

Got Milk? Optimizing Nutrition of Human Milk for Premature Infants

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Objectives

- Review the nutritional goals for premature infants.
- List the macronutrient requirements for premature infants.
- Describe the unique nutritional challenges of premature infants.
- Describe the need for fortification of human milk to meet the nutritional goals of premature infants.
- Identify key differences between human milk fortifiers.



Human Milk is Preferred Feeding for All Infants

- American Academy of Pediatrics support feeding of human milk for all infants, term and preterm
- And....
- Human milk is nutritionally insufficient to fully support the growth needs of very low birth weight and extremely low birth weight infants



Human Milk and Prematurity

Benefits of HM in Premature Infants
Preterm Infant Nutrition and Growth Goals



Human Milk and Prematurity

- Over 63,000 very preterm (<32 weeks) infants born in US
- At risk for undernutrition during long NICU stay
- Critical time for organ development
- Short- and long- term benefits of HM for preterm infants
- Addition of fortifiers to HM is standard practice
- Fortifiers designed to meet recommended nutrient goals when added to milk with average nutrient values at typical volumes
- Several products and strategies are available to fortify HM

Beckford, M. Macronutrient Intake from Human Milk, Infant Growth, and Body Composition at Term Equivalent Age: A Longitudinal Study of Hospitalized Very Preterm Infants. *Nutrients* 2020.



Human Milk and Prematurity

- NICU growth outcomes have improved in recent years
- Fortified HM-fed infants have shown slower weight gain and head growth compared to preterm formula-fed infants
- Current fortification strategies may not meet nutritional requirements for all infants
- Increase in use of maternal and donor human milk
- Macronutrient content of HM highly variable

Ballon, M. Macronutrient Intake from Human Milk, Infant Growth, and Body Composition at Term Equivalent Age: A Longitudinal Study of Hospitalized Very Preterm Infants. *Nutrients* 2020.



Human Milk Benefits for Preterm

- Protection against Necrotizing Enterocolitis
- Protection against Late Onset Sepsis
- Priming of the immature gut
- ?Protection against Severe Retinopathy of Prematurity
- ?Protection against Bronchopulmonary Dysplasia
- ?Improvement of long-term Neurocognitive Development
- ?Improvement of Cardiovascular Health

JPGN Human Milk in Feeding Premature Infants
Consensus Statement September 2015



Preterm Nutrition and Growth Goals

- Meet goals of *in utero* growth of normal fetus of same post-conceptual age
 - Body weight and length
 - Body composition
 - Organ development and maturity
- Catch up growth for deficiencies

AAP Committee on Nutrition (2019). *Pediatric Nutrition*, 8th Ed



Preterm Nutrition and Growth Goals

- Achieving adequate/optimal growth in preterm infants
- Extremely relevant for long-term neurodevelopment
- Reducing extrauterine growth restriction (EUGR)
- Goal not to lose more than 1 standard deviation in weight and HC from birth to discharge
- Growth ➡ only weight gain, don't forget length and HC

JPGN Human Milk in Feeding Premature Infants
Consensus Statement September 2015



Preterm Nutritional Requirements

- Energy
- Protein
- Fat
- Carbohydrates
- Oligosaccharides
- Sodium, Potassium, Chloride
- Calcium, Phosphorus, Magnesium
- Iron
- Zinc, Copper, Iodine, other trace elements

AAP Committee on Nutrition (2019). *Pediatric Nutrition*, 8th Ed



Preterm Nutritional Requirements

Table 1
Requirements for protein and energy; best estimates by factorial and empirical methods (14).

Body weight, g	500-1,000	1,001-1,500	1,501-2,000
Weight gain of fetus, g/kg/d	19.0	17.4	16.4
Protein, g/kg/d	4.0	3.9	3.7
Energy, Kcal/kg/d	106	115	123
Protein:energy, g/100 kcal	3.8	3.4	3.0

Aslanoglu S et al. Fortification of Human Milk for Preterm Infants: Update and Recommendations of ELMA Working Group. *Front Pediatr*. 2019



Preterm Nutritional Requirements

Table 2

Requirements for major minerals and electrolytes determined by factorial method, listed by body weight (31).

	800-1,000 g		1,001-1,500 g		1,501-2,000 g	
	Accretion	Requirement	Accretion	Requirement	Accretion	Requirement
Ca (mg)	102	184	99	178	96	173
P (mg)	66	126	65	124	63	120
Mg (mg)	2.8	6.9	2.7	6.7	2.5	6.4
Na (mmol)	1.54	3.3	1.37	3.0	1.06	2.6
K (mmol)	0.78	2.4	0.72	2.3	0.63	2.2
Cl (mmol)	1.28	2.8	0.99	2.7	0.74	2.5

Antonangelo S et al. Fortification of Human Preterm Infants: Update and Recommendations of EMBA Working Group. *Front Pediatr*. 2019



Preterm Nutritional Requirements

Table 3

Recommended enteral protein and energy intakes for clinically stable very low birthweight infants (30, 32, 33).

	Monich consensus 2014	ESPGHAN 2010	Ziegler et al.
Energy (kcal/kg/d)	110-130	110-135	105-127
Protein (g/kg/d)	3.5-4.5	4.0-4.5 (<1 kg)	3.9-4.6
		3.5-4.0 (1-1.8 kg)	
Protein:Energy (g/100 kcal)	3.2-4.1	3.2-4.1	3.1-3.8
Lipids (g/kg/d)	4.8-6.6	4.8-6.6	-
Carbohydrates (g/kg/d)	11.6-13.2	11.6-13.2	-

Antonangelo S et al. Fortification of Human Preterm Infants: Update and Recommendations of EMBA Working Group. *Front Pediatr*. 2019



Human Milk: Known vs Unknown

Table 1 The knowns and unknowns about human milk and its use in preterm infants.

Knowns	Unknowns
Human milk: <ul style="list-style-type: none"> • Most rapid achievement of full term • NEC • NEC • Improved brain development and neurodevelopmental outcome • Hospital admission up to 30 months • Feeding (RDP) • Cost of care • Many effects documented • Human protein (protein with RDP) 	<ul style="list-style-type: none"> • Uncertainty of size of effect on morbidity in context of modern neonatal care • What size the critical periods of exposure • Variability in composition • Effect on nutrient composition of standing, refrigeration and freeze-thawing • Possibility of substitution to human protein with RDP • Optimal approach to risk of transmission of virus and bacteria
ESBM: <ul style="list-style-type: none"> • Improved feed tolerance • NEC • Improved pulmonary health • Improved cognition • Better bone mineral content 	<ul style="list-style-type: none"> • Duration size of effect on protein metabolism of ESBM versus MBSM • Possible mechanism to increase stress with less absorption of nutrients • Variability in composition • Uncertainty about effect of maternal nutrient and milk intake • Small concerns about emerging pathogens
Defects: <ul style="list-style-type: none"> • Less nutrient rich than proteins MBSM • Bacteria and blood borne viruses inactivated by pasteurization • Pasteurization reduces concentration of immune factors 	

ESBM, donor breast milk; RDP, human milk receptor; MBSM, mother's expressed breast milk; NEC, necrotizing enterocolitis.

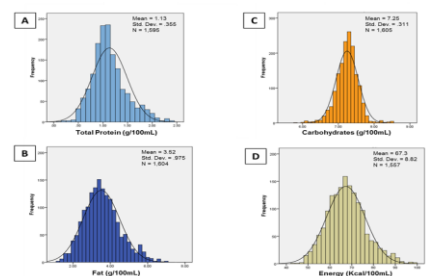
Merion G. et al. *Arch Dis Child Fetal Neonatal* E5 2013;95:F59-F62.



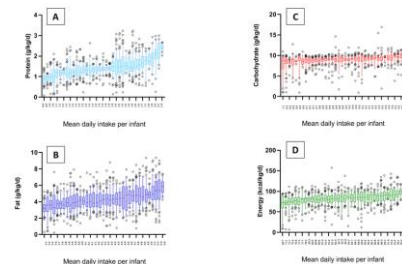
Macronutrient Intake from HM Varies

- Longitudinal study
- 37 infants <32 weeks gestation
- Analyzed 1626 HM samples
- Study aims:
 - Determine between-infant variation in macronutrient intake from HM
 - Examine associations of macronutrient intake with growth outcomes

Belfort M. Macronutrient Intake from Human Milk, Infant Growth, and Body Composition at Term Equivalent Age: A Longitudinal Study of Hospitalized Very Preterm Infants. *Nutrients* 2020.



Belfort M. Macronutrient Intake from Human Milk, Infant Growth, and Body Composition at Term Equivalent Age: A Longitudinal Study of Hospitalized Very Preterm Infants. *Nutrients* 2020.



Belfort M. Macronutrient Intake from Human Milk, Infant Growth, and Body Composition at Term Equivalent Age: A Longitudinal Study of Hospitalized Very Preterm Infants. *Nutrients* 2020.



Macronutrient Intake from HM Varies

- Greater intakes of fat and energy associated with higher weight
- Greater protein intake associated with greater body length
- Higher fat intake associated with higher fat mass and fat-free mass
- Macronutrient intakes from HM highly variable and associated with growth outcomes despite routine fortification

Bellizzi M. Macronutrient Intake from Human Milk, Infant Growth, and Body Composition at Term-Equivalent Age: A Longitudinal Study of Hospitalized Very Preterm Infants. *Nutrients* 2020.



Sources of Human Milk

Mother's Milk
Donor Milk



Sources of Human Milk

- Mother's milk
- Donor milk
- **NOT** the internet

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Cow's Milk Contamination of Human Milk Purchased via the Internet
Sarah A. Keim, Manjusha M. Kulkarni, Kelly McNamara, Sheela R. Geraghty,
Rachel M. Billock, Rachel Roman, Joseph S. Hogan and Jesse J. Kwitek
Pediatrics 2015;135:e1157
DOI: 10.1542/peds.2014-3554 originally published online April 6, 2015.



Breastmilk Black Market

- Discourage families from direct HM sharing/purchasing online
- Increased risks of bacterial or viral contamination
- Exposure to medications, drugs, other substances
- No guarantee it was stored properly
- Cow's milk Contamination

Keim, Sarah et al. *Pediatrics* 2015;135:31157.



Donor Human Milk

- Prioritization for preterm infants <1500 g
- Ideally a temporary bridge to obtaining mother's milk
- Does not compete with mother's own milk
- Growth outcomes:
 - Lower protein content
 - Lower energy content
 - Loss of bile salt-dependent lipase activity
- Pasteurization:
 - Loss of nutrients
 - Anti-inflammatory factors
 - Can eliminate bacterial strains with probiotic properties
 - Bioactive components substantially decreased
 - Much less effect on macro- and micro- nutrients

AMP Committee on Nutrition, AMP Section on Breastfeeding, AMP Committee on Fetus and Neonatal 2017



Donor Human Milk

- Donor HM should be obtained from a well-established milk bank
- HMB must follow specific safety guidelines
- Collection, treatment, distribution of DHM processes
- Need universal quality principles for all HMB
- DHM currently requires pasteurization, freezing, thawing
- Currently recommend Holder pasteurization for DHM
- New methods of DHM treatment are under investigation

JPDN Human Milk in Feeding Premature Infants
Consensus Statement September 2015



Promotion of Breast Feeding in the NICU

- Begin milk expression as soon after delivery as possible
- Use colostrum for oral cares
- Encourage kangaroo care
- Strategies to promote and support breast-feeding for preterm infants in every maternity or children's hospital
- Hospital-based lactation programs
- Fresh mother's own milk is first choice
- Ensure processes in place for safe centralized handling of HM

JPDN Human Milk Feeding/Premature Infants
Consensus Statement September 2015



Fortification of Human Milk

Multi-nutrient Fortifiers
Single-nutrient Supplements
Fortification Strategies



Multi-Nutrient Fortifiers

- Most multi-nutrient fortifiers contain bovine milk protein
- Donkey milk recently proposed as composition similar to HM
- HM based fortifier

Aslanoglu S et al. Fortification of HM for Preterm Infants: Update and
Recommendations of EMBA Working Group. *Front Pediatr*. 2019



Human Milk Fortifiers

- Formula
- Human Milk Fortifier
 - Powder vs Liquid
 - Sterilization: heat vs acidification
 - Human vs Bovine vs Donkey?
- Supplements
 - Protein
 - Lipids
 - Carbohydrates

Aslanoglu S et al. Fortification of HM for Preterm Infants: Update and
Recommendations of EMBA Working Group. *Front Pediatr*. 2019



Table 4

Nutrient composition of selected fortifiers and supplements.

Fortifier	Bovine-based products (per gram of powder)										Human milk-based fortifier (per volume)			
	Multicomponent fortifiers					Protein supplements					A	B	M	N
Volume (ml)	/	/	/	/	/	/	/	/	/	/	20	30	40	50
Energy (kcal)	4.4 (5)	3.5	3.6	4.9 (5)	3.9 (5)	3.4	3.6	3.6	4	3.7	28	42	56	71
Protein (g)	0.3 ^{DEF}	0.3 ^{DEF}	0.4	0.3	0.2 ^{DEF}	0.3 ^{DEF}	0.3 ^{DEF}	0.3 ^{DEF}	0.3 ^{DEF}	0.3 ^{DEF}	1.2	1.8	2.4	3
Na (mg)	9.2	8.6	1.4	5.6	4.2	7.8	9.2	2.1	3	0	20	40	42	45
Ca (mg)	18.9	14.9	10	32	33	5.2	12.8	0	4	0	100	100	100	111
P (mg)	11	8.7	7	18	19	5.2	6.73	0	3	0	53.8	54.9	56	57.5
Iron (mg)	0.5	0	0	0.5	0.1	0	0.007	0	0	0	0.1	0.15	0.2	0.25

C, IgHb; FFE, partially hydrolyzed; EEE, extensively hydrolyzed; FF, whole protein; EEEFF, human milk-based fortifier; A, FortiPreM; B, FortiPreM; D, Donkey; C, FFE; E, IgHb; F, IgHb; G, IgHb; H, IgHb; I, IgHb; J, IgHb; K, IgHb; L, IgHb; M, IgHb; N, IgHb; O, IgHb; P, IgHb; Q, IgHb; R, IgHb; S, IgHb; T, IgHb; U, IgHb; V, IgHb; W, IgHb; X, IgHb; Y, IgHb; Z, IgHb; AA, IgHb; AB, IgHb; AC, IgHb; AD, IgHb; AE, IgHb; AF, IgHb; AG, IgHb; AH, IgHb; AI, IgHb; AJ, IgHb; AK, IgHb; AL, IgHb; AM, IgHb; AN, IgHb; AO, IgHb; AP, IgHb; AQ, IgHb; AR, IgHb; AS, IgHb; AT, IgHb; AU, IgHb; AV, IgHb; AW, IgHb; AX, IgHb; AY, IgHb; AZ, IgHb; BA, IgHb; BB, IgHb; BC, IgHb; BD, IgHb; BE, IgHb; BF, IgHb; BG, IgHb; BH, IgHb; BI, IgHb; BJ, IgHb; BK, IgHb; BL, IgHb; BM, IgHb; BN, IgHb; BO, IgHb; BP, IgHb; BQ, IgHb; BR, IgHb; BS, IgHb; BT, IgHb; BU, IgHb; BV, IgHb; BW, IgHb; BX, IgHb; BY, IgHb; BZ, IgHb; CA, IgHb; CB, IgHb; CC, IgHb; CD, IgHb; CE, IgHb; CF, IgHb; CG, IgHb; CH, IgHb; CI, IgHb; CJ, IgHb; CK, IgHb; CL, IgHb; CM, IgHb; CN, IgHb; CO, IgHb; CP, IgHb; CQ, IgHb; CR, IgHb; CS, IgHb; CT, IgHb; CU, IgHb; CV, IgHb; CW, IgHb; CX, IgHb; CY, IgHb; CZ, IgHb; DA, IgHb; DB, IgHb; DC, IgHb; DD, IgHb; DE, IgHb; DF, IgHb; DG, IgHb; DH, IgHb; DI, IgHb; DJ, IgHb; DK, IgHb; DL, IgHb; DM, IgHb; DN, IgHb; DO, IgHb; DP, IgHb; DQ, IgHb; DR, IgHb; DS, IgHb; DT, IgHb; DU, IgHb; DV, IgHb; DW, IgHb; DX, IgHb; DY, IgHb; DZ, IgHb; EA, IgHb; EB, IgHb; EC, IgHb; ED, IgHb; EE, IgHb; EF, IgHb; EG, IgHb; EH, IgHb; EI, IgHb; EJ, IgHb; EK, IgHb; EL, IgHb; EM, IgHb; EN, IgHb; EO, IgHb; EP, IgHb; EQ, IgHb; ER, IgHb; ES, IgHb; ET, IgHb; EU, IgHb; EV, IgHb; EW, IgHb; EX, IgHb; EY, IgHb; EZ, IgHb; FA, IgHb; FB, IgHb; FC, IgHb; FD, IgHb; FE, IgHb; FF, IgHb; FG, IgHb; FH, IgHb; FI, IgHb; FJ, IgHb; FK, IgHb; FL, IgHb; FM, IgHb; FN, IgHb; FO, IgHb; FP, IgHb; FQ, IgHb; FR, IgHb; FS, IgHb; FT, IgHb; FU, IgHb; FV, IgHb; FW, IgHb; FX, IgHb; FY, IgHb; FZ, IgHb; GA, IgHb; GB, IgHb; GC, IgHb; GD, IgHb; GE, IgHb; GF, IgHb; GG, IgHb; GH, IgHb; GI, IgHb; GJ, IgHb; GK, IgHb; GL, IgHb; GM, IgHb; GN, IgHb; GO, IgHb; GP, IgHb; GQ, IgHb; GR, IgHb; GS, IgHb; GT, IgHb; GU, IgHb; GV, IgHb; GW, IgHb; GX, IgHb; GY, IgHb; GZ, IgHb; HA, IgHb; HB, IgHb; HC, IgHb; HD, IgHb; HE, IgHb; HF, IgHb; HG, IgHb; HH, IgHb; HI, IgHb; HJ, IgHb; HK, IgHb; HL, IgHb; HM, IgHb; HN, IgHb; HO, IgHb; HP, IgHb; HQ, IgHb; HR, IgHb; HS, IgHb; HT, IgHb; HU, IgHb; HV, IgHb; HW, IgHb; HX, IgHb; HY, IgHb; HZ, IgHb; IA, IgHb; IB, IgHb; IC, IgHb; ID, IgHb; IE, IgHb; IF, IgHb; IG, IgHb; IH, IgHb; II, IgHb; IJ, IgHb; IK, IgHb; IL, IgHb; IM, IgHb; IN, IgHb; IO, IgHb; IP, IgHb; IQ, IgHb; IR, IgHb; IS, IgHb; IT, IgHb; IU, IgHb; IV, IgHb; IW, IgHb; IX, IgHb; IY, IgHb; IZ, IgHb; JA, IgHb; JB, IgHb; JC, IgHb; JD, IgHb; JE, IgHb; JF, IgHb; JG, IgHb; JH, IgHb; JI, IgHb; JJ, IgHb; JK, IgHb; JL, IgHb; JM, IgHb; JN, IgHb; JO, IgHb; JP, IgHb; JQ, IgHb; JR, IgHb; JS, IgHb; JT, IgHb; JU, IgHb; JV, IgHb; JW, IgHb; JX, IgHb; JY, IgHb; JZ, IgHb; KA, IgHb; KB, IgHb; KC, IgHb; KD, IgHb; KE, IgHb; KF, IgHb; KG, IgHb; KH, IgHb; KI, IgHb; KJ, IgHb; KK, IgHb; KL, IgHb; KM, IgHb; KN, IgHb; KO, IgHb; KP, IgHb; KQ, IgHb; KR, IgHb; KS, IgHb; KT, IgHb; KU, IgHb; KV, IgHb; KW, IgHb; KX, IgHb; KY, IgHb; KZ, IgHb; LA, IgHb; LB, IgHb; LC, IgHb; LD, IgHb; LE, IgHb; LF, IgHb; LG, IgHb; LH, IgHb; LI, IgHb; LJ, IgHb; LK, IgHb; LL, IgHb; LM, IgHb; LN, IgHb; LO, IgHb; LP, IgHb; LQ, IgHb; LR, IgHb; LS, IgHb; LT, IgHb; LU, IgHb; LV, IgHb; LW, IgHb; LX, IgHb; LY, IgHb; LZ, IgHb; MA, IgHb; MB, IgHb; MC, IgHb; MD, IgHb; ME, IgHb; MF, IgHb; MG, IgHb; MH, IgHb; MI, IgHb; MJ, IgHb; MK, IgHb; ML, IgHb; MN, IgHb; MO, IgHb; MP, IgHb; MQ, IgHb; MR, IgHb; MS, IgHb; MT, IgHb; MU, IgHb; MV, IgHb; MW, IgHb; MX, IgHb; MY, IgHb; MZ, IgHb; NA, IgHb; NB, IgHb; NC, IgHb; ND, IgHb; NE, IgHb; NF, IgHb; NG, IgHb; NH, IgHb; NI, IgHb; NJ, IgHb; NK, IgHb; NL, IgHb; NM, IgHb; NO, IgHb; NP, IgHb; NQ, IgHb; NR, IgHb; NS, IgHb; NT, IgHb; NU, IgHb; NV, IgHb; NW, IgHb; NX, IgHb; NY, IgHb; NZ, IgHb; OA, IgHb; OB, IgHb; OC, IgHb; OD, IgHb; OE, IgHb; OF, IgHb; OG, IgHb; OH, IgHb; OI, IgHb; OJ, IgHb; OK, IgHb; OL, IgHb; OM, IgHb; ON, IgHb; OO, IgHb; OP, IgHb; OQ, IgHb; OR, IgHb; OS, IgHb; OT, IgHb; OU, IgHb; OV, IgHb; OW, IgHb; OX, IgHb; OY, IgHb; OZ, IgHb; PA, IgHb; PB, IgHb; PC, IgHb; PD, IgHb; PE, IgHb; PF, IgHb; PG, IgHb; PH, IgHb; PI, IgHb; PJ, IgHb; PK, IgHb; PL, IgHb; PM, IgHb; PN, IgHb; PO, IgHb; PP, IgHb; PQ, IgHb; PR, IgHb; PS, IgHb; PT, IgHb; PU, IgHb; PV, IgHb; PW, IgHb; PX, IgHb; PY, IgHb; PZ, IgHb; QA, IgHb; QB, IgHb; QC, IgHb; QD, IgHb; QE, IgHb; QF, IgHb; QG, IgHb; QH, IgHb; QI, IgHb; QJ, IgHb; QK, IgHb; QL, IgHb; QM, IgHb; QN, IgHb; QO, IgHb; QP, IgHb; QQ, IgHb; QR, IgHb; QS, IgHb; QT, IgHb; QU, IgHb; QV, IgHb; QW, IgHb; QX, IgHb; QY, IgHb; QZ, IgHb; RA, IgHb; RB, IgHb; RC, IgHb; RD, IgHb; RE, IgHb; RF, IgHb; RG, IgHb; RH, IgHb; RI, IgHb; RJ, IgHb; RK, IgHb; RL, IgHb; RM, IgHb; RN, IgHb; RO, IgHb; RP, IgHb; RQ, IgHb; RR, IgHb; RS, IgHb; RT, IgHb; RU, IgHb; RV, IgHb; RW, IgHb; RX, IgHb; 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VU, IgHb; VV, IgHb; VW, IgHb; VX, IgHb; VY, IgHb; VZ, IgHb; WA, IgHb; WB, IgHb; WC, IgHb; WD, IgHb; WE, IgHb; WF, IgHb; WG, IgHb; WH, IgHb; WI, IgHb; WJ, IgHb; WK, IgHb; WL, IgHb; WM, IgHb; WN, IgHb; WO, IgHb; WP, IgHb; WQ, IgHb; WR, IgHb; WS, IgHb; WT, IgHb; WU, IgHb; WV, IgHb; WW, IgHb; WX, IgHb; WY, IgHb; WZ, IgHb; XA, IgHb; XB, IgHb; XC, IgHb; XD, IgHb; XE, IgHb; XF, IgHb; XG, IgHb; XH, IgHb; XI, IgHb; XJ, IgHb; XK, IgHb; XL, IgHb; XM, IgHb; XN, IgHb; XO, IgHb; XP, IgHb; XQ, IgHb; XR, IgHb; XS, IgHb; XT, IgHb; XU, IgHb; XV, IgHb; XW, IgHb; XX, IgHb; XY, IgHb; XZ, IgHb; YA, IgHb; YB, IgHb; YC, IgHb; YD, IgHb; YE, IgHb; YF, IgHb; YG, IgHb; YH, IgHb; YI, IgHb; YJ, IgHb; YK, IgHb; YL, IgHb; YM, IgHb; YN, IgHb; YO, IgHb; YP, IgHb; YQ, IgHb; YR, IgHb; YS, IgHb; YT, IgHb; YU, IgHb; YV, IgHb; YW, IgHb; YX, IgHb; YY, IgHb; YZ, IgHb; ZA, IgHb; ZB, IgHb; ZC, IgHb; ZD, IgHb; ZE, IgHb; ZF, IgHb; ZG, IgHb; ZH, IgHb; ZI, IgHb; ZJ, IgHb; ZK, IgHb; ZL, IgHb; ZM, IgHb; ZN, IgHb; ZO, IgHb; ZP, IgHb; ZQ, IgHb; ZR, IgHb; ZS, IgHb; ZT, IgHb; ZU, IgHb; ZV, IgHb; ZW, IgHb; ZX, IgHb; ZY, IgHb; ZZ, IgHb;

Aslanoglu S et al. Fortification of HM for Preterm Infants: Update and
Recommendations of EMBA Working Group. *Front Pediatr*. 2019



Single-Nutrient Supplements

- Protein
 - Many protein supplements not specifically designed for neonates
 - +/- Partially or extensively hydrolyzed protein
 - New products designed for preterm infants
 - No consensus on how to use these products
- Lipids
 - Medium chain triglycerides
 - HM derived cream supplement
- Carbohydrates
 - Dextrin maltose

Aslanoglu S et al. Fortification of HM for Preterm Infants: Update and
Recommendations of EMBA Working Group. *Front Pediatr*. 2019



Fortification Strategies

- Standard Fortification
- Individualized Fortification
 - Adjustable Fortification
 - Targeted Fortification

Arslanoglu S et al. Fortification of HM for Preterm Infants: Update and Recommendations of EBMA Working Group. *Front Pediatr*. 2019



Table 5

Current human milk fortification methods (43, 74, 78–79).

Fortification method	Principle	Advantages/Disadvantages
1. Standard (STD) Fortification	Fortification method currently in use in most of the neonatal units. A fixed amount of fortifier is added to a fixed volume of HM according to the manufacturer's instructions.	Practical. But has not solved the problem of protein undernutrition for VLBW infants. Despite STD fortification many VLBW infants continue to have suboptimal growth.
2. Individualized HM Fortification Methods	Protein adequacy is monitored by BCN twice weekly, cut-off levels of BCN are 10–18 mg/dL. If the level is <10 mg/dL extra protein is added to the STD fortification.	Practical, not labor intensive. Doesn't need expensive devices. Monitor protein status of each infant.
a. Adjustable (ADJ) Fortification	Macronutrient concentrations in HM are analyzed and based on the results milk is supplemented with extra protein and/or fat.	Infants also against excessive protein intake. Protein to be effective in optimizing growth and protein status with a BCT.
b. Targeted Fortification		A real individualized method taking into consideration each infant's protein requirement. All macronutrients can be supplemented. Bioactive HM analytes are required. May be labor intensive. Supplementation is done according to the population recommendations, does not take into consideration that each individual infant's requirement may be different.

BM, breast milk; VLBW, very low birth weight; BCN, blood urea nitrogen; BCT, randomized controlled trial.

*BCN levels of 10–18 mg/dL correspond to blood urea concentrations of 2.2–4.0–24.28 mg/dL (0.17–0.77 mmol/L).

Arslanoglu S et al. Fortification of HM for Preterm Infants: Update and Recommendations of EBMA Working Group. *Front Pediatr*. 2019



Table 6

The products required and the threshold values of the metabolic marker used for the Adjustable (ADJ) fortification method (72).

Fortifier/supplement required
1. A multi-nutrient fortifier
2. A protein supplement
Metabolic marker and threshold values used to adjust protein supply
Blood urea nitrogen (BCN) <10 mg/dL increase the fortification to the next level 10–18 mg/dL no change
>18 mg/dL decrease the fortification by one level

Table 7

The scheme for adjustable fortification (updated in 2012) (72).

Fortifier/supplement	Fortification levels and the amount of fortifier/supplement to be added (g per 100 mL BM)
	-1 -2 0 Standard (STD) -1 -2 -3
Multi-nutrient HM fortifier	1/4 strength Half strength Full strength Full strength Full strength Full strength
Protein supplement	- - - 0.4 0.8 1.2

Arslanoglu S et al. Fortification of HM for Preterm Infants: Update and Recommendations of EBMA Working Group. *Front Pediatr*. 2019



Conclusions

Conclusions/Comments EBMA

- HM is first choice in preterm feeding
- Unfortified HM insufficient amount of nutrients when fed at usual feeding volumes
- To prevent EUGR, poor neurocognitive outcome and specific nutrient deficiencies, need fortification of HM
- Despite standard fortification, many VLBW infants continue to have suboptimal growth
- Targeted fortification needs to be improved
- HM-based fortification seems promising, still concerns on efficacy, safety, ethical issues
- No strong evidence to support use of hydrolyzed protein source

Arslanoglu S et al. Fortification of HM for Preterm Infants: Update and Recommendations of EBMA Working Group. *Front Pediatr*. 2019



Recommendations EBMA

- HM feeding is basic right for preterm infants
- Mother's own milk is first choice in preterm infant feeding
- When mother's milk unavailable, donor HM is best alternative
- HM fortification recommended for preterm with BW <1800g
- HM fortification can be started when feeds 50–80 mL/kg/day
- Optimization of HM fortification is required



Conclusions/Comments JPGN

- All preterm infants <1800 grams should be fed fortified HM
- HM should be fortified with protein, vitamins and minerals
- Quantity of HM fortification should optimize growth in NICU stay
- HM fortification should start with standard fortification
- If infants do not grow appropriately, advise individualized fortification
 - Targeted fortification (based on milk analysis)
 - Adjustable fortification (based on BUN measurements)
 - Both advisable depending on the NICU experience and facilities

JPGN Human Milk Feeding/Premature Infants
Consensus Statement September 2015



Future Research

- Address nutritional management in specific preterm groups
- Randomized controlled trials assessing efficacy/safety of HM fortification
 - After discharge
 - Adjusted vs targeted
- Defining reasonable and replicable study endpoints in large cohorts
 - Neurocognitive outcomes
 - Body composition
- Optimization of quality of fortifiers

Aslanoglu Serial Fortification of Human Preterm Infants: Update and
Recommendations of EMBA Working Group, Front Pediatr, 2019



Nutrition at Discharge

- No consensus about post discharge nutrition
- Nutritional supplementation for premature infants should be continued for 3-6 months to optimize growth and development
- Studies that evaluated post discharge HM fortification showed no deleterious effect on breastfeeding rates
 - Suggested some advantages

Aslanoglu Serial Fortification of Human Preterm Infants: Update and
Recommendations of EMBA Working Group, Front Pediatr, 2019



Changes You May Wish to Make in Practice

CPQCC Potentially Better Practices



PBP #15: Start Fortification Before Full Feeds are Reached

- Early fortification of HM minimizes nutrition gap
- Best to follow standardized local guidelines
- No clear evidence when it is safe to introduce fortification
- Protocols have increasingly used earlier fortification steps without intestinal complications
- Increase in osmolality with addition of fortifiers does not exceed significant levels of risk that were associated with NEC
- Powdered fortifiers no longer recommended in NICU

CPQCC Quality Improvement Toolkit: Nutritional Support of the VLBW Infant, September 2018



PBP #16: Enteral Feeds Should be Advanced and Concentrated Until Providing Adequate Nutrition to Sustain Optimal Growth

- Provide optimal nutrition/growth, replace need for TPN
- Advance volume to deliver more nutrients 150-200 ml/kg/d +/-
- May need fortification beyond 24 kcal/oz
 - Not well evaluated, but common practice
- Proactive rather than reactive approach
- Adjust feedings based on daily weights
- Customized fortification may be required
 - Adjustable approach: growth and BUN <9 mg/dL
 - Targeted approach: technology to measure macronutrients in milk*

CPQCC Quality Improvement Toolkit: Nutritional Support of the VLBW Infant, September 2018



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