their effects acting through enrichment of *Lactobacillus* and/or *Bifidobacterium* spp. FOS and GOS currently dominate the prebiotic category as evidenced by numerous studies on their prebiotic effects. Today, the prebiotic concept has expanded, in part, because of advances in tools for microbiome research (for example, high-throughput sequencing), which have improved our knowledge of the composition of the microbiota and enabled identification of additional substances influencing colonization. Concurrent with this progress is the realization that a broader range of beneficial microorganisms are affected by prebiotics and also that they might be effective at extraintestinal sites directly or indirectly[5]. Furthermore, the use of prebiotics has expanded to production and companion animals[6,7] and categories beyond food. Accordingly, researchers have advocated for reconsideration of the contemporary nature of prebiotics, which formed the aim of the consensus panel that was convened on 9 December 2016 in London, UK. The various aspects looked at in this review of evidence were: evolution of the term prebiotic; effects and selectivity; substrates that

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doi:10.1038/nrgastro.2017.75
Published online 14 Jun 2017

A substract utilized **selectively** by the host microorganisms and **confers health benefits**

HHS Public Access
Author manuscript
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Bifidobacterium longum subspecies *infantis*: champion colonizer of the infant gut

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Abstract

Oligosaccharides are abundant in human milk. Production of these highly diverse structures requires significant energy expenditure by the mother and yet these human milk oligosaccharides offer no direct nutritive value to her infant. A primary function of human milk oligosaccharides is to shape the infant's intestinal microbiota with life-long consequences. *Bifidobacterium longum* subspecies *infantis* (*B. infantis*) is unique among gut bacteria in its prodigious capacity to digest and consume any human milk oligosaccharide structure, the result of a large repertoire of bacterial genes encoding an array of glycosidases and oligosaccharide transporters not found in other bacterial species. *In vitro*, *B. infantis* grows better than other bacterial strains in the presence of human milk oligosaccharides, displays anti-inflammatory activity in premature intestinal cells, and decreases intestinal permeability. In premature infants, *B. infantis* given in combination with human milk increases *B. infantis* and decreases Enterobacteriaceae in the feces. Probiotics containing *B. infantis* decrease the risk of necrotizing enterocolitis in premature infants. Colonization with *B. infantis* is also associated with increased vaccine responses. Probiotic organisms have historically been selected based on ease of production and stability. The advantages of *B. infantis*, selected through coevolution with human milk glycans, present an opportunity for focused manipulation of the infant intestinal microbiota.

The colonization of the fetal gut begins *in utero* with swallowing of amniotic fluid. At that point, infants begin a lifelong relationship with their gut microbiota. Major shifts in the community of microbes inhabiting the intestinal tract (the gut microbiota) and the genes expressed by these microbes (the gut microbiome) and presumably the health consequences of the phenotype of the gut microbiota occur with rupture of the fetal membranes, birth, initiation of feeding, addition of solid foods, weaning, and interventions such as antibiotics,

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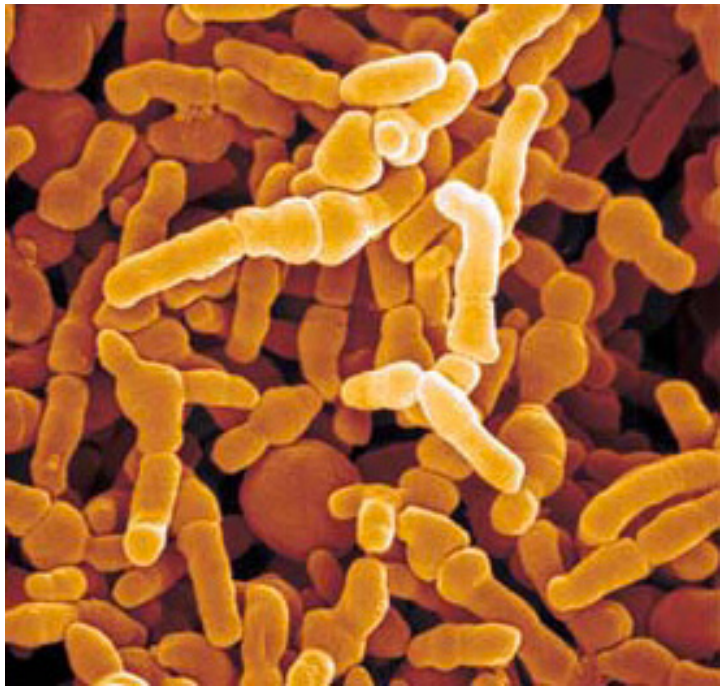
Disclosure: Three of the authors (J.B.G., C.B.L., D.A.M.) are the cofounders of Evolve Biosystems, a company focused on diet-based manipulation of the gut microbiota.

Selectivity



SCIENTIFIC REPORTS

OPEN

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Fucosylated oligosaccharides in mother's milk alleviate the effects of caesarean birth on infant gut microbiota

Katri Korpela[1,2], Anne Salonen[1], Brandon Hickman[1], Clemens Kunz[3], Norbert Sprenger[4], Kaarina Kukkonen[5], Erkki Savilahti[6], Mikael Kuitunen[6] & Willem M. de Vos[1,7]

One of the most abundant components in human milk is formed by oligosaccharides, which are poorly digested by the infant. The oligosaccharide composition of breast milk varies between mothers, and is dependent on maternal secretor (FUT2) genotype. Secretor mothers produce milk containing α1-2 fucosylated human milk oligosaccharides, which are absent in the milk of non-secretor mothers. Several strains of bacteria in the infant gut have the capacity to utilise human milk oligosaccharides (HMOs). Here we investigate the differences in infant gut microbiota composition between secretor (N = 76) and non-secretor (N = 15) mothers, taking into account birth mode. In the vaginally born infants, maternal secretor status was not associated with microbiota composition. In the caesarean-born, however, many of the caesarean-associated microbiota patterns were more pronounced among the infants of non-secretor mothers compared to those of secretor mothers. Particularly bifidobacteria were strongly depleted and enterococci increased among the caesarean-born infants of non-secretor mothers. Furthermore, *Akkermansia* was increased in the section-born infants of secretor mothers, supporting the suggestion that this organism may degrade HMOs. The results indicate that maternal secretor status may be particularly influential in infants with compromised microbiota development, and that these infants could benefit from corrective supplementation.

Infants are adapted to obtaining all of their nutrition from human milk during the first months of life. In addition to nutrients for the infant, breast milk contains a diverse mixture of complex oligosaccharides, termed human milk oligosaccharides (HMOs), at an abundance of approximately 10 g/l[1]. These oligosaccharides are poorly digested by the infant, but are favoured growth substrates for intestinal bacteria that have the appropriate enzymatic degradation capacity. The oligosaccharide composition and abundance in breast milk is dependent on maternal genetics, particularly the FUT2 gene, which encodes an enzyme responsible for the addition of fucose at the α1-2 position on a backbone of abundant glycans containing galactose[1]. The breast milk of mothers with a functional FUT2 allele, the so-called secretors, contains a large amount of α1-2 fucosylated HMOs, most abundantly 2′fucosyllactose (2′FL), and in lesser amounts lactodifucotetraose (LDFT), lacto-N-difucohexaose I (LNDFH I) and lacto-*N*-fucopentaose I (LNFP I)[1,2]. The breast milk of non-secretor mothers lacks or has only traces of these α1-2 fucosylated oligosaccharides, thus containing a lower total amount of HMOs[1,2], although this lack may be partly compensated by higher abundances of lacto-N-tetraose (LNT), LNFP II, and III and LNDFH II[1]. The abundance of 2′FL in breast milk has been shown to be a reliable indicator of secretor status[2].

Maternal secretor phenotype has been recently linked with reduced risk of atopic dermatitis in a cohort of caesarean-born infants[3], and individual HMOs were related to reduced risk of cow's milk allergy[4]. Although HMOs are reported to have immunomodulatory effects, these are mainly restricted to sialylated HMOs[5,6], which

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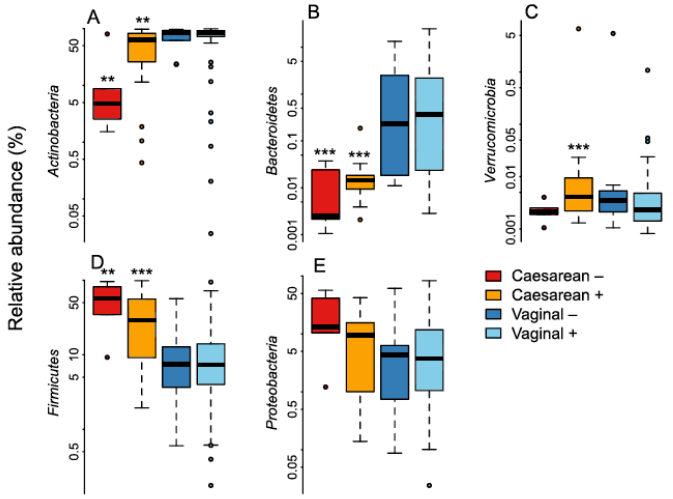
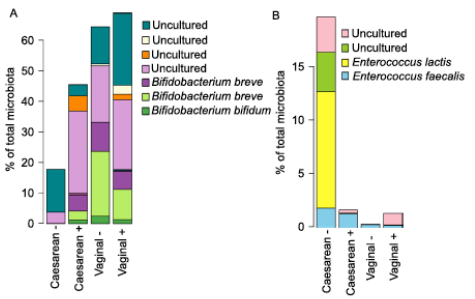


Figure 2. Relative abundance of the bacterial phyla by birth mode and maternal secretor status. The asterisks indicate the significance of the difference to the vaginally born infants of secretor mothers: $^{**}p < 0.01$, $^{***}p < 0.001$.



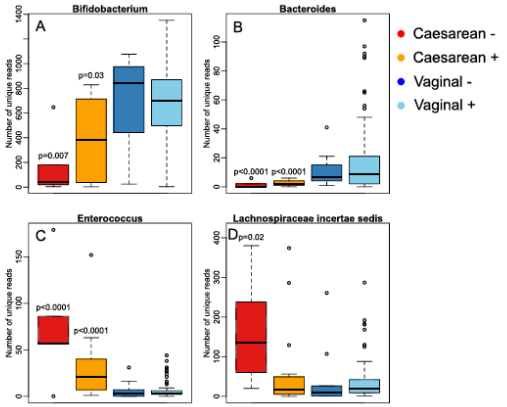


Figure 4. Sequence-level diversity (richness) within selected genera. The p-values represent the significance of the difference to the vaginally born infants of secretor mothers ("Vaginal +"), from negative binomial regression.

WHEN SCIENCE IS TRANSLATED INTO PRACTICE

In Infants With Necrotizing Enterocolitis, Gut Dysbiosis Precedes Disease

Julie A. Jacob, MA

When Edward McCabe, MD, PhD, was a pediatric resident in the mid-1970s, he often treated preterm infants with necrotizing enterocolitis (NEC). "It's a horrible disease," he said. Forty years later, when he retired from clinical practice in 2012, few strides had been made in prevention, treatment, or mortality. The lack of significant advances to prevent or treat NEC in fragile preterm infants is frustrating to clinicians who care for them, McCabe said.

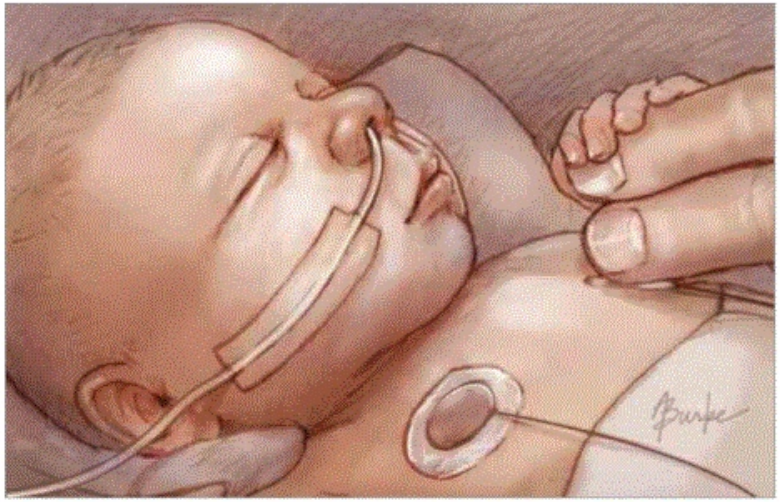
"There have been lots of studies on [causes and treatments] with essentially no change in mortality," said McCabe, the senior vice president and chief medical officer for the March of Dimes. Currently, about 12% of preterm infants weighing less than 1500 g develop NEC, and about one-third die from sepsis or other complications (Gephart SM et al. *Adv Neonatal Care*. 2012;12[2]:77-87; http://1.usa.gov/21IRhiH).

However, a new prospective case-control study by researchers at Washington University School of Medicine in St Louis provides a preliminary road map for additional investigation into causes and potential treatments (Warner BB et al. *Lancet*. doi: 10.1016/S0140-6736(16)00081-7 [published online March 8, 2016]). The research team sequenced DNA extracted from 3586 stool samples retrieved from 166 preterm infants who were hospitalized in neonatal intensive care units at 3 hospitals: St Louis (Missouri) Children's Hospital; Kosair Children's Hospital in Louisville, Kentucky; and Children's Hospital at Oklahoma University in Oklahoma City. All babies weighing less than 1500 g without congenital heart disease or intestinal perforations who were expected to survive more than 1 week were eligible for the study. The babies' stool samples were analyzed from neonatal admission to 60 days of age or until a NEC diagnosis, whichever occurred first.

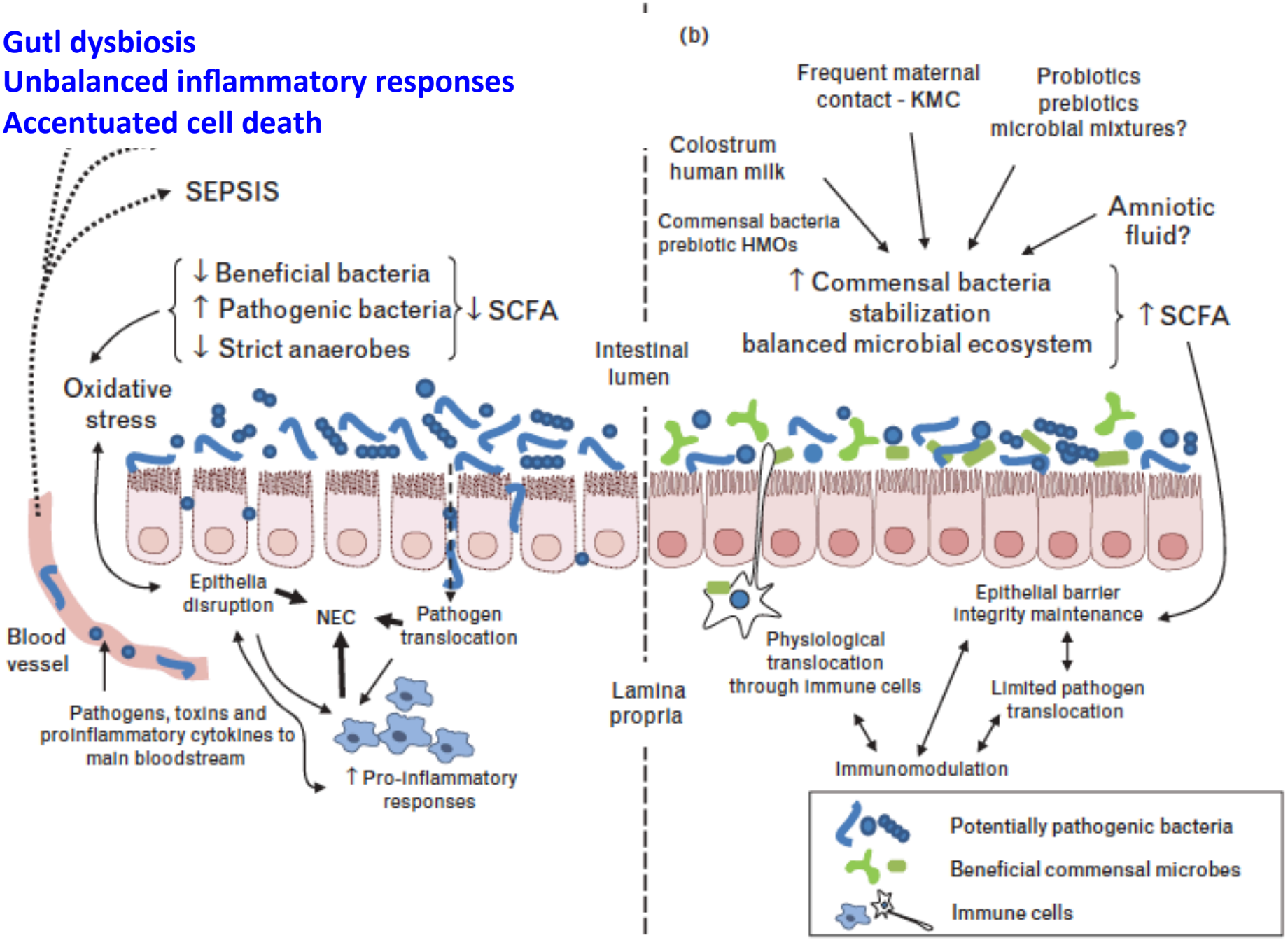
Investigators discovered that the gastrointestinal bacterial microbiome of 46 preterm babies who developed NEC contained significantly more gram-negative gammaproteobacteria, such as *Escherichia coli*, and less anaerobic bacteria, particularly *Negativicutes*, compared with preterm babies who did not develop the disease.

"Neonatologists have long believed that gut bacteria could have a bearing on developing or being protected from necrotizing enterocolitis," said Phillip I. Tarr, MD, the study's senior author and a professor of pediatrics and microbiology at the Washington University School of Medicine in St Louis. That hypothesis, he explained, is based on several factors, including the association between greater antibiotic use and NEC and the protective factor of breastfeeding. "However, the identity of the risk-conferring microbes had not been clarified," Tarr added.

It was the study's scope and methodology, however, that enabled the researchers to demonstrate that the gut microbiome transition occurs before infants develop NEC, noted Scott Lorch, MD, a neonatologist and director of the Neonatal-Perinatal Medicine Fellowship at the Children's Hospital of Philadelphia, who was not involved in the study. Because thousands of stool samples were sequenced from the time the infants were admitted to neonatal intensive care—before any were diagnosed with NEC—researchers were able to study how the infants' gut microbiomes evolved over several



Gutl dysbiosis
Unbalanced inflammatory responses
Accentuated cell death



July 2017

PAEDIATRICS

Are human milk oligosaccharides the magic bullet for necrotizing enterocolitis?

Michael S. Caplan

There have been no major improvements in the prevention or treatment of necrotizing enterocolitis (NEC) over the past several decades, and therefore a 'magic bullet' is urgently needed. However, new data demonstrate that disialyllacto-*N*-tetraose levels in breast milk can predict the risk of NEC, and these findings might provide a strategy for successful intervention.

Refers to Autran, C. A. *et al.* Human milk oligosaccharide compostion predicts risk of necrotizing enterocolitis in preterm infants. *Gut* http://dx.doi.org/10.1136/gutjnl-2016-312819 (2017)

Necrotizing enterocolitis (NEC) is an acute, inflammatory necrosis of the intestine that primarily affects premature infants and continues to account for substantial morbidity and mortality in neonatal intensive care units worldwide. Despite >30 years of intensive research, the precise aetiology of this disease remains unknown, although studies suggest that intestinal dysbiosis, unbalanced inflammatory responses and accentuated cell death contribute to the development of this unique disease (FIG. 1). Unfortunately, fully effective preventive and treatment approaches are unavailable[1]. Nonetheless, human milk has long been known to reduce the risk of NEC compared with infant formula, yet the specific factor(s) responsible for this effect are not well delineated[2]. Now, in new research published in *Gut*, Autran *et al.*[3] demonstrate that one specific human milk oligosaccharide (HMO), disialyllacto-*N*-tetraose (DSLNT), had lower levels in breast milk fed to babies who developed NEC than in breast milk fed to age-matched healthy controls. The implication is that milk DSLNT levels might be an effective biomarker to identify infants at high-risk of NEC and that DSLNT supplementation could ultimately prove to be an effective preventive strategy.

HMOs are a diverse group of complex glycans with multiple effects and are the third largest component of human milk[4]. HMOs stimulate the growth of beneficial intestinal commensal bacteria such as *Bifidobacteria* spp., and many randomized trials and meta-analyses have demonstrated that probiotic supplementation can reduce the risk of NEC in preterm infants[5]. In addition, specific isotypes of HMOs, of which >150 exist, bind to various microbial pathogens in a specific manner and this process might reduce the inflammatory response to bacteria at the mucosal surface. A previous study from authors of the new research demonstrated that DSLNT supplementation reduced the risk of NEC in a neonatal rat model, whereas all other HMOs had much less or no effect[6]. The latest study demonstrating that low milk DSLNT levels are associated with NEC in humans supports the animal observations and has provocative implications.

An urgent need exists to identify a reliable biomarker for NEC that can be measured before the onset of clinical symptoms and signs. Many representative molecules have been evaluated, including faecal calprotectin, intestinal fatty acid binding protein, platelet activating factor, among others[7]. However, the specificity, sensitivity and, more importantly, the positive and negative predictive values have not been robust enough to reliably identify clinically significant cases of NEC[7]. Furthermore, biomarker development has been hampered by imprecise definitions and categorization of NEC, which currently depends on the modified Bell Staging system and is not a reliable differentiator between NEC and a variety of acquired intestinal pathologies of the neonate, such as spontaneous intestinal perforation, cow's milk protein allergy or feeding intolerance[8]. Notably, of the cases included in Autran *et al.*[3], 3 of 10 patients might not be 'true' NEC at all, and might represent feeding intolerance or dysmotility.

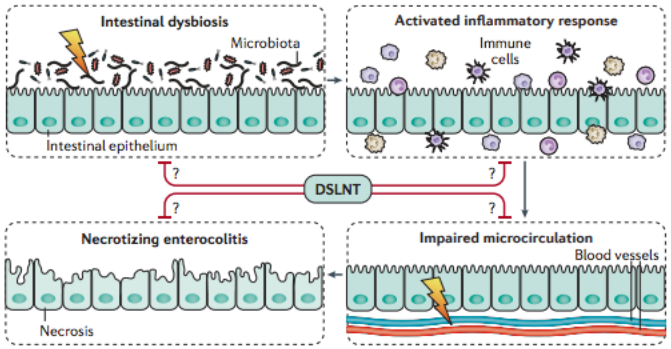


Figure 1 | **Proposed pathophysiology and inhibition of necrotizing enterocolitis.** Possible mechanisms for how disialyllacto-*N*-tetraose (DSLNT) might inhibit necrotizing enterocolitis are shown, including via the gut microbiota, inflammatory responses and impaired microcirculation.

Provision of HM is vital for the preterm infants!

SCIENTIFIC AUTHORITIES

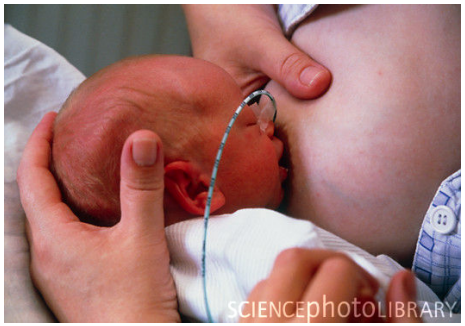
POLICY STATEMENT

Breastfeeding and the Use of Human Milk

Recommendations on Breastfeeding Management for Preterm Infants

1

- All preterm infants should receive human milk. Human milk should be fortified, with protein, minerals, and vitamins to ensure optimal nutrient intake for infants weighing <1500 g at birth.



- Pasteurized donor human milk, appropriately fortified, should be used if mother's own milk is unavailable or its use is contraindicated.

2

Donor Human Milk for Preterm Infants: Current Evidence and Research Directions

*†Sertac Arslanoglu, ‡Willemijn Corpeleijn, *Guido Moro, §Christian Braegger, ||Cristina Campoy, ¶Virginie Colomb, #Tamas Decsi, **Magnus Domellöf, ††Mary Fewtrell, ‡‡Iva Hojsak, §§Walter Mihatsch, ||||Christian Mølgaard, ¶¶Raanan Shamir, ##Dominique Turck, and ‡Johannes van Goudoever, ESPGHAN Committee on Nutrition

ABSTRACT

The Committee on Nutrition of the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition aims to document the existing evidence of the benefits and common concerns deriving from the use of donor human milk (DHM) in preterm infants. The comment also outlines gaps in knowledge and gives recommendations for practice and suggestions for future research directions. Protection against necrotizing enterocolitis is the major clinical benefit deriving from the use of DHM when compared with formula. Limited data also suggest unfortified DHM to be associated with improved feeding tolerance and with reduced cardiovascular risk factors during adolescence. Presence of a human milk bank (HMB) does not decrease breast-feeding rates at discharge, but decreases the use of formula during the first weeks of life. This commentary emphasizes that fresh own mother's milk (OMM) is the first choice in preterm infant feeding and strong efforts should be made to promote lactation. When OMM is not available, DHM is the recommended alternative. When neither OMM nor guidelines. Storage and processing of human milk reduces some biological components, which may diminish its health benefits. From a nutritional point of view, DHM, like HM, does not meet the requirements of preterm infants, necessitating a specific fortification regimen to optimize growth. Future research should focus on the improvement of milk processing in HMB, particularly of heat treatment; on the optimization of HM fortification; and on further evaluation of the potential clinical benefits of processed and fortified DHM.

Key Words: donor milk, human milk, human milk banking, pasteurization, preterm infant

(*JPGN* 2013;57: 535–542)

ESPGHAN 2013

Recommendations

1. OMM is the first choice in preterm infant feeding, and strong efforts should be made to promote lactation.
2. When mother's milk is not available, DHM is the preferred choice. When mother's milk and DHM are not available, PF should be used.
3. No DHM should be provided outside the organization of an established HMB.
4. Adequate screening of donors and pasteurization of the donor milk should be performed.
5. DHM should be fortified to meet early nutrient requirements and achieve better short-term growth, which is associated with improved neurocognitive outcome. Individualized fortification is advised.

3

Human Milk in Feeding Premature Infants: From Tradition to Bioengineering

Proceedings of a Consensus Development Conference–EXPO 2015, Milan, Italy, May 15–16

*Guido E. Moro, †Sertac Arslanoglu, ‡Enrico Bertino, §Luigi Corvaglia, ||Rosario Montirosso, ¶Jean-Charles Picaud, #Staffan Polberger, **Richard J. Schanler, ††Caroline Steele, ‡‡Johannes van Goudoever, and §§Ekhard E. Ziegler

American Academy of Pediatrics
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FROM THE AMERICAN ACADEMY OF PEDIATRICS

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

POLICY STATEMENT

Breastfeeding and the Use of Human Milk

SECTION ON BREASTFEEDING

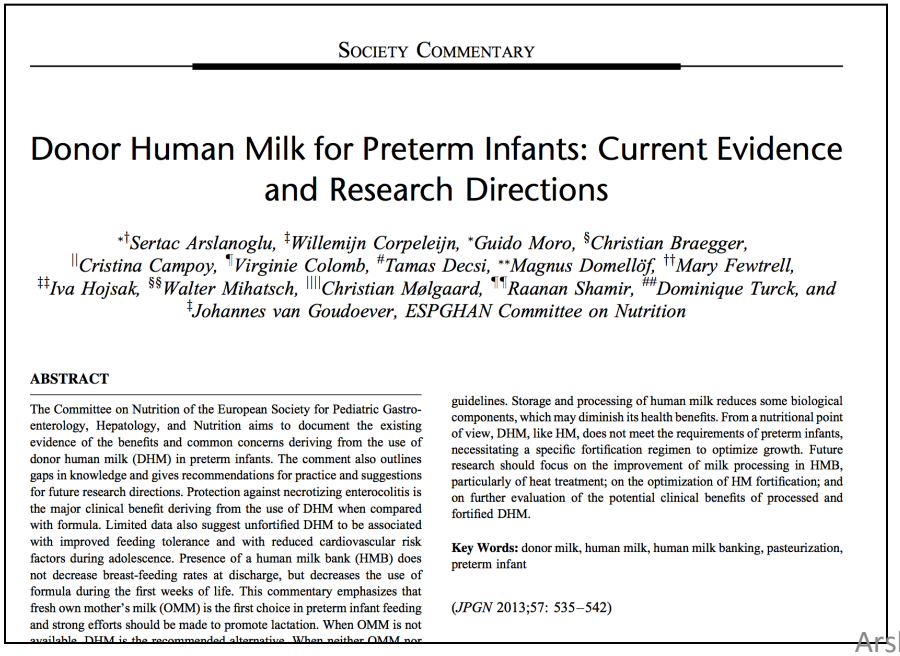
KEY WORDS
breastfeeding, complementary foods, infant nutrition, lactation, human milk, nursing

ABBREVIATIONS
AAP—American Academy of Pediatrics
AHRQ—Agency for Healthcare Research and Quality
CDC—Centers for Disease Control and Prevention
CI—confidence interval
CMV—cytomegalovirus
DHA—docosahexaenoic acid
NEC—necrotizing enterocolitis
OR—odds ratio
SIDS—sudden infant death syndrome
WHO—World Health Organization

abstract

FREE

Breastfeeding and human milk are the normative standards for infant feeding and nutrition. Given the documented short- and long-term medical and neurodevelopmental advantages of breastfeeding, infant nutrition should be considered a public health issue and not only a lifestyle choice. The American Academy of Pediatrics reaffirms its recommendation of exclusive breastfeeding for about 6 months, followed by continued breastfeeding as complementary foods are introduced, with continuation of breastfeeding for 1 year or longer as mutually desired by mother and infant. Medical contraindications to breastfeeding are rare. Infant growth should be monitored with the World Health Organization (WHO) Growth Curve Standards to avoid mislabeling infants as underweight or failing to thrive. Hospital routines to encourage and support the initiation and sustaining of exclusive breastfeeding should be based on the American Academy of Pediatrics-endorsed WHO/UNICEF "Ten Steps to Successful Breastfeeding." National strategies supported by the US Surgeon General's Call to Action, the Centers for Disease Control and Prevention, and The



SOCIETY COMMENTARY

Donor Human Milk for Preterm Infants: Current Evidence and Research Directions

*†Sertac Arslanoglu, ‡Willemijn Corpeleijn, *Guido Moro, §Christian Braegger, ||Cristina Campoy, ¶Virginie Colomb, #Tamas Decsi, **Magnus Domellöf, ††Mary Fewtrell, ‡‡Iva Hojsak, §§Walter Mihatsch, ||||Christian Mølgaard, ¶¶Raanan Shamir, ###Dominique Turck, and ‡Johannes van Goudoever, ESPGHAN Committee on Nutrition

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Key Words: donor milk, human milk, human milk banking, pasteurization, preterm infant

(*JPGN* 2013;57: 535–542)

- All preterm infants should be fed human milk.
- Human milk should be fortified for the infants < 1800 g.
- When breast milk is unavailable donor milk should be used.

4

frontiers

In Press

FORTIFICATION OF HUMAN MILK FOR PRETERM INFANTS: Update and Recommendations of the European Milk Bank Association (EMBA) Working Group on Human Milk Fortification

Sertac Arslanoglu[1*], Clair-Yves Boquien[2], Caroline King[3], Delphine Lamireau[4], Paola Tonetto[5], Debbie Barnett[6], Enrico Bertino[5], Antoni Gaya[7], Corinna Gebauer[8], Anne Grovslien[9], Guido E. Moro[10], Gillian Weaver[11], Aleksandra M. Wesolowska[12], Jean-charles Picaud[13, 14]

[1]Istanbul Medeniyet University, Turkey, [2]INRA UMR1280 Physiologie des Adaptations Nutritionnelles, France, [3]Department of Nutrition and Dietetics, Imperial College Healthcare NHS Trust, United Kingdom, [4]Lactariums Et Biberonnerie, Pôle pédiatrique, Centre Hospitalo-universitaire de Bordeaux, France, [5]Unità di Neonatologia, AOU Città della Salute e della Scienza di Torino, Italy, [6]NHS Greater Glasgow and Clyde, United Kingdom, [7]Fundació Banc Sang i Teixits de les Illes Balears, Spain, [8]Klinik und Poliklinik für Kinder und Jugendmedizin, Universitätsklinikum Leipzig, Germany, [9]Oslo University Hospital, Norway, [10]Associazione Italiana delle Banche del Latte Umano Donato (AIBLUD), Italy, [11]Hearts Milk Bank, United Kingdom, [12]Department of Neonatology, Faculty of Health Science, Medical University of Warsaw, Poland, [13]INSERM U1060 Laboratoire de Recherche en Cardiovasculaire, Métabolisme, diabétologie et Nutrition, France, [14]Service de Néonatalogie, Hôpital de la Croix-Rousse, France

PROVEN BENEFITS OF DONOR HUMAN MILK

Donor Human Milk for Preterm Infants: Current Evidence and Research Directions

*†Sertac Arslanoglu, ‡Willemijn Corpeleijn, *Guido Moro, §Christian Braegger, ||Cristina Campoy, ¶Virginie Colomb, #Tamas Decsi, **Magnus Domellöf, ††Mary Fewtrell, ‡‡Iva Hojsak, §§Walter Mihatsch, ||||Christian Mølgaard, ¶¶Raanan Shamir, ##Dominique Turck, and ‡Johannes van Goudoever, ESPGHAN Committee on Nutrition

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Key Words: donor milk, human milk, human milk banking, pasteurization, preterm infant

(*JPGN* 2013;57: 535–542)

ESPGHAN 2013

CONCLUSIONS, RECOMMENDATIONS, FUTURE RESEARCH DIRECTIONS

Conclusions

Based on the evidence presented in this Comment, the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition Committee on Nutrition concludes the following:

1. DHM is associated with reduced NEC rates compared with cow's milk–based formula.
2. Unfortified DHM, like HM, is associated with slower neonatal growth when compared with PF.
3. Appropriately handled and pasteurized DHM is microbiologically safe.
4. Presence of an HMB does not decrease the breast-feeding rates at discharge, but may decrease formula use during the first weeks of life.

Pediatrics 2016

Impact of Donor Milk Availability on Breast Milk Use and Necrotizing Enterocolitis Rates

Agata Kantorowska, BS,[a] Julia C. Wei, MPH,[b] Ronald S. Cohen, MD,[c] Ruth A. Lawrence, MD,[d] Jeffrey B. Gould, MD,[c,e] Henry C. Lee, MD, MS[c,e]

abstract

OBJECTIVES: To examine the availability of donor human milk (DHM) in a population-based cohort and assess whether the availability of DHM was associated with rates of breast milk feeding at NICU discharge and rates of necrotizing enterocolitis (NEC).

METHODS: Individual patient clinical data for very low birth weight infants from the California Perinatal Quality Care Collaborative were linked to hospital-level data on DHM availability from the Mothers' Milk Bank of San José for 2007 to 2013. Trends of DHM availability were examined by level of NICU care. Hospitals that transitioned from not having DHM to having DHM availability during the study period were examined to assess changes in rates of breast milk feeding at NICU discharge and NEC.

RESULTS: The availability of DHM increased from 27 to 55 hospitals during the study period. The availability increased for all levels of care including regional, community, and intermediate NICUs, with the highest increase occurring in regional NICUs. By 2013, 81.3% of premature infants cared for in regional NICUs had access to DHM. Of the 22 hospitals that had a clear transition to having availability of DHM, there was a 10% increase in breast milk feeding at NICU discharge and a concomitant 2.6% decrease in NEC rates.

CONCLUSIONS: The availability of DHM has increased over time and has been associated with positive changes including increased breast milk feeding at NICU discharge and decrease in NEC rates.

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2018

Formula versus donor breast milk for feeding preterm or low birth weight infants (Review)

Quigley M, Embleton ND, McGuire W

Quigley M, Embleton ND, McGuire W.
Formula versus donor breast milk for feeding preterm or low birth weight infants.
Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD002971.
DOI: 10.1002/14651858.CD002971.pub4.

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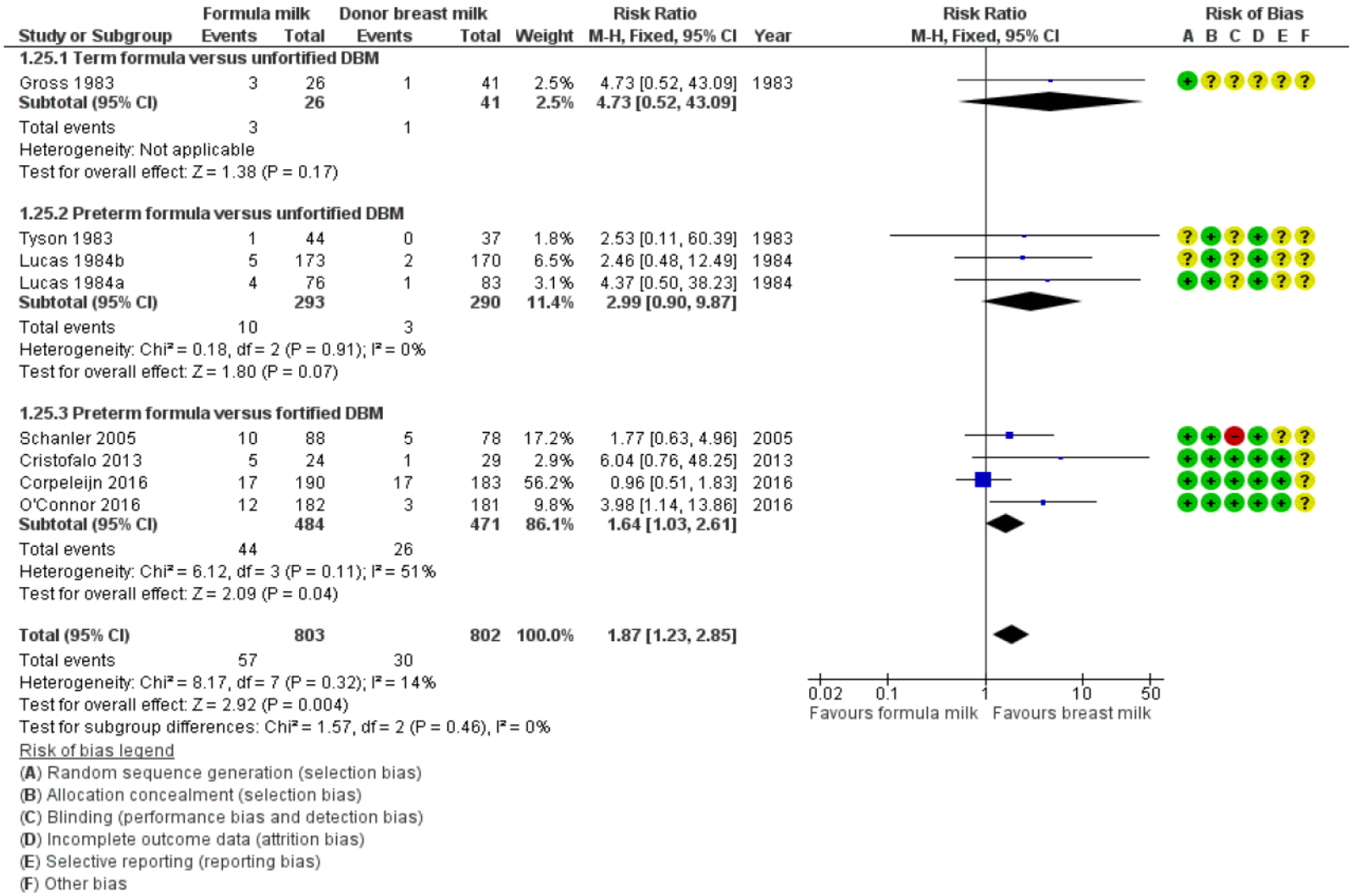
Figure 7. Forest plot of comparison: 1 Formula (term or preterm) versus DBM (unfortified of fortified), outcome: 1.25 Necrotising enterocolitis.



Risk of bias legend

(**A**) Random sequence generation (selection bias)

(**B**) Allocation concealment (selection bias)

(**C**) Blinding (performance bias and detection bias)

(**D**) Incomplete outcome data (attrition bias)

(**E**) Selective reporting (reporting bias)

(**F**) Other bias

NEC

Authors' conclusions

In preterm and LBW infants, feeding with formula compared with donor breast milk, either as a supplement to maternal expressed breast milk or as a sole diet, results in higher rates of weight gain, linear growth, and head growth and a higher risk of developing necrotising enterocolitis. The trial data do not show an effect on all-cause mortality, or on long-term growth or neurodevelopment.

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ARTICLE

Low rate of necrotizing enterocolitis in extremely low birth weight infants using a hospital-based preterm milk bank

Swati Murthy[1,2] · Pamela R. Parker[1,2] · Steven J. Gross[1,2]

Received: 21 May 2018 / Revised: 16 August 2018 / Accepted: 10 September 2018 / Published online: 5 October 2018

Abstract

Objective We examined the effect of two strategies to prevent necrotizing enterocolitis (NEC) in extremely low birth weight (ELBW) infants—adherence to a standardized feeding protocol and use of a hospital-based milk bank to provide exclusive preterm human milk feedings.

Study design We conducted a single-center observational study from 2010 to 2015. Infants received preterm human milk, initially trophic feeds from days 7 to 14 after birth, followed by advancement of 15 mL/kg/day to reach a goal of 180 mL/kg/day. Fortification was used selectively for weight gain < 15 g/kg/day. We determined the incidence of NEC, other morbidities, and growth.

Results The cohort included 398 ELBW infants who survived to day 14 without congenital anomalies. Mean gestational age was 26.2 ± 1.9 weeks. Maternal milk was used as the sole feeding in 62% of infants; preterm donor milk was used solely or as supplement in 29%. Full feeds were reached at a median of 27 (IQR 23, 33) days. Four infants (1%) developed NEC.

Conclusion Use of standardized feedings with a hospital-based milk bank is associated with an incidence of NEC lower than previously reported.

Introduction

Although advances in the care of extremely low birth weight (ELBW) infants have led to improved survival, it has become increasingly clear that the nutritional management of these infants plays a large role in their immediate survival and subsequent growth and development. Therefore, nutritional care goals have expanded from optimizing short term growth to include preventing feeding-related morbidities such as complications of parenteral nutrition, necrotizing enterocolitis (NEC) and sepsis [1, 2].

NEC is a serious gastrointestinal disease affecting > 10% of ELBW infants with a mortality of up to 50% [3]. The pathophysiology is poorly understood, but intestinal immaturity, microbial colonization, hypoxic ischemia, and diet have all been implicated. Use of human milk and standardized feedings are the only strategies that consistently have been shown to decrease the incidence of disease [4, 5]. The continued increase in NEC suggests that these strategies are not being fully utilized [6, 7].

Our neonatal intensive care unit (NICU) has been using a standardized feeding protocol with an emphasis on human milk for over 20 years. In 1995, we became a licensed human milk bank, which only accepts donors that have delivered preterm. All ELBW infants in our NICU receive preterm human milk—maternal or donor. They begin enteral feeds 7 days after birth. Trophic feeds are maintained for 7 days and followed by slow advancement over the next 10 days [8]. Fortification was used selectively based on growth after full human milk feeds were achieved. This protocol has been associated with a 1% rate of NEC for ELBW infants for over two decades. In this study, we present detailed feeding outcomes including the incidence of NEC for ELBW infants in our regional center over a recent 6-year period.

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DE GRUYTER DOI 10.1515/jpm-2012-0196 — J. Perinat. Med. 2013; 41(2): 129–131

Recommendation and Guidelines for Perinatal Practice

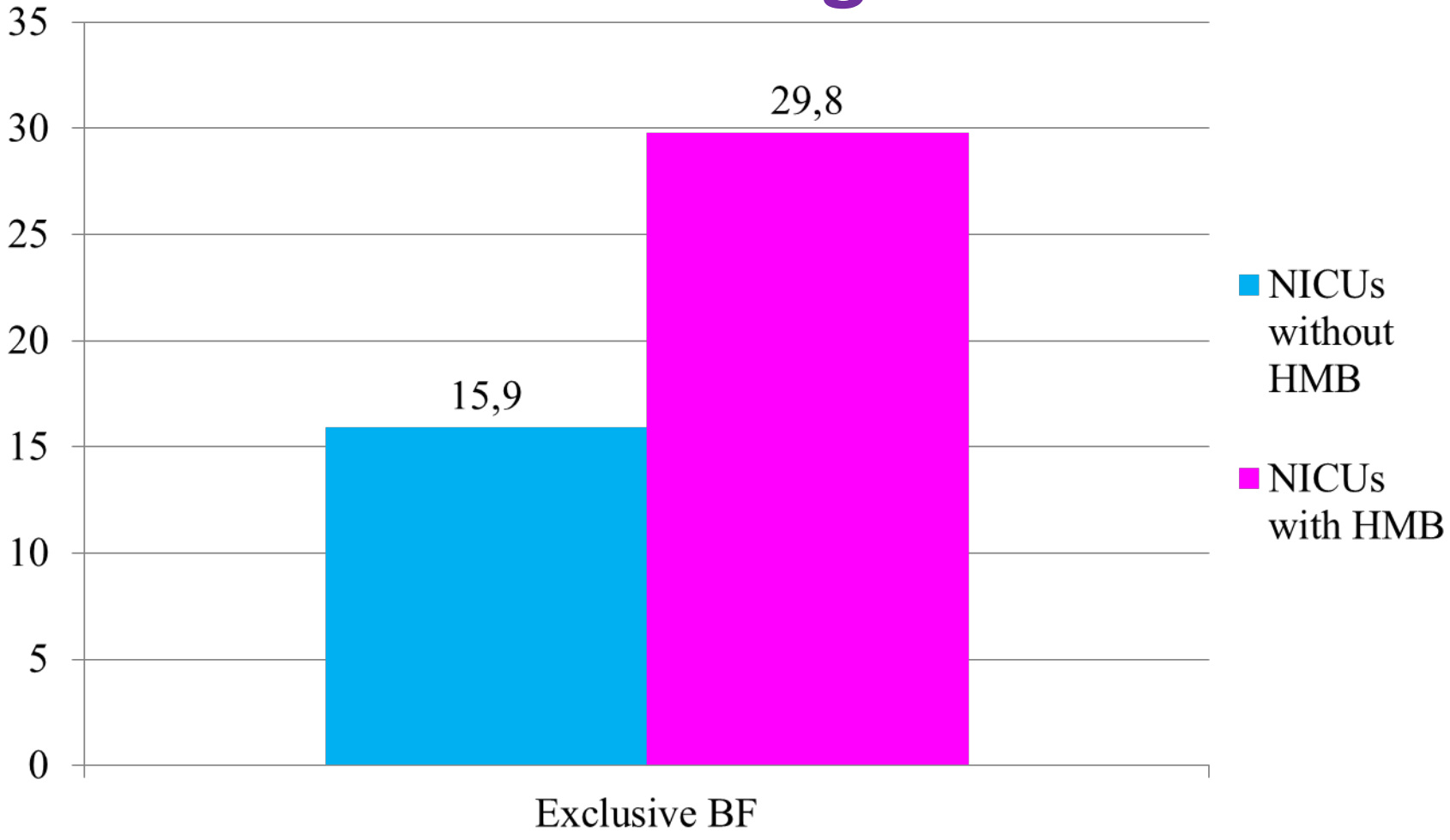
Sertac Arslanoglu[a], Guido E. Moro[a,*], Roberto Bellù, Daniela Turoli, Giuseppe De Nisi, Paola Tonetto and Enrico Bertino

Presence of human milk bank is associated with elevated rate of exclusive breastfeeding in VLBW infants

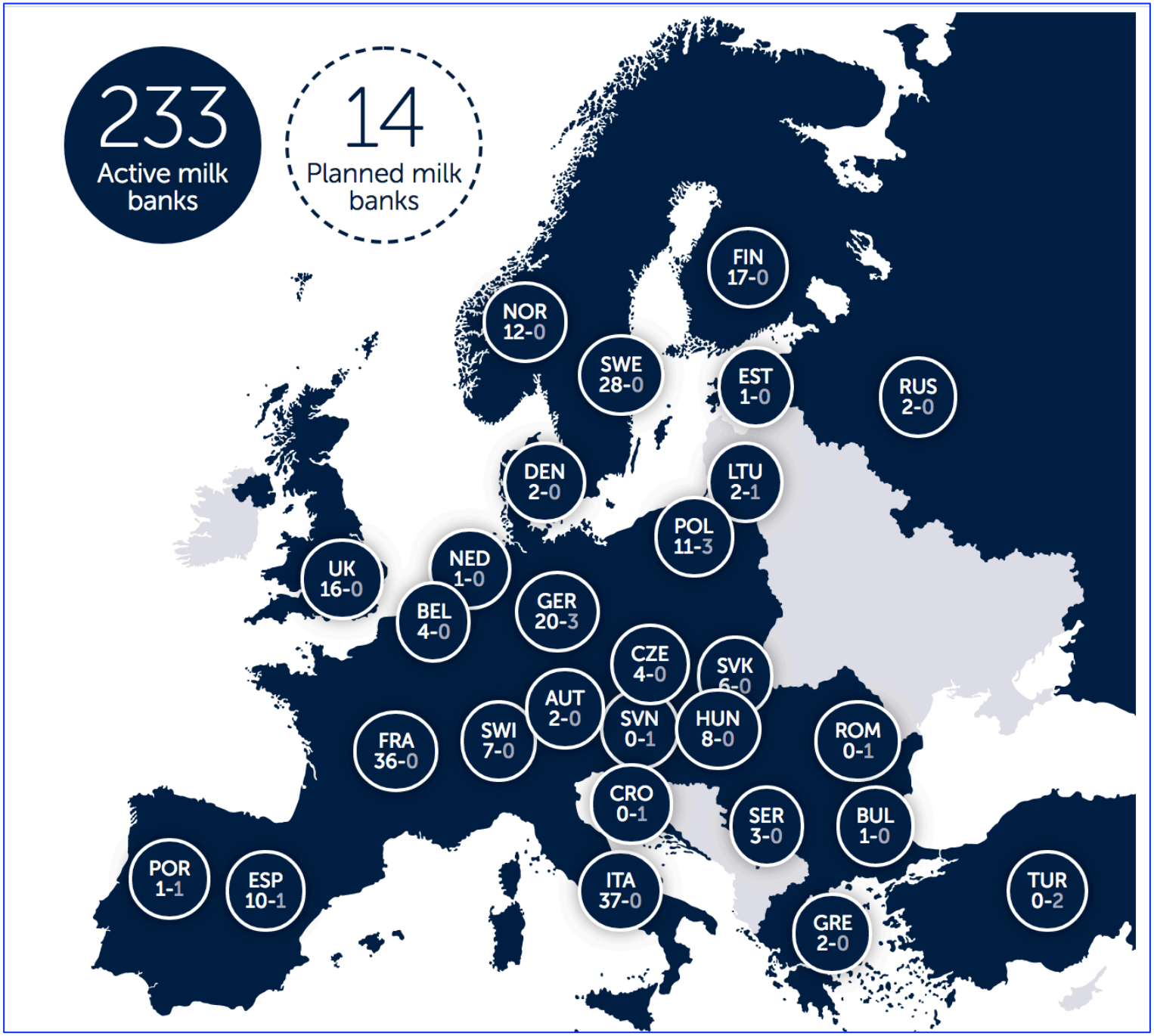
ITALIAN NEONATAL NETWORK-VON 2010 Data

- **Data from 83 NICUs participating to VON**
- **Subjects: 4277 VLBW infants**
- **Breastfeeding at discharge**
  - **Any**
  - **Exclusive**
- **Centers without HMB: 64**
  3333 infants
- **Centers with HMB: 19**
  944 infants

Exclusive breastfeeding at discharge

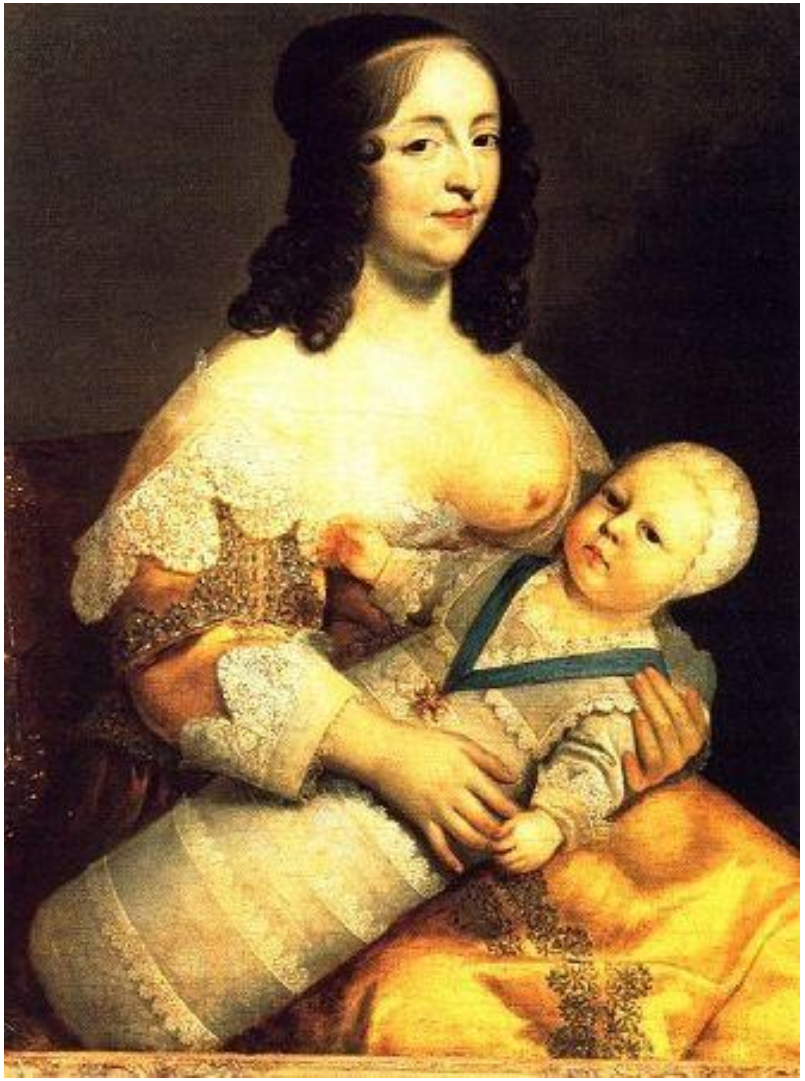


Italian Neonatal Network- VON 2010


233
Active milk banks
14
Planned milk banks
FIN 17-0
NOR 12-0
SWE 28-0
EST 1-0
RUS 2-0
DEN 2-0
LTU 2-1
POL 11-3
UK 16-0
NED 1-0
BEL 4-0
GER 20-3
CZE 4-0
SVK 6-0
AUT 2-0
SVN 0-1
HUN 8-0
ROM 0-1
FRA 36-0
SWI 7-0
CRO 0-1
SER 3-0
BUL 1-0
POR 1-1
ESP 10-1
ITA 37-0
GRE 2-0
TUR 0-2

Alexey Venetsianov
Wet-Nurse with a Child, 1830.

- The origins of donor milk banking go back to earlier times when children were breast fed by friends, relatives or strangers - a practice referred to as "wet nursing".



Among the wealthy upper class in European countries from 1500 to 1700 the hiring of wet nurses was the norm.

Babylonia 1780 BC

Evidence of the support for "wet nursing" is already present in the Code of Hammurabi.

Transition from wetnursing to HM banking in 1909

Theodor Escherich (1857–1911)

The first human milk bank in Vienna - 1909

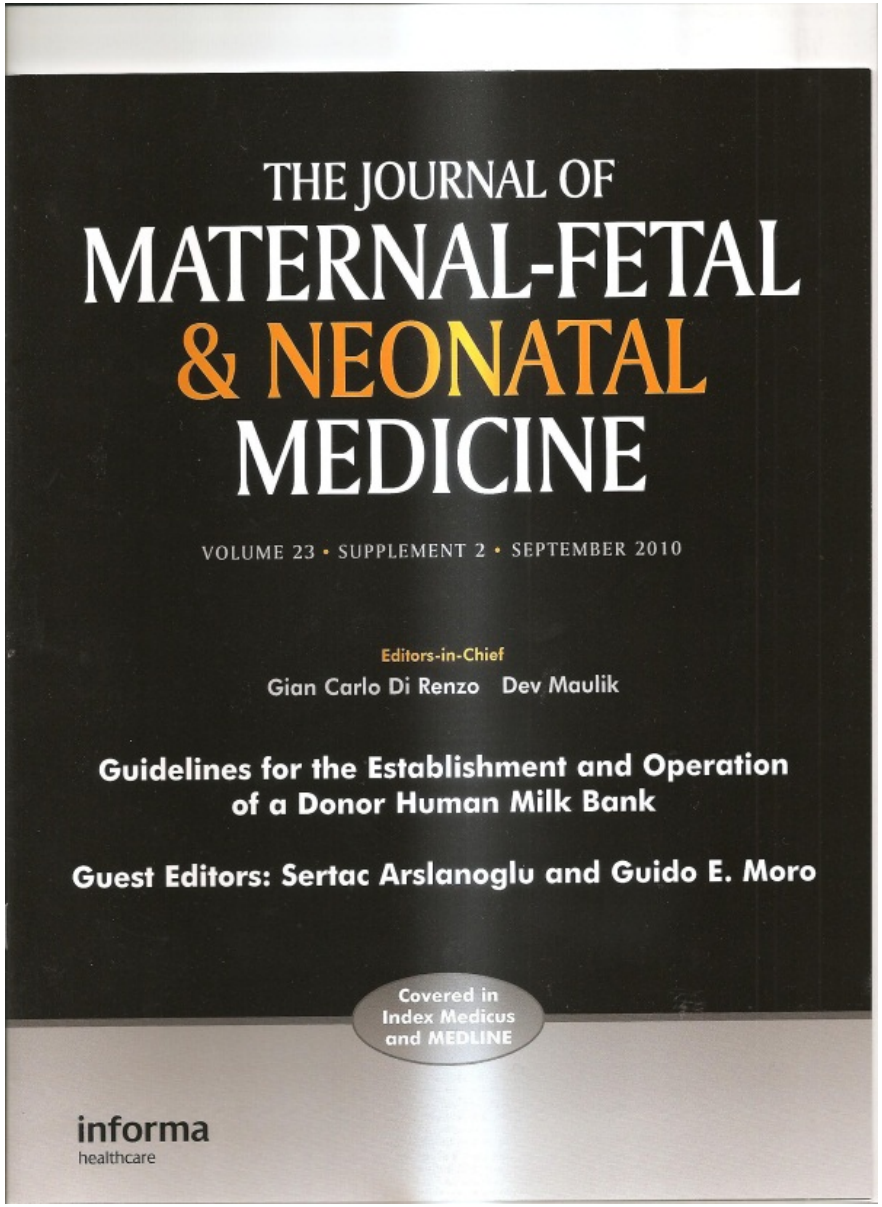
It has been integrated into the national strategies to improve health in the developed countries.

EMBA:

- Officially founded in 2010
- Not for profit
- No 1 aim: to promote breastfeeding

a. Promote breast feeding
b. Promote the donation of human milk to Human Milk Banks (HMB)
c. Promote the utilization of donor human milk for premature infants and other infants with specific needs who do not have access to their own mother's milk
d. Promote milk banking and the establishment of new human milk banks
e. Promote international co-operation between HMBs and between National Associations/Groups of Human Milk Banks in Europe
f. Prepare international and regularly revised guidelines to set standards for the practice of milk banking
g. Promote quality control of donor human milk banking among member banks through adherence to guidelines
h. Provide a forum for the exchange of information about milk banking
i. Promote continual education and updating of health and social workers

Guidelines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Guidelines for the Establishment and Operation of a Donor Human Milk Bank
Guest Editors: Sertac Arslanoglu and Guido E. Moro
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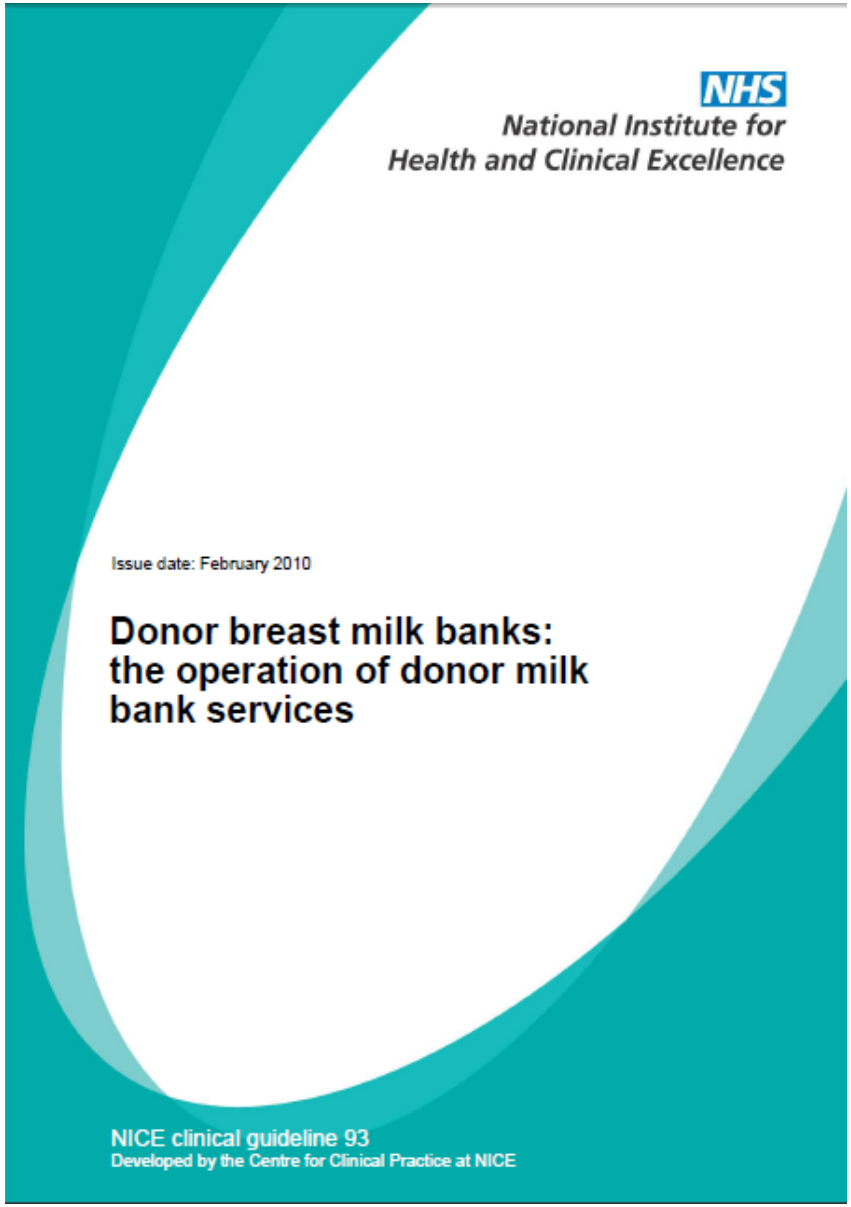
NHS
National Institute for Health and Clinical Excellence
Issue date: February 2010
Donor breast milk banks: the operation of donor milk bank services
NICE clinical guideline 93
Developed by the Centre for Clinical Practice at NICE

PATH Technical Advisory Group Meeting

frontiers in Pediatrics

REVIEW
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Fortification of Human Milk for Preterm Infants: Update and Recommendations of the European Milk Bank Association (EMBA) Working Group on Human Milk Fortification

Sertac Arslanoglu[1*†], Clair-Yves Boquien[2†], Caroline King[3†], Delphine Lamireau[4†], Paola Tonetto[5†], Debbie Barnett[6], Enrico Bertino[5], Antoni Gaya[7], Corinna Gebauer[8], Anne Grovslien[9], Guido E. Moro[10], Gillian Weaver[11], Aleksandra Maria Wesolowska[12] and Jean-Charles Picaud[13,14†]

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frontiers

Processing of donor human milk: Update and recommendations from the European Milk Bank Association (EMBA)

Guido E. Moro[1*], Claude Billeaud[2], BUFFIN RACHEL[3], Javier Calvo[4], Laura Cavallarin[5], Lukas Christen[6], Diana Escuder[7], Antoni Gaya[4], David Lembo[8], Aleksandra Wesolowska[9], Sertac Arslanoglu[10], Debbie Barnett[11], Enrico Bertino[12], Clair-Yves BOQUIEN[13], Corinna Gebauer[14], Anne Grovslien[15], Gillian A. Weaver[16], Jean-charles PICAUD[17]

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frontiers in Microbiology

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Strategies for the Preservation, Restoration and Modulation of the Human Milk Microbiota. Implications for Human Milk Banks and Neonatal Intensive Care Units

*Leónides Fernández[1], Lorena Ruiz[2], Josué Jara[1], Belén Orgaz[2] and Juan M. Rodríguez[3]**

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Studies carried in the last years have revealed that human milk contains a site-specific microbiota and constitutes a source of potentially beneficial bacteria to the infant gut. Once in the infant gut, these bacteria contribute to the assembly of a physiological gut microbiota and may play several functions, contributing to infant metabolism, protection against infections, immunomodulation or neuromodulation. Many preterm neonates are fed with pasteurized donor's human milk (DHM) or formula and, therefore, are devoid of contact with human milk microbes. As a consequence, new strategies are required to allow the exposition of a higher number of preterm infants to the human milk microbiota early in life. The first strategy would be to promote and to increase the use of own mother's milk (OMM) in Neonatal Intensive Care Units (NICUs). Even small quantities of OMM can be very valuable since they would be added to DHM in order to microbiologically "customize" it. When OMM is not available, a better screening of donor women, including routine cytomegalovirus (CMV) screening of milk, may help to avoid the pasteurization of the milk provided by, at least, a relevant proportion of donors. Finally, when pasteurized DHM or formula are the only feeding option, their supplementation with probiotic bacteria isolated from human milk, such as lactic

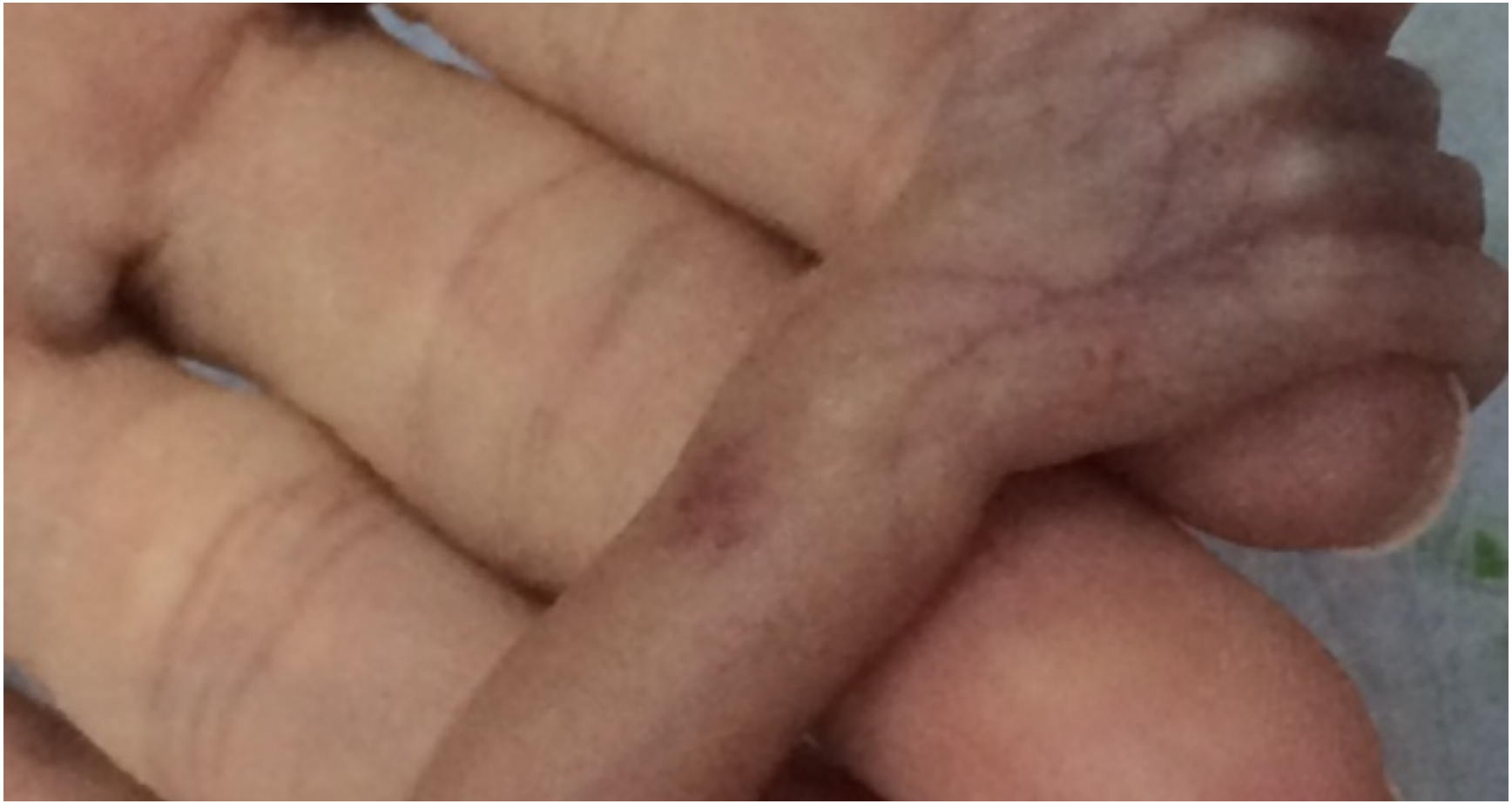
Take Home Messages

1. Human milk is the best food for all neonates and has vital importance for sick and preterm infants in NICU
2. Absence of human milk is associated with NEC, infection, ROP, BPD, mortality, and neurocognitive deficits
3. OMM is the first choice, every effort should be done to promote lactation
4. When OMM is not available, DHM is the recommended choice
5. DHM has to be obtained from HMBanks following specific guidelines

Take Home Messages II

5. DHM should be fortified for preterm infants weighing less than 1800 g
6. Individualized fortification is recommended
7. DHM is pasteurized to ensure microbiological and viral safety
8. At the moment Holder pasteurization is the best compromise to ensure safety and attain milk quality
9. New methods are under investigation. Some are promising (ex:Flash)
10. Cultural, religious believes are not barriers to milk banking, alternative models are available

Providing human milk for preterm infants has become a human right to give a good start to life …



EVERY DROP IS GOLD

THANK YOU…

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