Importance of Adequate DHA/ARA in Preterm Infants

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Pediatric Nutrition
CONTINUING EDUCATION FOR CLINICIANS

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Mead Johnson Nutrition.

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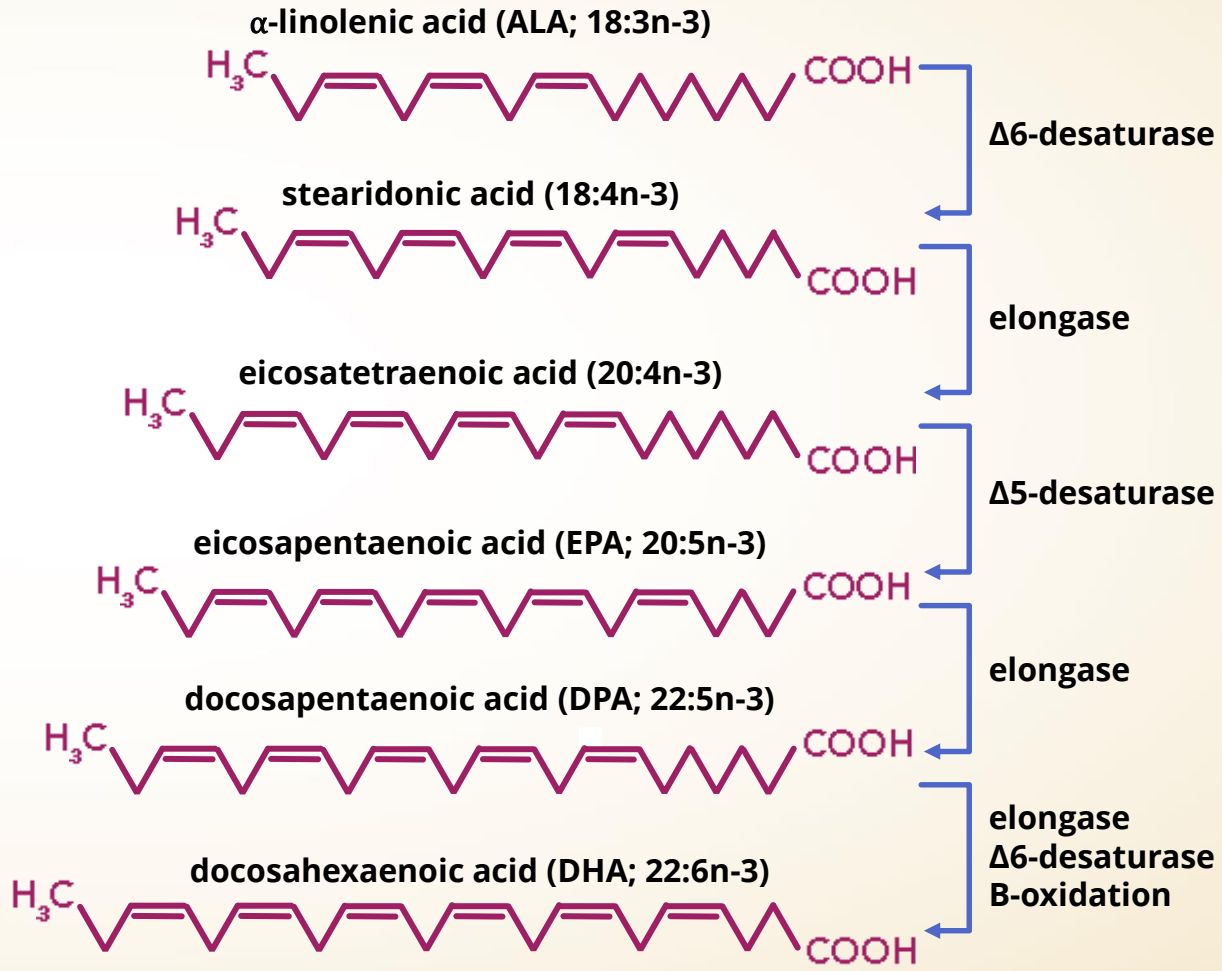
Learning Objectives

- Describe the role DHA/ARA plays in developing infants
- Recognize the importance of adequate DHA/ARA balance in preterm infants
- Associate current NICU practices with DHA/ARA accretion rates in preterm infants

THE ROLE OF DHA/ARA IN INFANT GROWTH

Overview of Docosahexaenoic Acid (DHA)

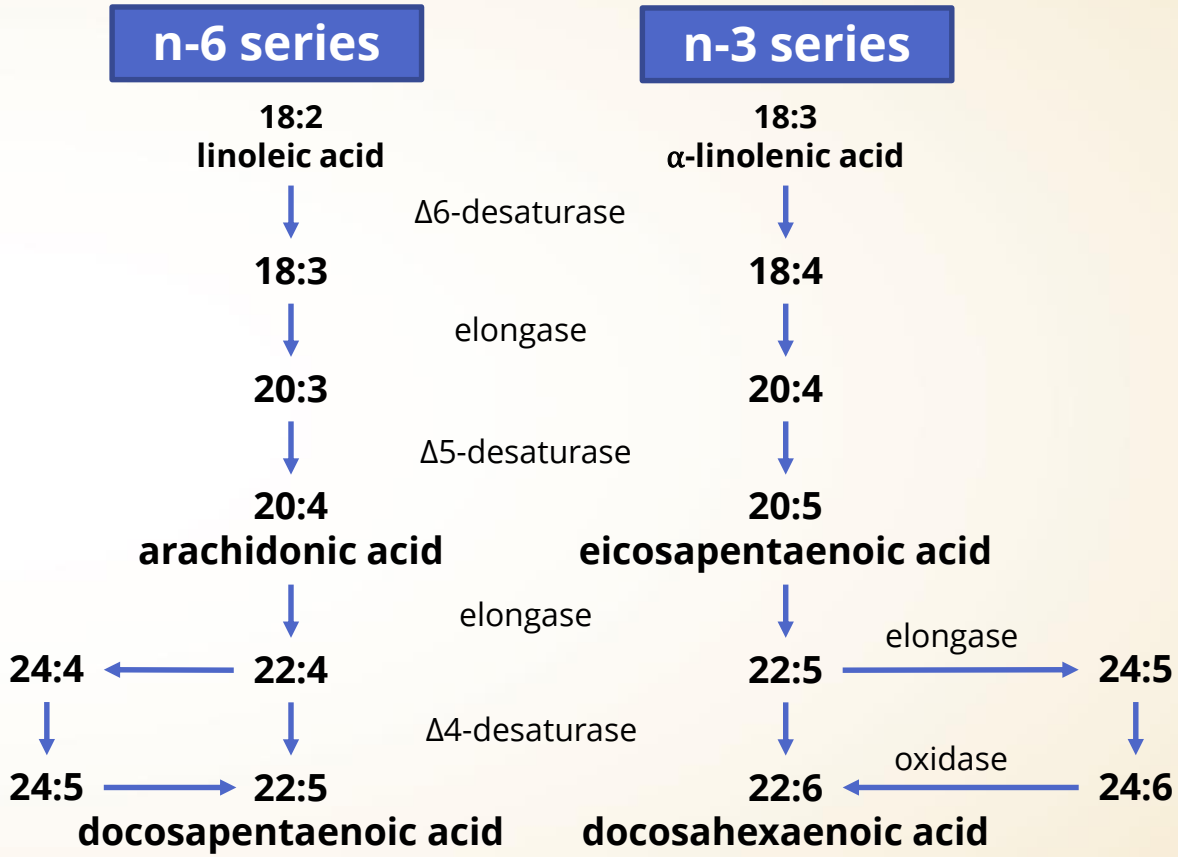
- Long-chain, highly unsaturated omega-3 fatty acid (22:6*n*-3)
- Metabolized from α-linolenic acid
- Found in seafood, especially fatty fish, and products derived from seafood



Calder PC. *Ann Nutr Metab*. 2016;69 Suppl 1:7-21.

Overview of Arachidonic Acid (ARA)

- Long-chain, highly unsaturated omega-6 fatty acid (20:4*n*-6)[1]
- Abundant in brain, muscles, and liver[1]
- Immediate precursor for adrenic acid[2]
  - Pathway for ARA utilization in infants to meet increase needed for neural tissue development



1. Hadley KB, et al. *Nutrients*. 2016;8(4):216. 2. Wijendran V, et al. *J Lipid Res*. 2002;43(5):762-767.

Functions of DHA/ARA

Structure and function of tissues

Retinal development

Brain development

Immune function

Martinez M. *J Pediatr*. 1992;120(4 Pt 2):S129-S138.

DHA/ARA: Important Building Blocks of the Growing Brain

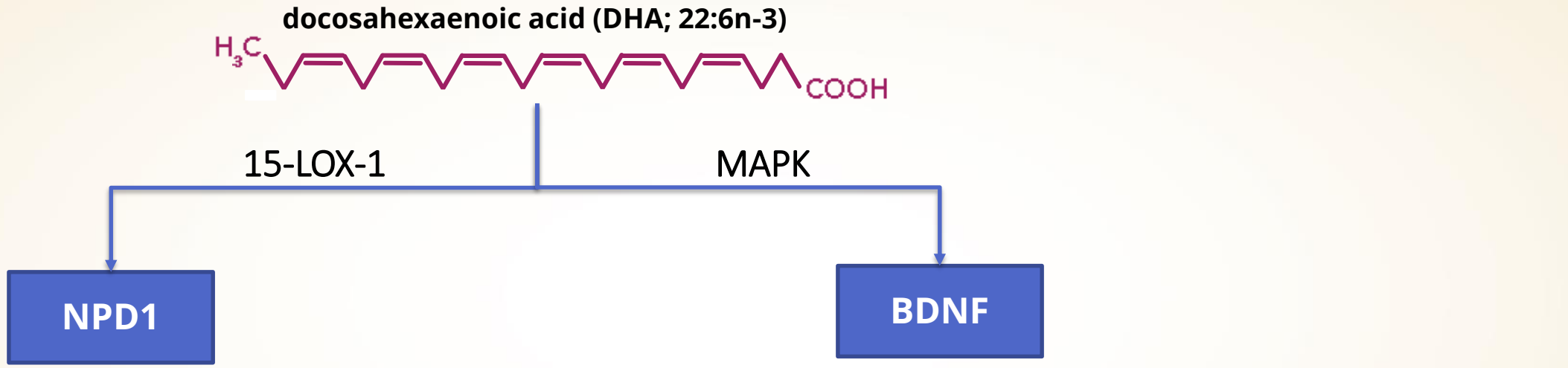
- DHA and ARA play an important role in neuronal cell division and signaling

- Mammalian brains are 60% fat
  - About **25% of the total fatty acid content of the brain** is made up of DHA or ARA

- DHA and ARA are primarily in the form of phospholipids
  - Found in **neural cell membranes**, providing structural support

Hadley KB, et al. *Nutrients*. 2016;8(4):216.

DHA Signaling: NPD1 and BDNF



Protective roles

- Inhibits retinal ganglion cell death
- Protects against oxidative stress
- Downregulates pro-inflammatory signaling
- Upregulates antiapoptotic proteins
- Downregulates proapoptotic proteins

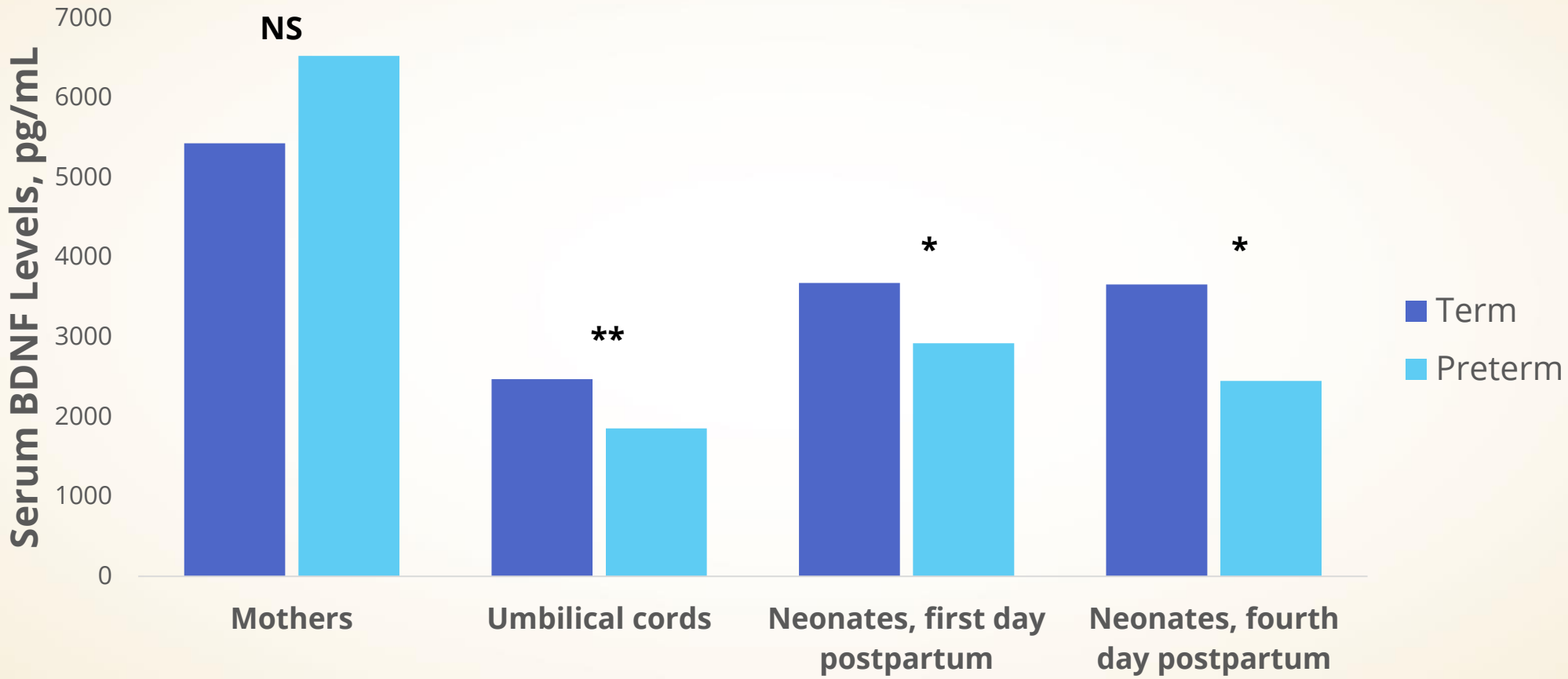
Protective roles

- Promotes neuronal survival
- Increases synaptic plasticity
- Plays a role in neurogenesis

BDNF, brain-derived neurotrophic factor; NPD1, neuroprotectin D1.

1. Niemoller TD, Bazan NG. *Prostaglandins Other Lipid Mediat*. 2010;91(3-4):85–89.

BDNF Levels Are Lower in Preterm Infants



BDNF, brain-derived neurotropic factor.
*P <.05; **P <.001.
Prospective study in 30 healthy term and 15 healthy preterm neonates. BDNF measured by enzyme immunoassay.

1. Malamitsi-Puchner A, et al. *Early Hum Dev*. 2004;76(1):17-22.

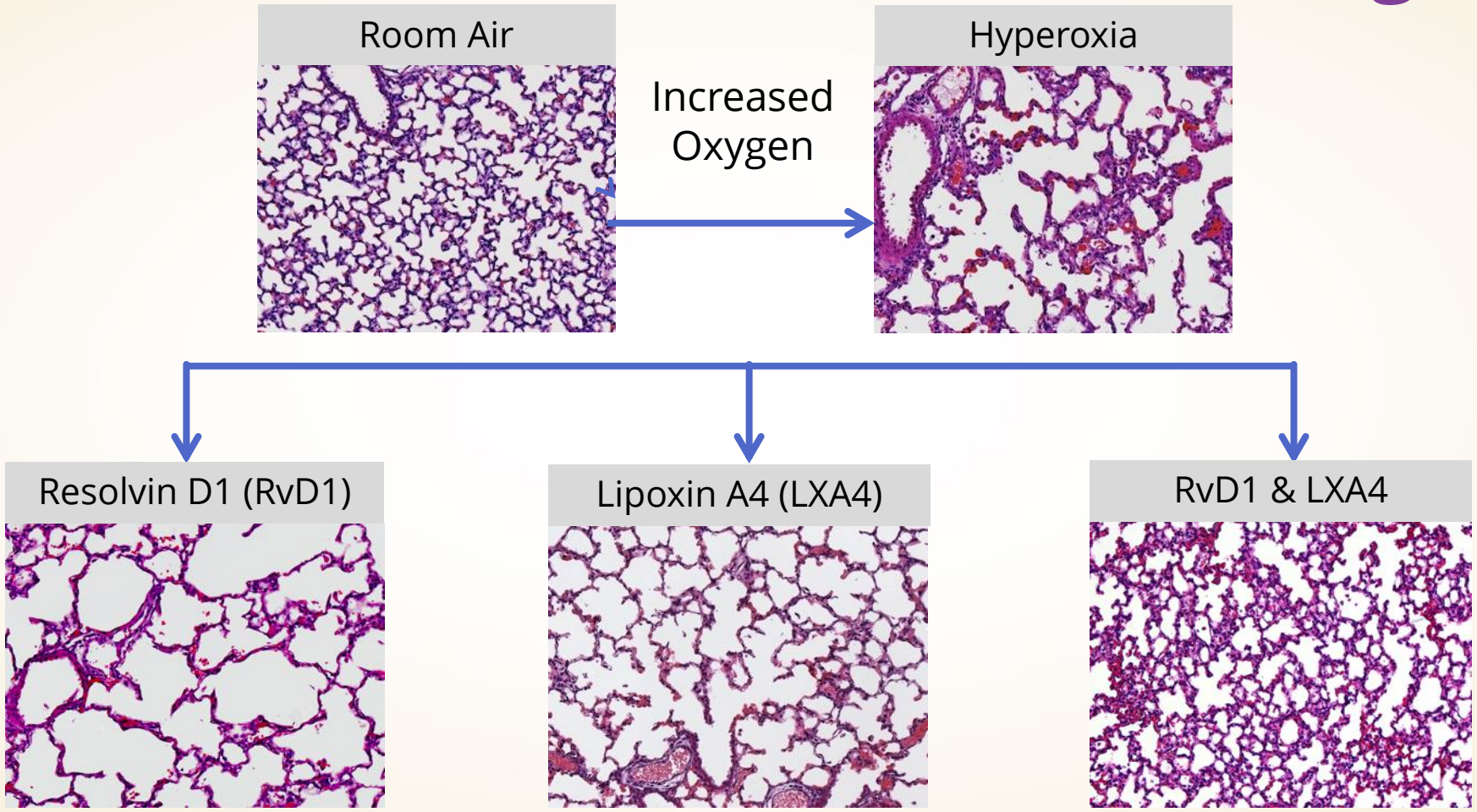
DHA/ARA in Infant Retinal Development

- DHA/ARA play a role in the maturation and survival of photoreceptor cells[1-3]
- Incorporation of DHA into phospholipids is important for retinal function[4]
- Animals raised on fatty acid–free diets develop abnormal electroretinograms[5]

Electroretinography (ERG) is an eye test that detects function of the retina by measuring electrical response of the light-sensitive cells in eyes.

1. Benolken RM, et al. *Science*. 1973;182:1253-1254. 2. Jastrzebska B, et al. *Prog Lipid Res*. 2011;50:267-277. 3. Jeffrey BG, et al. *Invest Ophthalmol Vis Sci*. 2009;50:4360-4367. 4. Shindou H, et al. *J Biol Chem*. 2017;292(29):12054-12064. 5. Neuringer M, et al. *J Clin Invest*. 1984;73:272-276.

DHA and ARA Metabolites Attenuate Lung Injury†

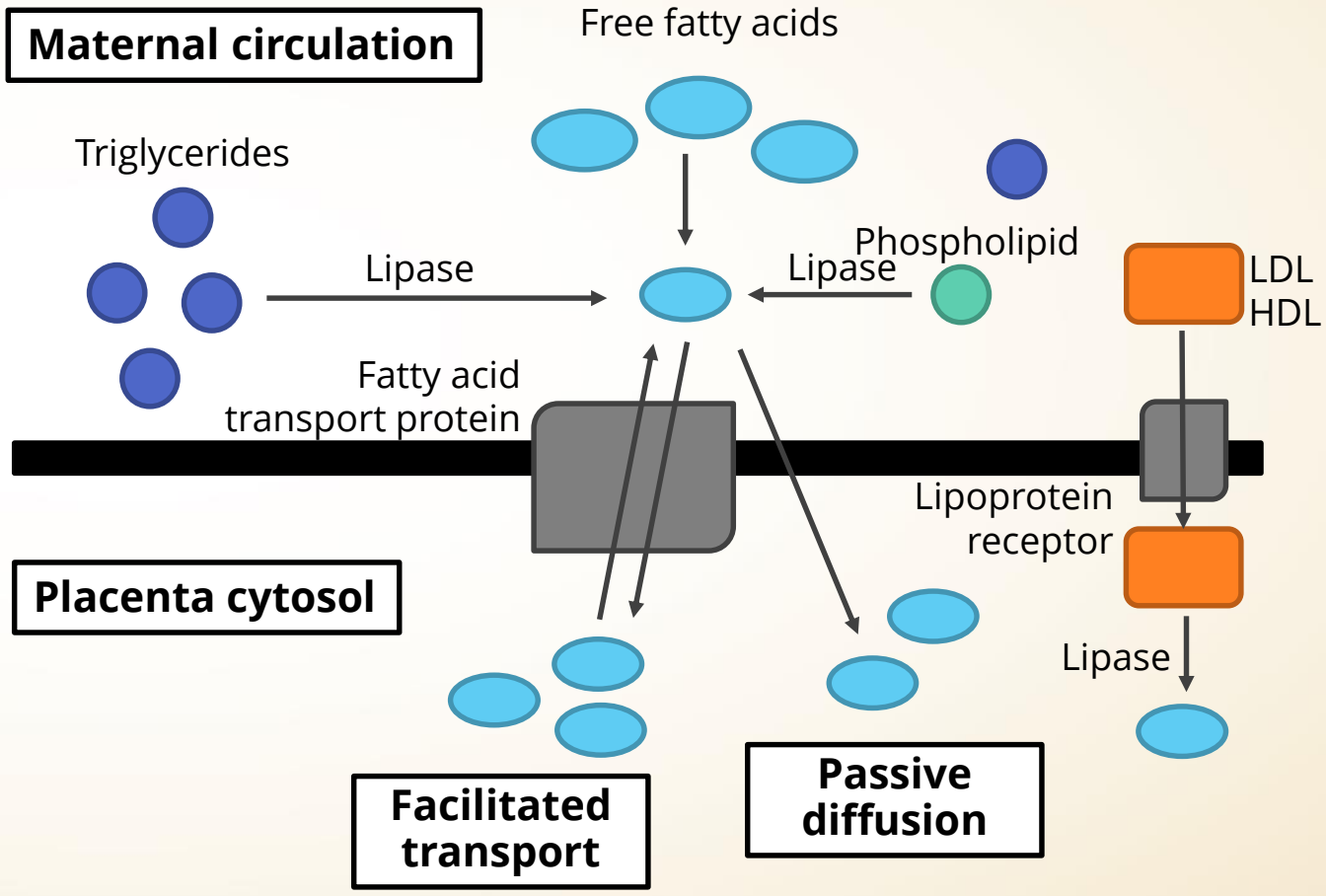


Histology (H&E): 200x.
†C57/BL6 pups were randomized at birth and treated IP on days 0, 3, 6, and 9. On day 10, mice were sacrificed and lungs were collected for morphometric analyses. Hyperoxia, >90% oxygen.

Martin CR, et al. *PLOS One*. 2014;9(6):e98773.

Mechanisms of Maternal-Fetal Fatty Acid Delivery

- Mechanisms involved in fatty acid transfer across placenta are poorly defined
- DHA may selectively accumulate in fetal tissue through higher placental uptake
- Fatty acid transfer can occur through passive diffusion or facilitated transfer

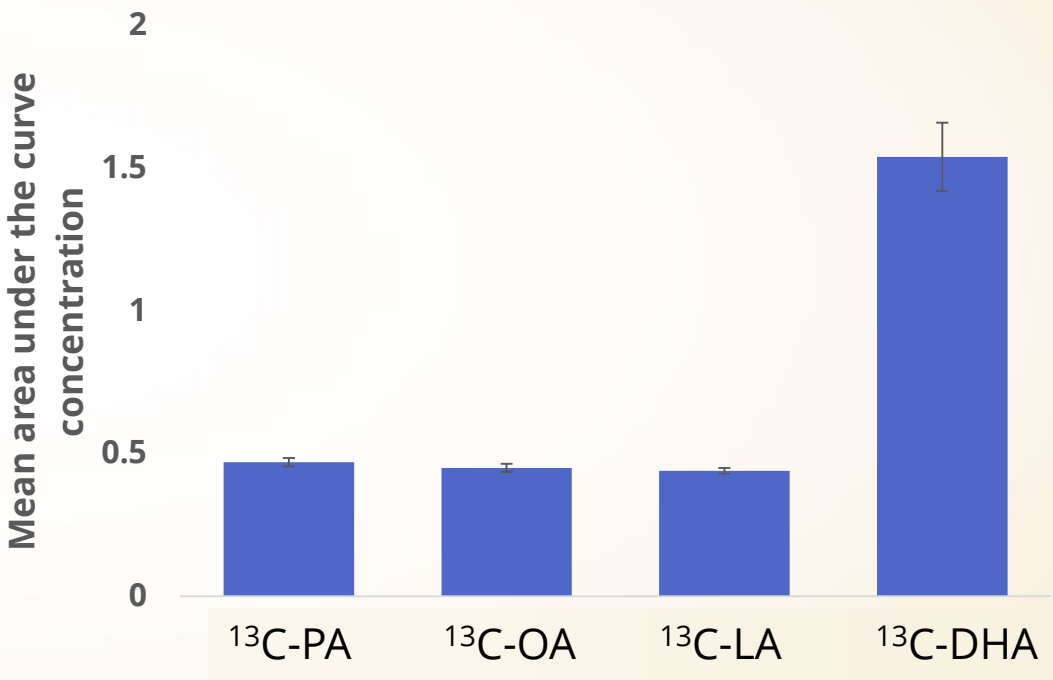


Larqué E, et al. *Am J Clin Nutr.* 2011;94(6 Suppl):1908S-1913S.

DHA Accumulates in the Placenta at a Higher Rate Than Other Fatty Acids[1,2]

- In a study of 11 pregnant women given radio-labeled fatty acids, the maternal-fetal distribution was evaluated
- Twelve hours after oral intake of fatty acids, an elective cesarean section was performed
- Mean ratios between cord and maternal plasma area under the curve (AUC) concentration of ^{13}C-fatty acids (expressed as percentages) are shown in the figure

Mean Cord:Maternal Plasma Ratios[2]

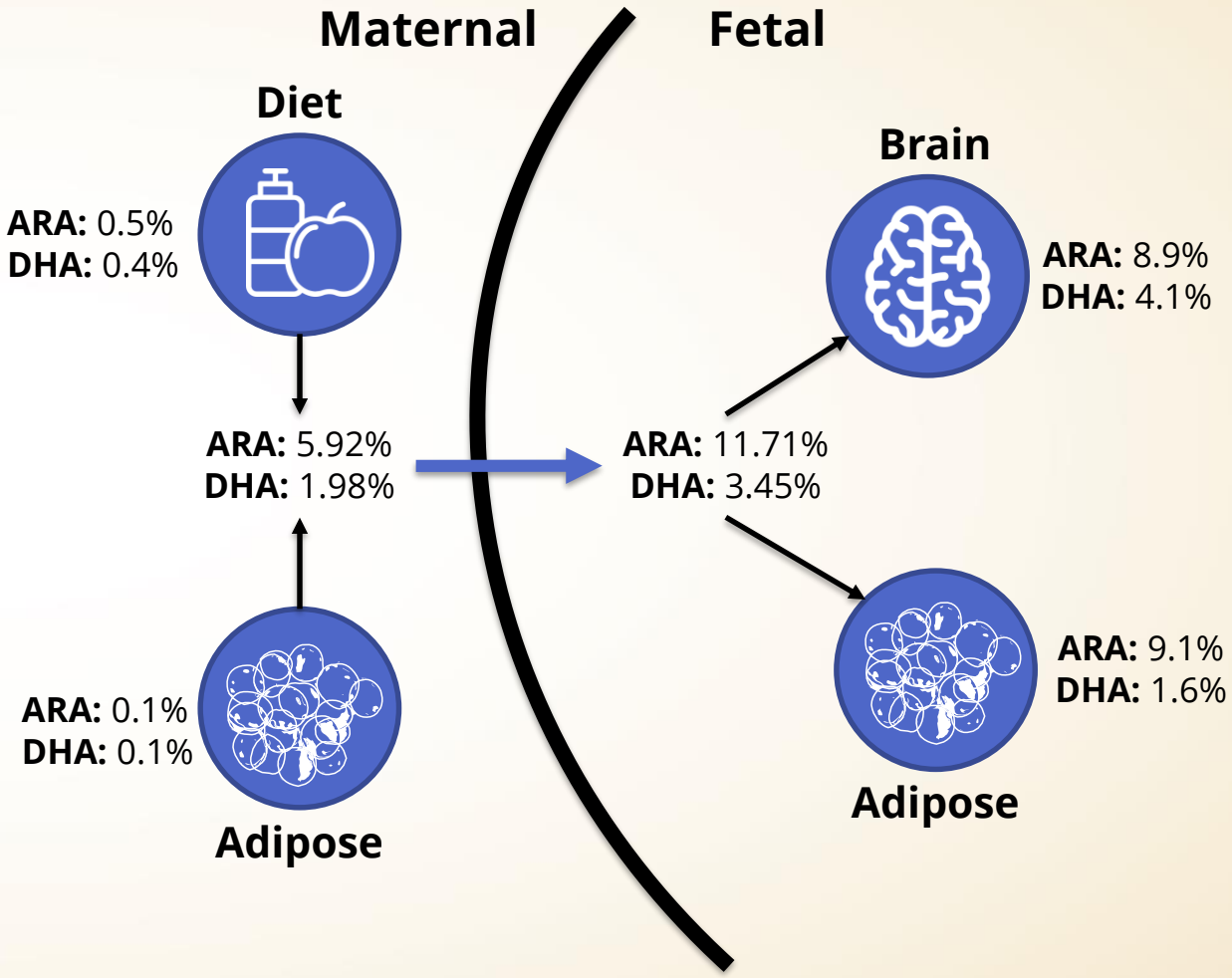


1. Hanebutt FL, et al. *Clin Nutr*. 2008;27(5):685-693. 2. Gil-Sanchez A, et al. *Am J Clin Nutr*. 2010;92(1):115-122.

Accumulation of DHA/ARA in Fetal Tissue at End of Pregnancy[1-5]

- During the final weeks of pregnancy, the DHA and ARA content in **fetal plasma is almost twice as high** as in the mother's blood[1-4]

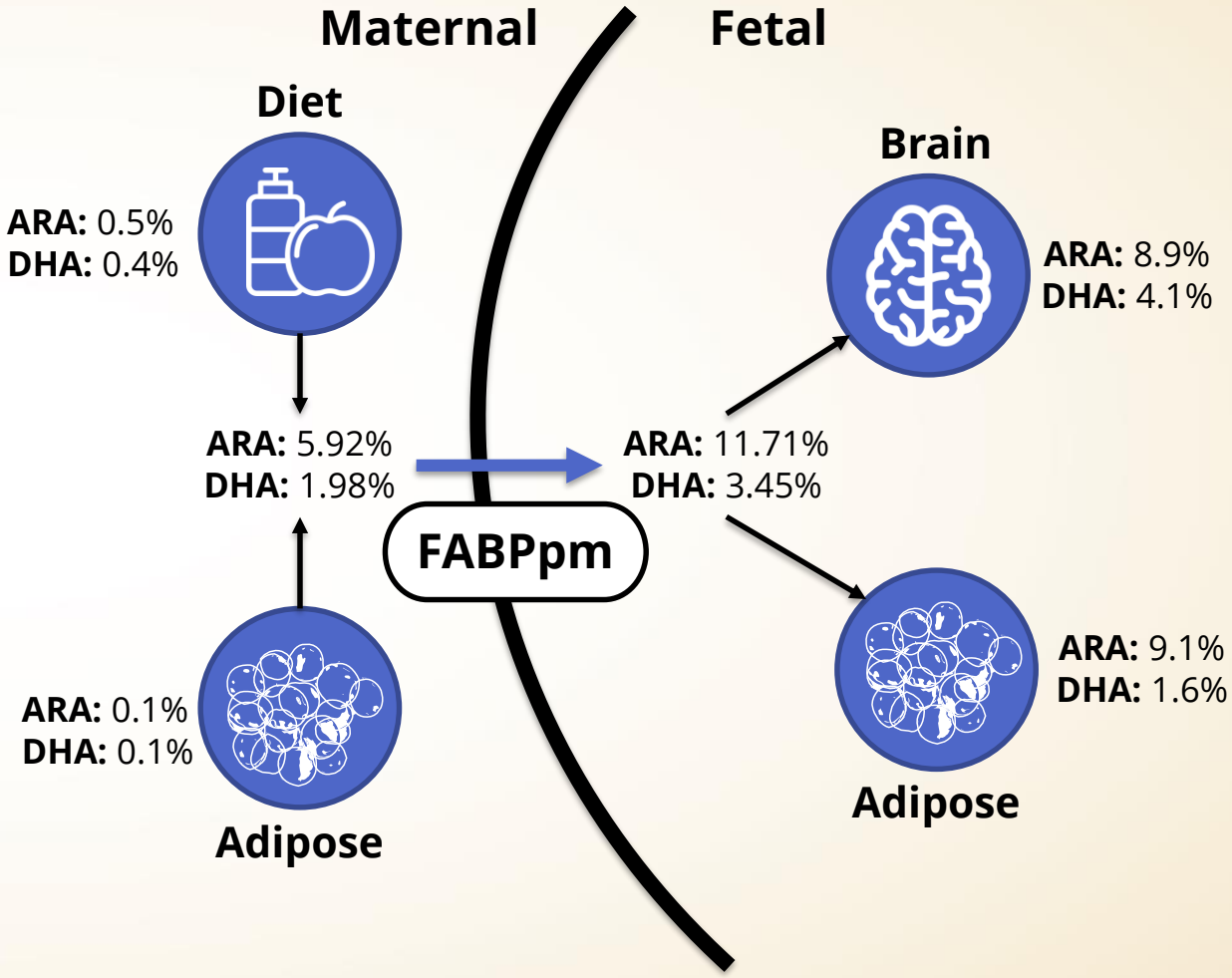
- Towards the end of the pregnancy, levels are **several times higher in fetal adipose tissue** than in the maternal adipose tissue:[1-4]
  - **DHA:** 16 times higher
  - **ARA:** 90 times higher



1. Haggarty P. *Placenta*. 2002;23 Suppl A:S28-S38. 2. Otto SJ, et al. *Eur J Clin Nutr*. 1997;51(4):232-242. 3. Lakin V, et al. *Prostaglandins Leukot Essent Fatty Acids*. 1998;59(3):209-220. 4. Clandinin MT, et al. *Early Hum Dev*. 1981;5(4):355-366. 5. Bobinski R, Mikulska M. *Acta Biiochim Pol*. 2015;62(3):499-507.

FABPpm Transports DHA Selectively Across the Placenta[1-4]

- **Membrane associated fatty acid binding protein (FABPpm)** is a peripheral membrane protein and fatty acid transporter
- FABPpm selectively binds LC-PUFA on the maternal side to transfer fatty acids to the placenta[1,2]
- FABPpm binds only 10% of total fatty acids, with a high affinity for DHA/ARA:
  - ARA: 98%
  - DHA: 87%
  - Smaller quantities of LA and OA (oleic acid)[3]



1. Kaufmann P, Scheffen I. In Fetal and Neonatal Physiology. 1998, pp 59–70. 2. Campbell FM, et al. *Life Sci*. 1998;63(4):235-240. 3. Schmitz G, et al. *Prog Lipid Res*. 2008;47(2):147-155. 4. Bobinski R, Mikulska M. *Acta Biochim Pol*. 2015;62(3):499-507.

Enteral Sources of DHA/ARA for Term Infants

- **Human milk:** DHA/ARA is always present[1]
  - Concentration of DHA/ARA is related to maternal diet
  - Breastfeeding is ideal, but the majority of infants receive some formula during the first year of life[2]

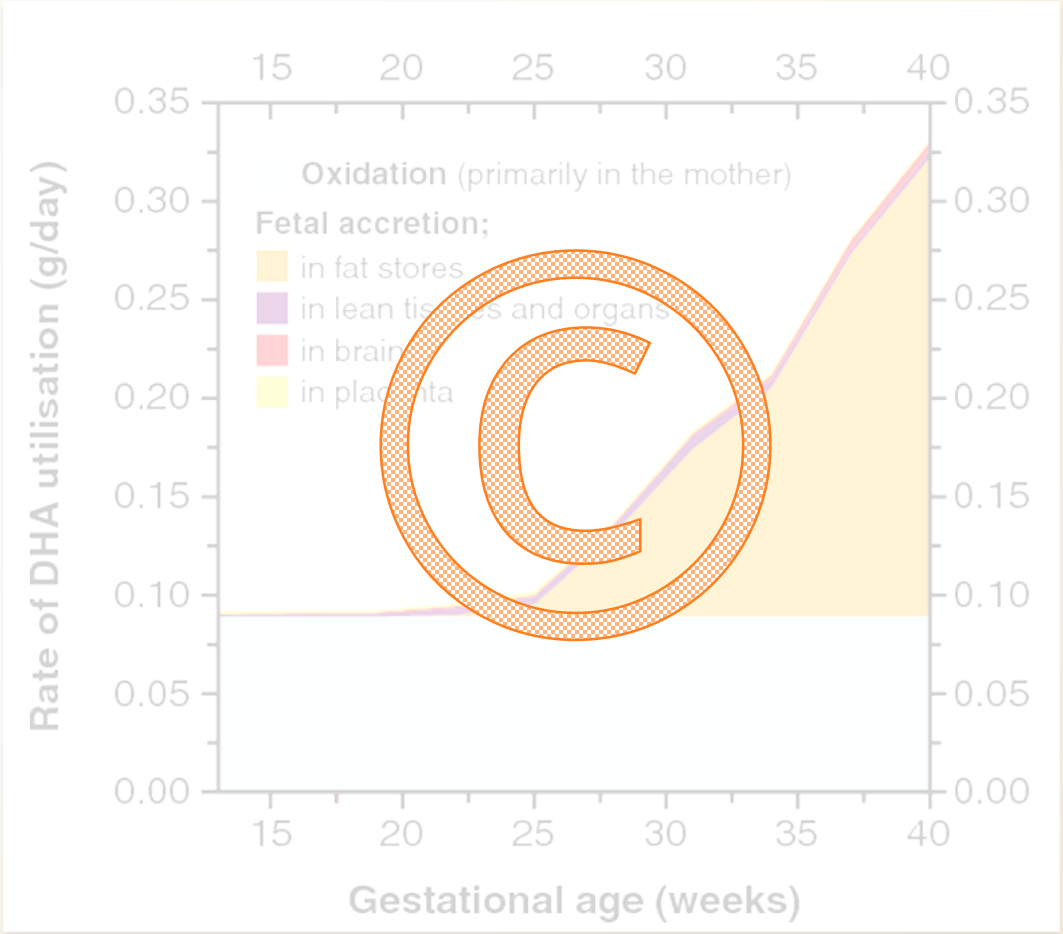
- **Formula:** DHA/ARA is added in the US since 2001 based on worldwide averages in human milk[3]
  - 0.2% to 0.4% DHA
  - 0.35% to 0.7% ARA

1. Hadley KB, et al. *Nutrients*. 2016;8(4):216. 2. http://www.cdc.gov/breastfeeding/data/reportcard.htm. Accessed October 28, 2019. 3. Brenna JT, et al. *Am J Clin Nutr*. 2007;85(6):1457-1464.

IMPORTANCE OF ADEQUATE DHA/ARA BALANCE IN PRETERM INFANTS

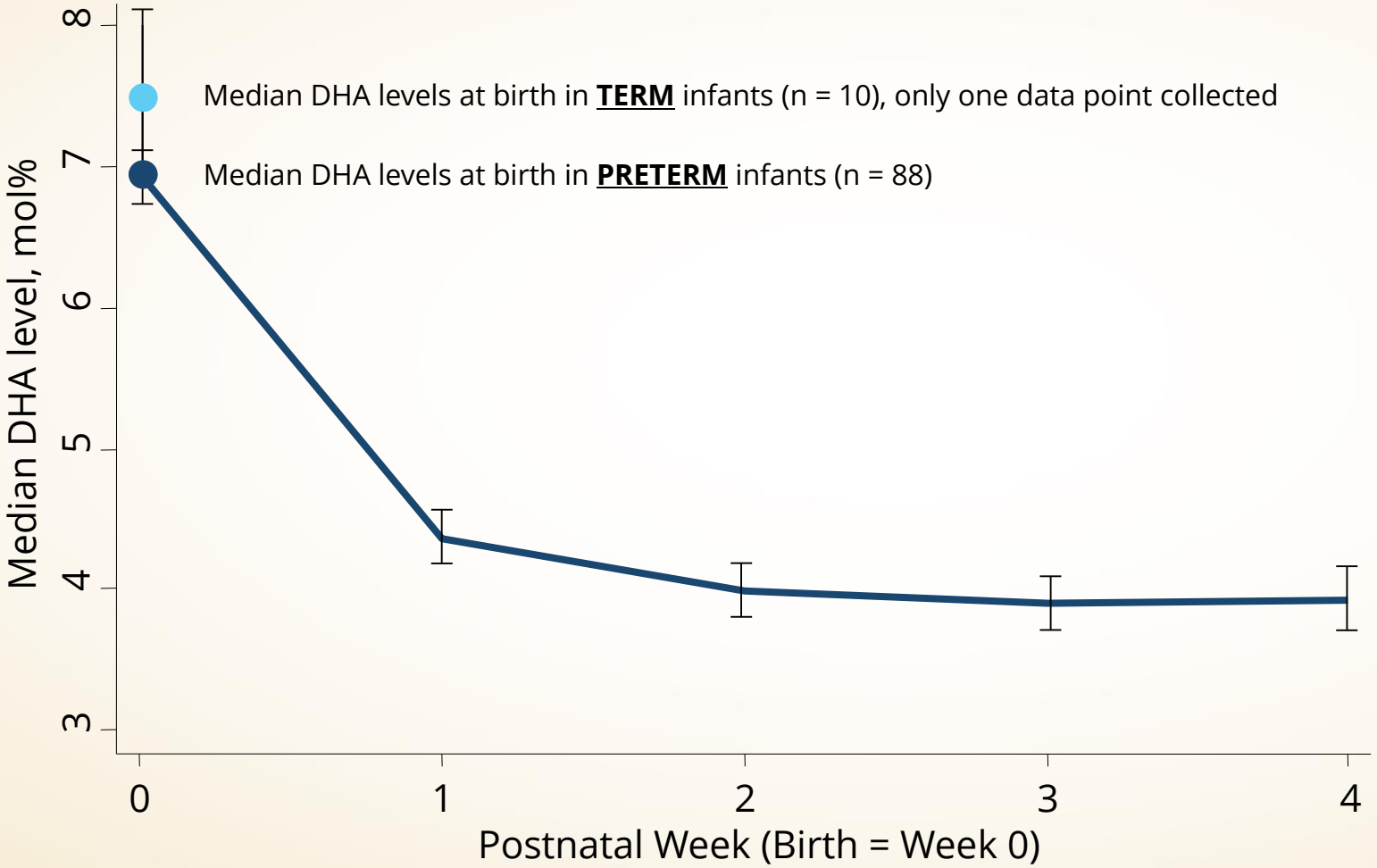
DHA/ARA Are Stored in the Brain and Adipose Tissue

- Since maternal diets may not always meet DHA/ARA needs, these fatty acids are stored in the adipose tissue for later use
- Storage in adipose tissue increases substantially in the final weeks of pregnancy
- Preterm infants may not have the same levels of DHA/ARA accretion as term infants



Haggarty P. *Annu Rev Nutr*. 2010;30:237-255.

DHA Levels Rapidly Decline in the First Postnatal Week

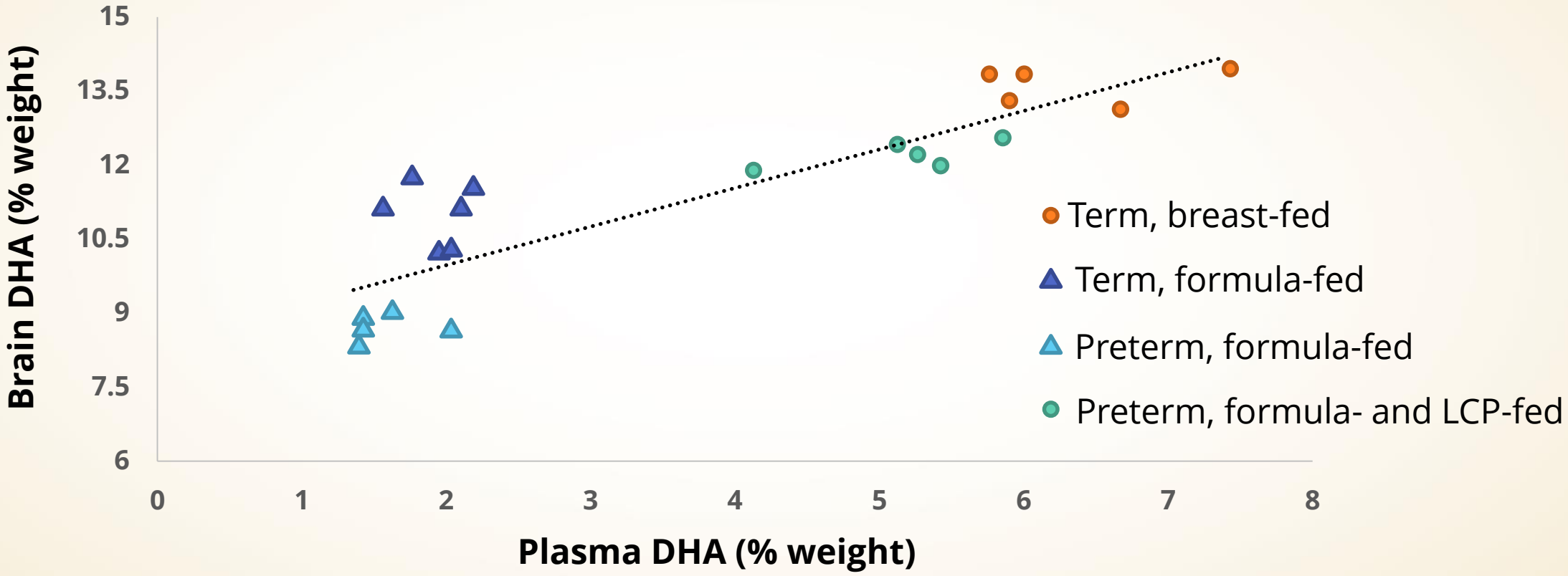


Median DHA levels at birth comparable across gestational age

Retrospective cohort study of 88 infants born at <30 weeks' gestation. Fatty acid profiles and infant outcomes were assessed during the first postnatal month.

Martin CR, et al. *J Pediatr*. 2011;159(5):743-749.e1-2.

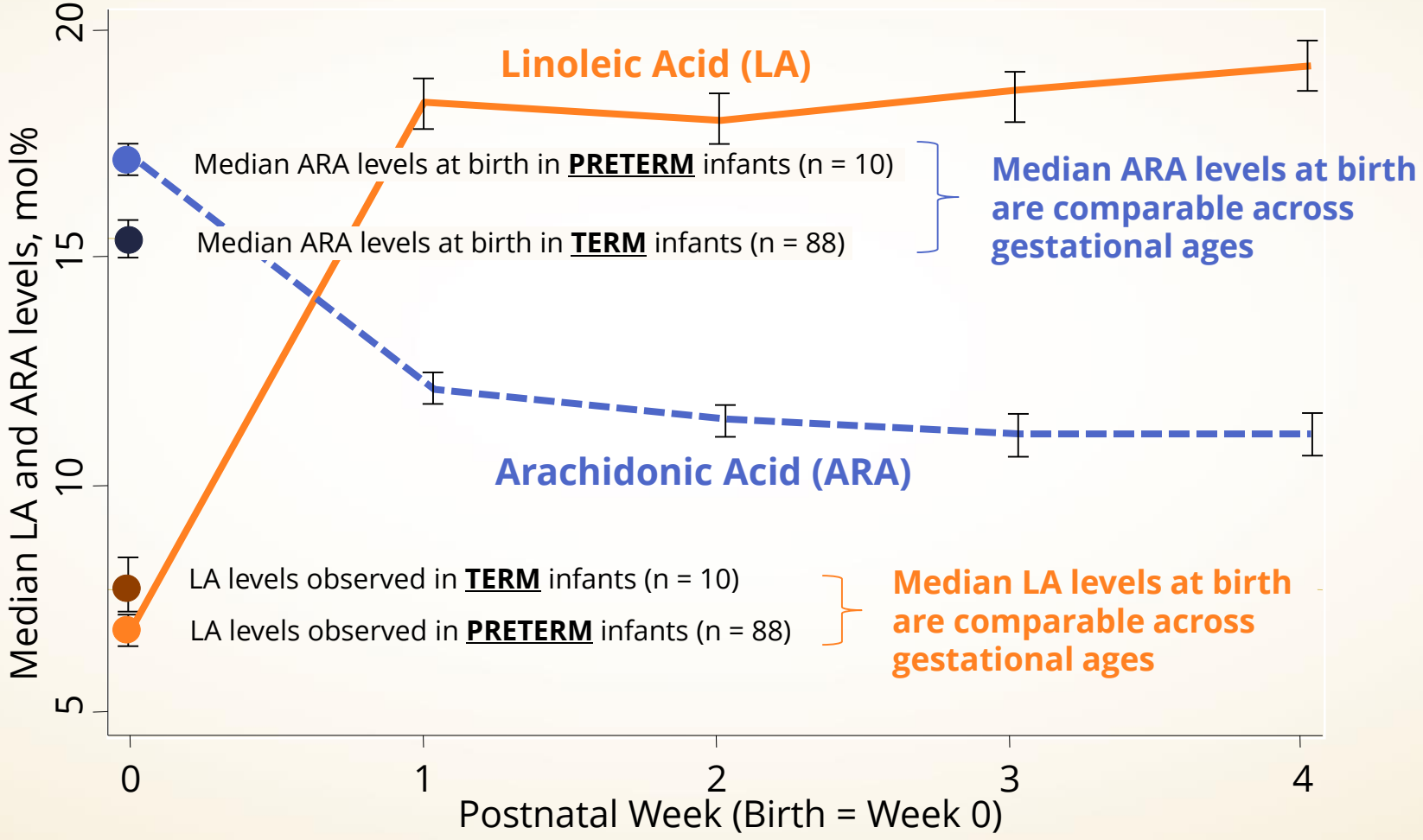
Plasma Levels of DHA Approximate Brain Levels†



†Study in 22 pregnant baboons/neonates randomized to term breast-fed, term formula-fed, preterm formula-fed, or preterm DHA/ARA-supplemented formula-fed

Sarkadi-Nagy E, et al. *Pediatr Res*. 2003;54(2):244-252.

ARA Levels Are Rapidly Altered in the First Postnatal Week



Retrospective cohort study of 88 infants born at <30 weeks' gestation. Fatty acid profiles and infant outcomes were assessed during the first postnatal month.

Martin CR, et al. *J Pediatr*. 2011;159(5):743-749.e1-2.

DHA/ARA Imbalance Associated With Disease in Preterm Infants

Suboptimal cognitive development

Retinopathy of prematurity

Chronic lung disease

Sepsis and infection

1. Martin CR, et al. *J Pediatr*. 2011;159(5):743-749.e1-2. 2. Martin CR, et al. *PLoS One*. 2014;9(6):e98773. 3. Lavoie JC, et al. *JPEN J Parenter Enteral Nutr*. 2018;42(8):1314-1321. 4. Löfqvist CA, et al. *JAMA Ophthalmol*. 2018;136(3):271-277.

DHA/ARA Levels Are Linked With Improved Neurodevelopment

- In a study of 60 preterm infants, red blood cell fatty acid composition was evaluated
- A 1% increase in DHA levels was associated with **4.3-fold reduced risk of intraventricular hemorrhage**
- Higher DHA and lower LA levels early after delivery were associated with **better developmental scores at a mean follow-up of 33 months**

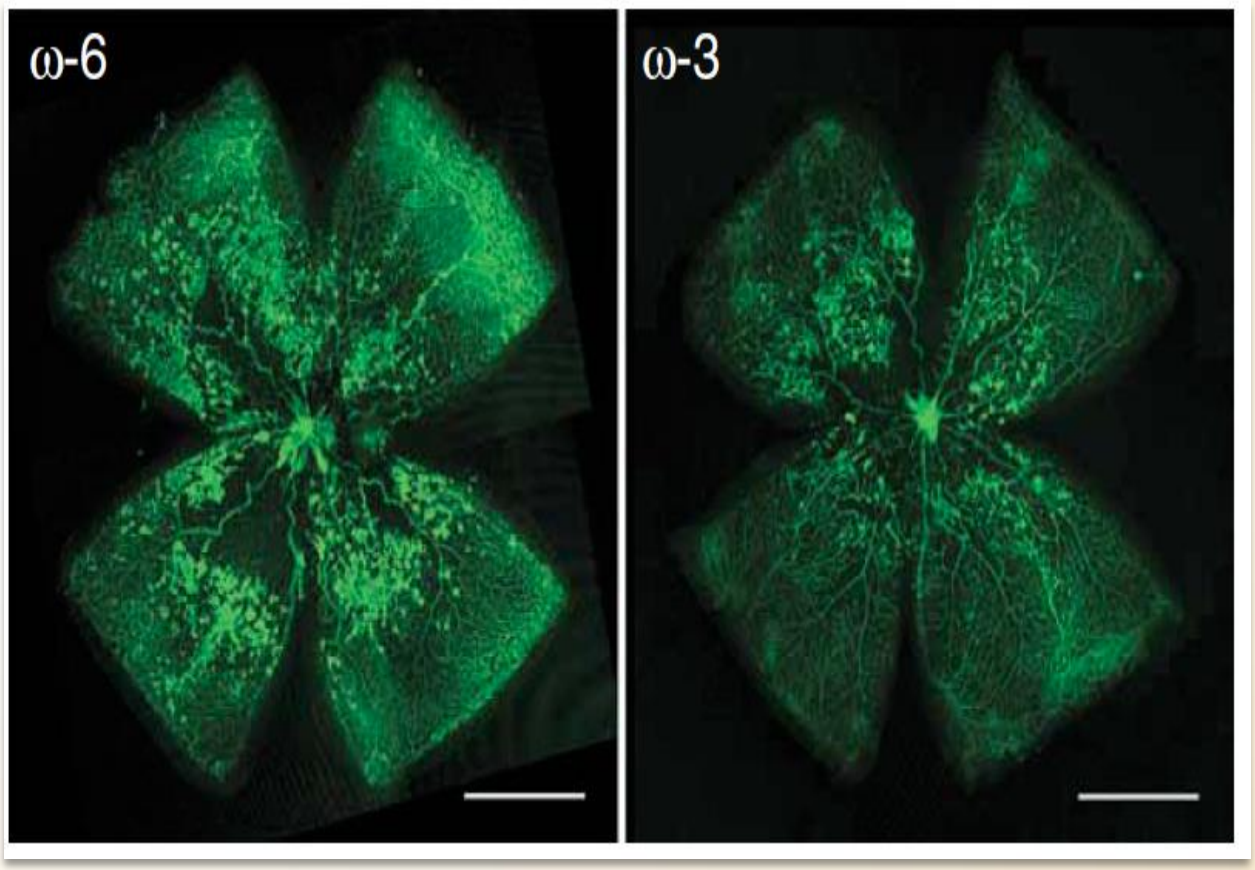
Tam EW, et al. *Pediatr Res.* 2016;79(5):723-30.

Omega-3 and Retinopathy of Prematurity†

- Mice receiving ω-6-PUFAs had a significantly greater vaso-obliterated/total retinal area of 21.5% vs 13.7% in those receiving ω-3-PUFAs
- Mice receiving ω-3-PUFAs were significantly protected from pathologic neovascularization (5.7% vs 9.0%)

Vaso-obliteration / Neovascularization:

21.5% / 9% **13.7% / 5.7%**

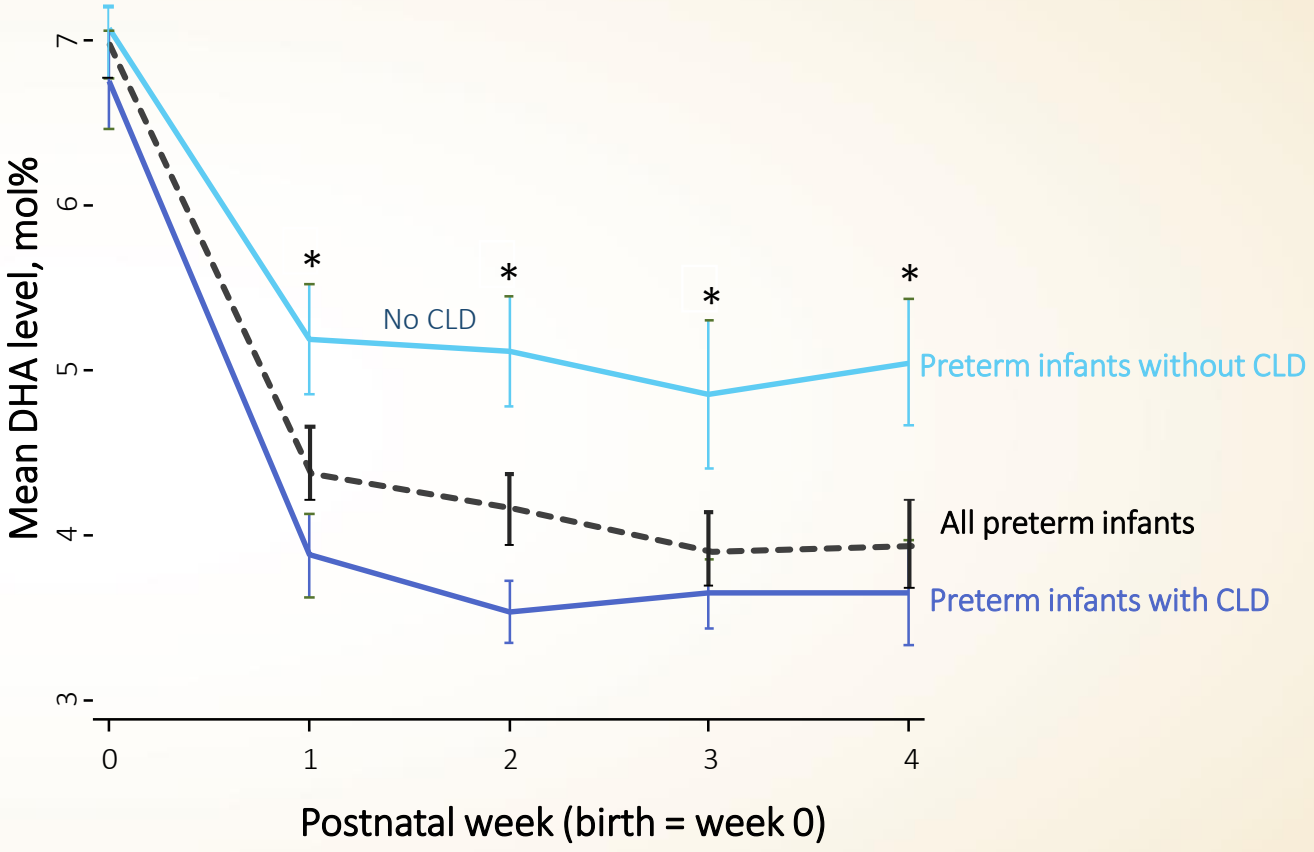


†Mouse pups exposed to 75% O_2 from P7-P12. Scale bar, 1 mm. P17 retinal vasculature stained with isolectin B4-FITC. Omega-6, n = 14; omega-3, n = 27.

Connor KM, et al. *Nat Med*. 2007;13(7):868-873. Reprinted by permission from Springer Nature.

Low DHA Levels Are Linked to the Development of Chronic Lung Disease

- In a retrospective cohort study of 88 preterm infants, fatty acid profiles were measured for the first 4 weeks
- Decreased levels of DHA were associated with a **2.5-fold increased risk of chronic lung disease (CLD)**
- Imbalanced DHA/LA levels were associated with an **8.6-fold increased risk of CLD**



Martin CR, et al. *J Pediatr*. 2011;159(5):743-749.e1-2.

Association With Increased Risk of Chronic Lung Disease and Late-onset Sepsis

- In the same study, fatty acid levels and imbalance were associated with late-onset sepsis
- Imbalanced LA:DHA was associated with a **4.6-fold increased risk** of late-onset sepsis

Chronic lung disease		
Fatty acid	**OR (95% CI)**	***P***
LA	0.9 (0.7, 1.1)	.4
ARA	0.9 (0.6, 1.3)	.6
DHA	2.5 (1.3, 5.0)	.001
LA: DHA	8.6 (1.4, 53.1)	.02
Late-onset sepsis		
Fatty acid	**Hazard ratio (95% CI)**	***P***
LA	0.8 (0.7, 0.96)	.02
ARA	1.4 (1.1, 1.7)	.02
DHA	1.4 (1.0, 2.0)	.08
LA: DHA	4.6 (1.5, 14.1)	.007

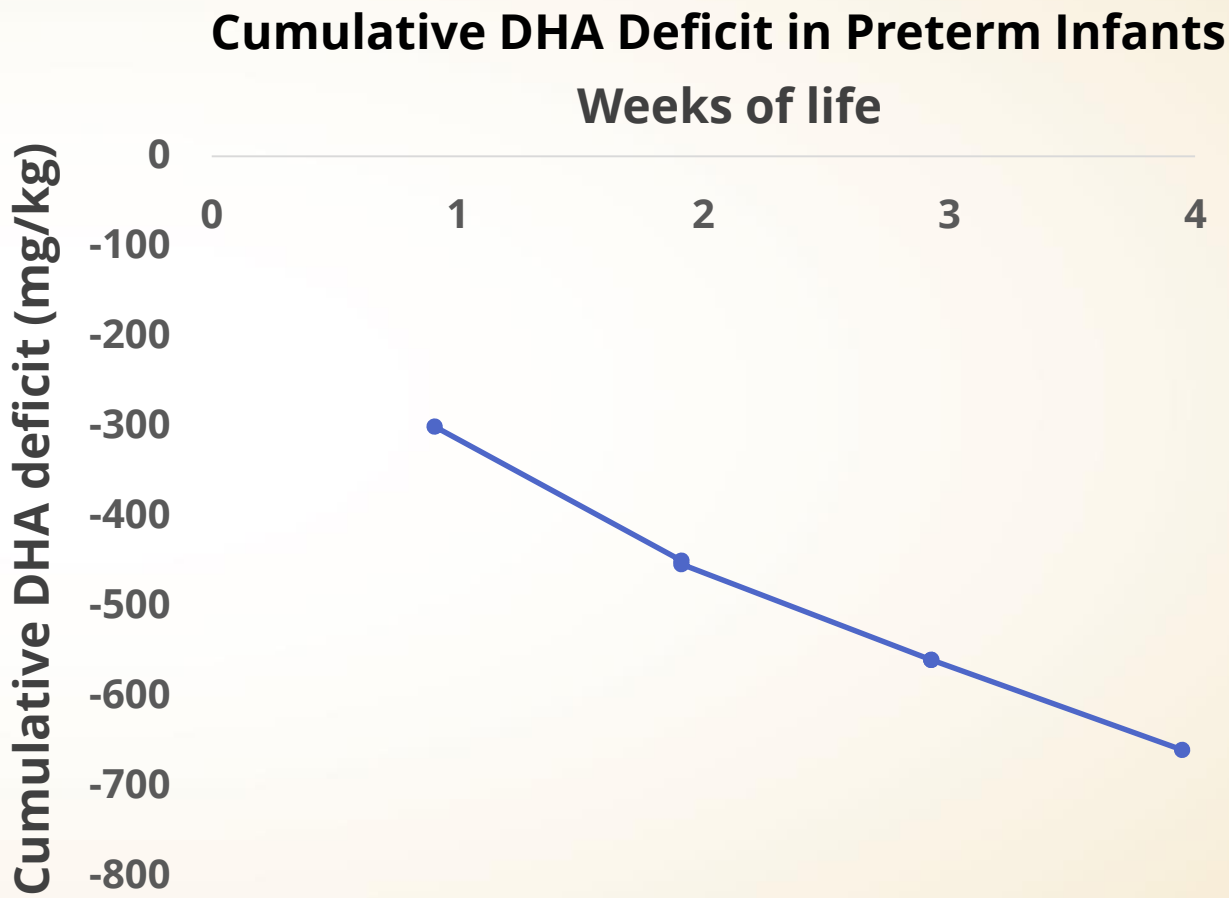
Models adjusted for gestational age, gender, growth restriction, severity of illness, total Intralipid intake.

Martin CR, et al. *J Pediatr*. 2011;159(5):743-749.e1-2.

DHA/ARA SUPPLEMENTATION IN PRETERM INFANTS

Current Nutritional Practices Are Inadequate to Maintain Optimal Levels of Fatty Acids in Preterm Infants†

- In a study of 40 preterm infants (≤28 weeks gestational age), nutritional data were collected for the first 4 weeks of life
- DHA deficit was greater for low-birth-weight infants
- In preterm infants, DHA accumulation is half that of term infants at 1 month of age



†Nutritional data were collected for the first 28 days of life in 40 preterm infants born with a gestational age ≤28 weeks at a single center.

Lapillonne A, et al. *Neonatology*. 2010;98(4):397-403.

Challenges in Achieving Adequate DHA/ARA Intake in Preterm Infants

- Delivery of DHA/ARA[1]
  - Breast milk and formulas provide DHA/ARA
  - Intravenous lipid emulsions available for routine use do not include DHA/ARA
  - Extremely premature infants may rely on intravenous lipid emulsion for the first weeks of life,[2] contributing to DHA/ARA deficiency

1. Robinson DT, et al. *J Pediatr*. 2013;162(1):56-61. 2. Ehrenkranz RA, et al. *Pediatrics*. 1999;104(2 Pt 1):280-289.

Challenges in Achieving Adequate DHA/ARA Intake in Preterm Infants

- Providing additional DHA is dependent on the infant's ability to tolerate full-volume enteral feedings
  - Variable among NICUs
  - Dependent on size, clinical status, and gestational age

Baack ML, et al. *Lipids*. 2016;51(4):423-433.

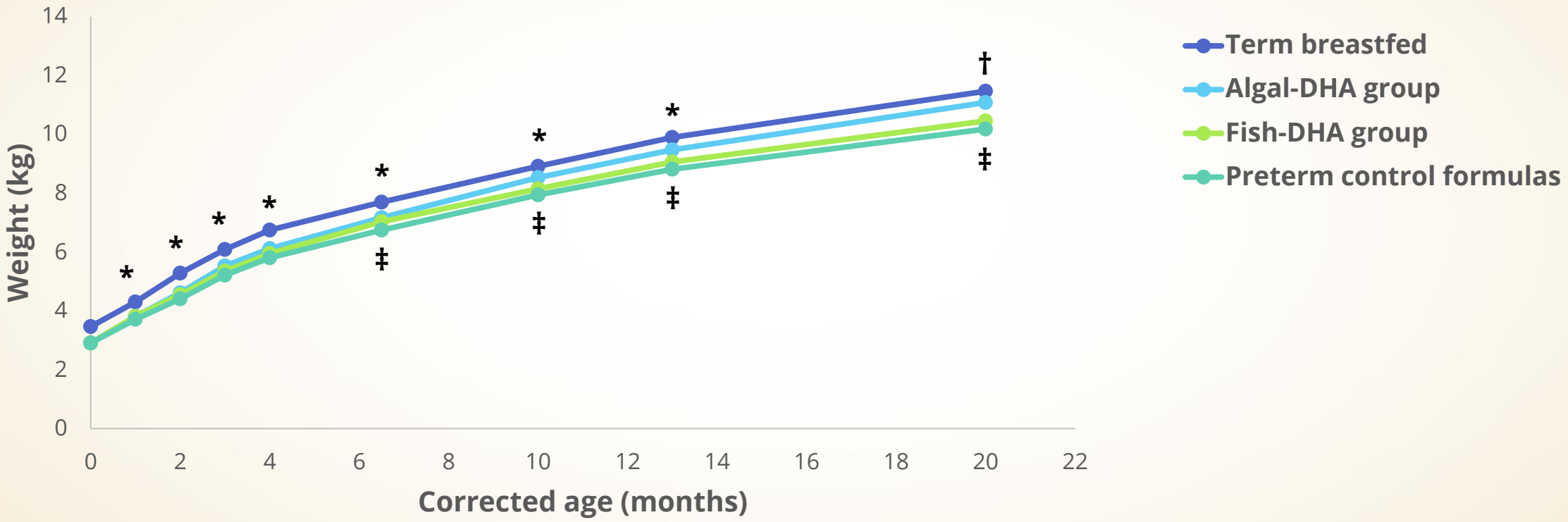
DHA Supplementation Alleviates DHA Deficiency in Preterm Infants†

	Baseline DHA, mol%	Full-Feedings, DHA mol%	Discharge, DHA mol%
Placebo preterm (n = 29)	2.91 (0.45)	2.83 (0.50)	2.87 (0.50)*
DHA preterm (n = 31)	2.88 (0.68)	3.03 (0.54)	3.55 (0.44)**
Term (n = 30)	4.31 (0.95)		

†Double-blind, randomized, controlled trial evaluating DHA supplementation (50 mg/day) for preterm infants (24-34 weeks gestational age) beginning in the first week of life.
Results expressed as mean (SD) mol%.
*Groups compared with term reference peers via ANOVA; $P < .001$.
**Placebo vs DHA comparison via linear mixed models; $P < .001$.

Baack ML, et al. *Lipids*. 2016;51(4):423-433.

Weight of Preterm Infants Fed DHA/ARA Formula Is Closer to Term Breast-fed Infants§

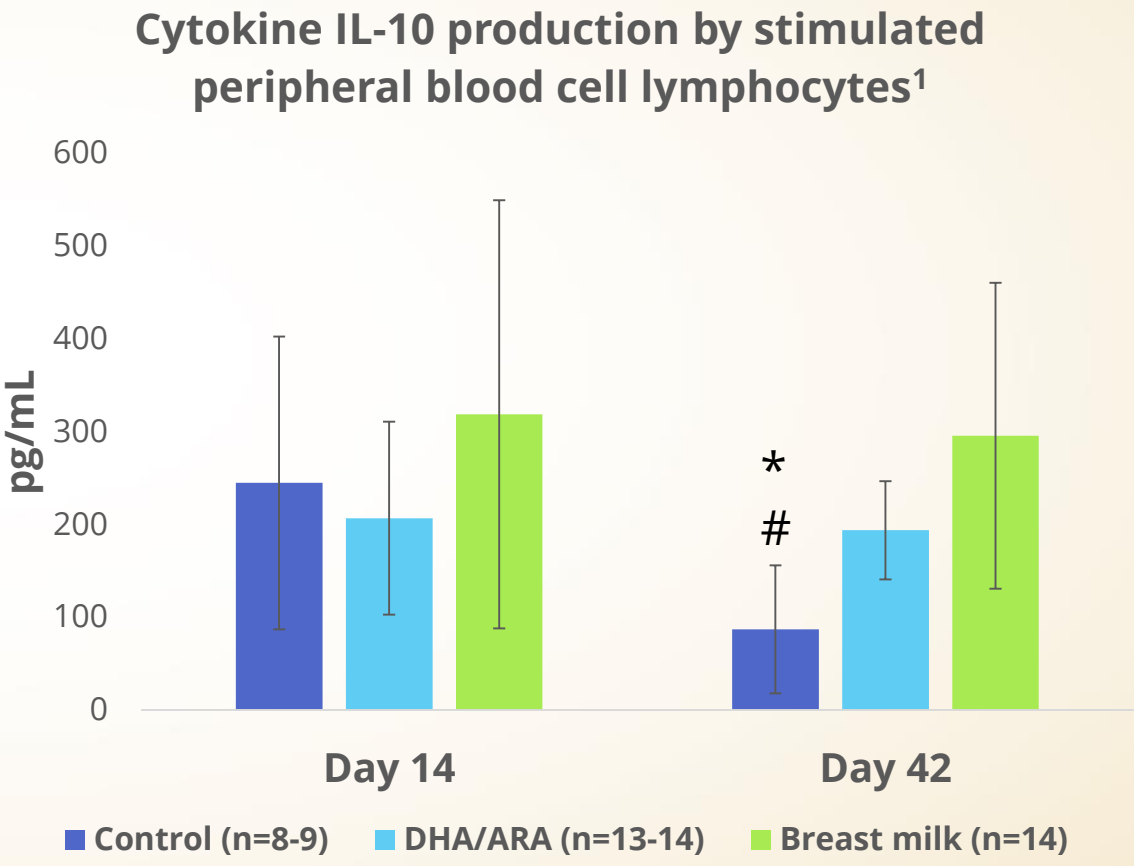


§Double-blinded study of 361 preterm infants fed until 92 weeks postmenstrual age, with follow-up to 118 weeks postmenstrual age
*Breast-fed term infants > all preterm groups ($P < .05$).
†Infant formulas not different from term breast milk, both > control and fish/fungal formulas.
‡Infant formulas > control formulas.

Clandinin MT, et al. *J Pediatr*. 2005;146(4):461-468.

Enhanced Immune Function With DHA/ARA Supplementation†

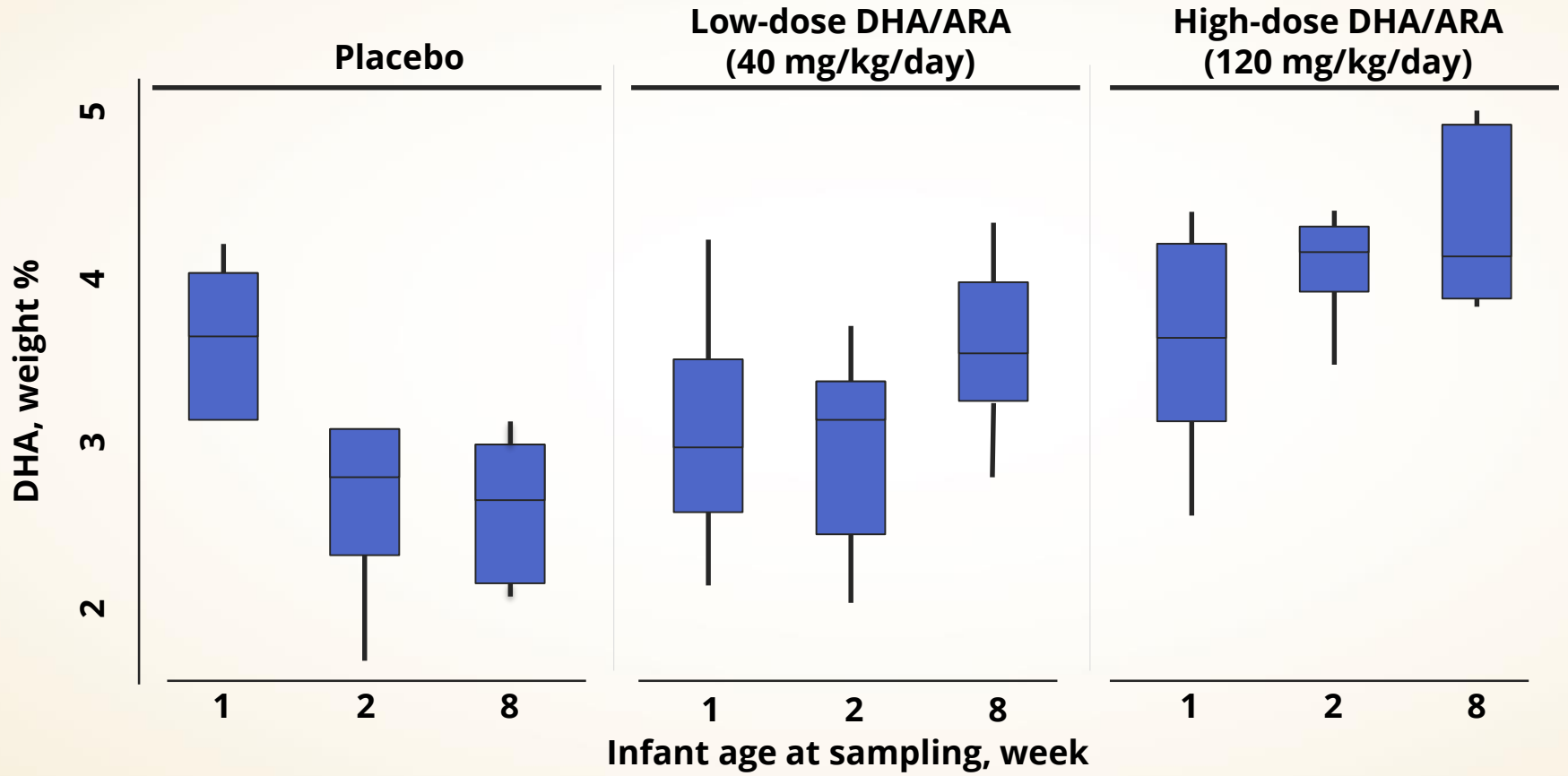
- Adding DHA/ARA to preterm formula resulted in immune function more consistent with breast milk-fed infants[1]
- In another study, infants supplemented with DHA had reduced levels of inflammatory cytokines believed to play a role in type 1 diabetes development[2]
- DHA/ARA supplementation may affect the ability of an infant to respond to immune challenges[1,2]



†Study of 44 preterm infants with gestational ages between 27 and 36 weeks receiving 100% enteral nutrition by day 14 of life.
*$P < .05$, compared with Day 14. #$P < .05$, compared with breast milk, Day 42.

1. Field CJ, et al. *J Pediatr Gastroenterol Nutr*. 2000;31(3):291-299. 2. Chase P, et al. American Diabetes Association Scientific Sessions 2010. Orlando, Florida: June 25-29. Abstract 1918-P.

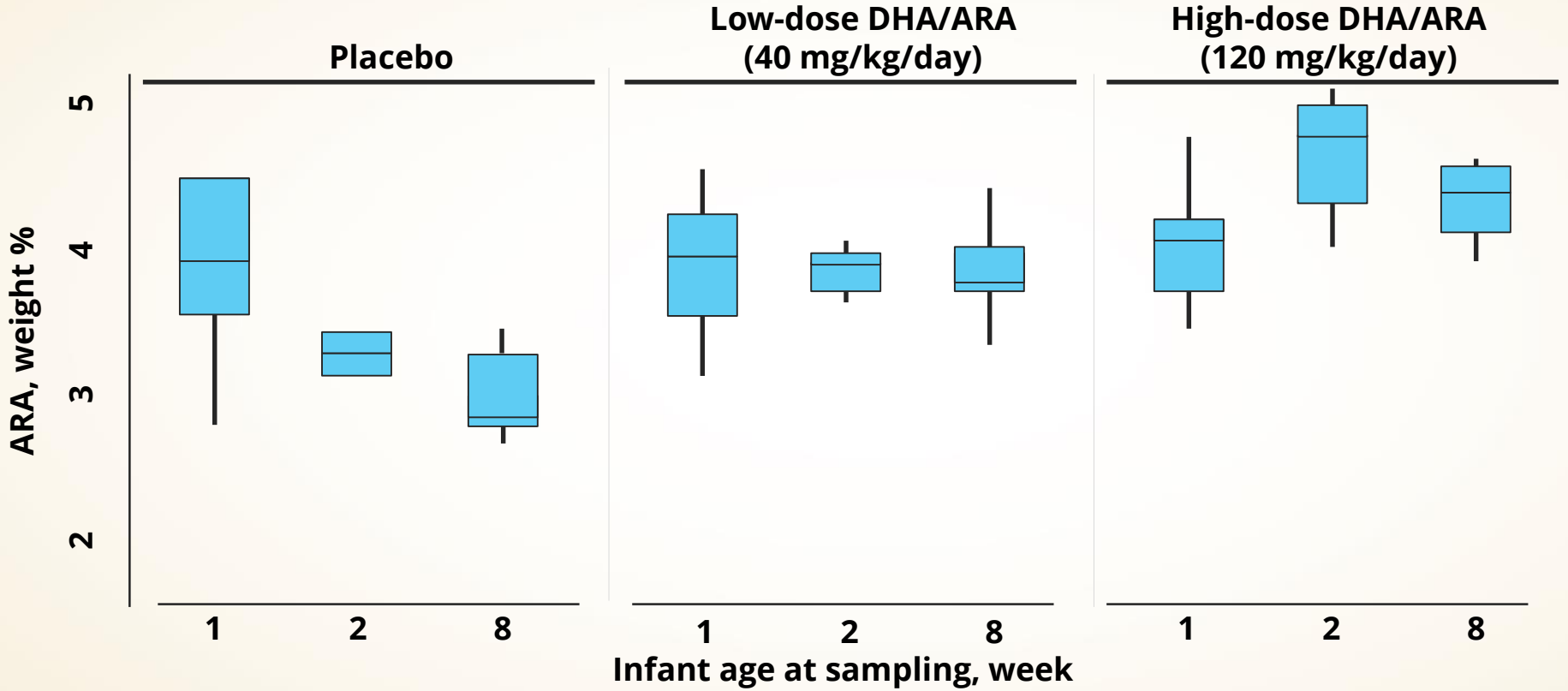
Effect of Emulsified DHA/ARA Enteral Supplementation on Serum DHA Levels in Preterm Infants



Randomized, double-blind, placebo-controlled trial of 30 very low-birth-weight infants given low dose or high dose PUFA via nasogastric tube. Dosing started within first 72 h of life and was given for 8 weeks or until discharge, whichever came first.

Frost B, et al. Pediatric Academic Societies Meeting. April 24 – May 1, 2019. Baltimore, MD.

Effect of Emulsified DHA/ARA Enteral Supplementation on Serum ARA Levels in Preterm Infants†



†Randomized, double-blind, placebo-controlled trial of 30 very low-birth-weight infants given low dose or high dose PUFA via nasogastric tube. Dosing started within first 72 h of life and was given for 8 weeks or until discharge, whichever came first.

DHA/ARA Supplementation and Neurodevelopment in Preterm Infant Neurodevelopment at 6 Months and 1 Year†

- In a double-blind study, preterm infants between gestational age of 30 and 37 weeks were randomly assigned to receive formula with or without DHA/ARA supplementation
- DHA/ARA supplementation for 6 months led to significantly increased measures of neurodevelopment in preterm infants

	Mean ± SD MDI score		Mean ± SD PDI score	
Age	**6 mo**	**1 y**	**6 mo**	**1 y**
+DHA/ARA (n = 16)	96.1±8.6	98.7±8.0	102.2±10.5	98.0±5.8
-DHA/ARA (n = 11)	91.7±10.4	90.5±6.9	95.4±13.2	86.7±11.1

†Double-blind, randomized study of preterm infants >2000 g body weight and >32 weeks of gestation in full feeding status who received formula with or without DHA/ARA for 6 months.
MDI, Mental Development Index; PDI, Psychomotor Development Index.

Fang PC, et al. *Chang Gung Med J*. 2005;28(10):708-715.

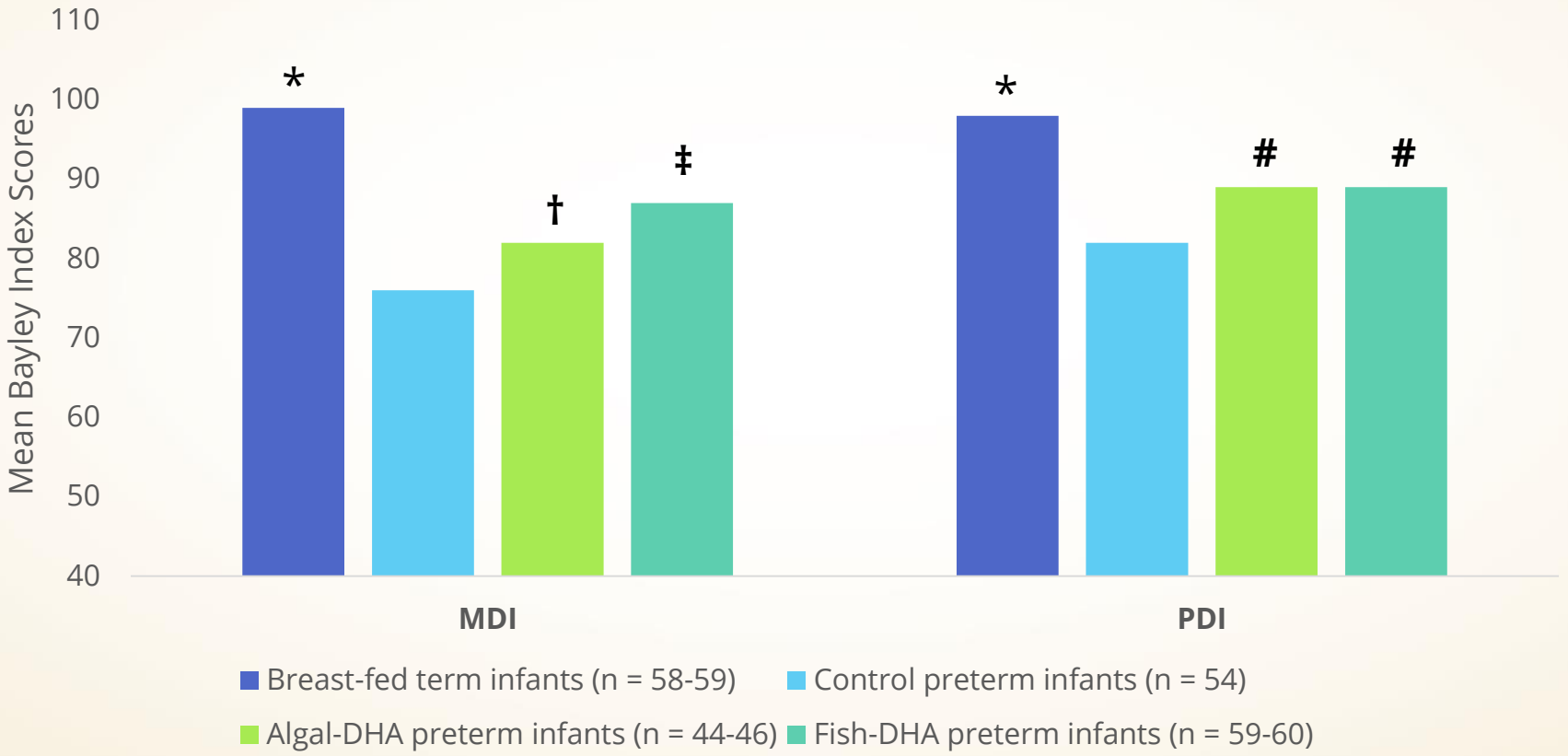
DHA/ARA Supplementation Improves Cognitive Development at 6 Months†

	Score, Mean (SD)	
	Control (n = 55)	**DHA/ARA supplementation (n = 50)**
Total score	215 (39)	221 (32)
Communication	46.6 (9.1)	45.4 (7.9)
Gross motor	30.9 (11.1)	33.3 (11.5)
Fine motor	45.8 (14.3)	45.2 (10.7)
Problem-solving	49.5 (9.5)	53.4 (7.0)*
Personal-social	42.2 (12.3)	43.2 (12.8)

†Randomized, double-blind, placebo-controlled study of 141 infants with birth weights <1500 g. Intervention = 32 mg DHA + 31 mg ARA per 100 mL human milk started 1 week after birth and continued through hospital discharge (mean, 9 weeks). Cognitive development assessed at 6 months of age using Ages and Stages Questionnaire.

Henriksen C, et al. *Pediatrics*. 2008;121(6):1137-1145.

DHA/ARA Supplementation Improves Bayley Scores at 118 Weeks Postmenstrual Age in a Double-Blind Study

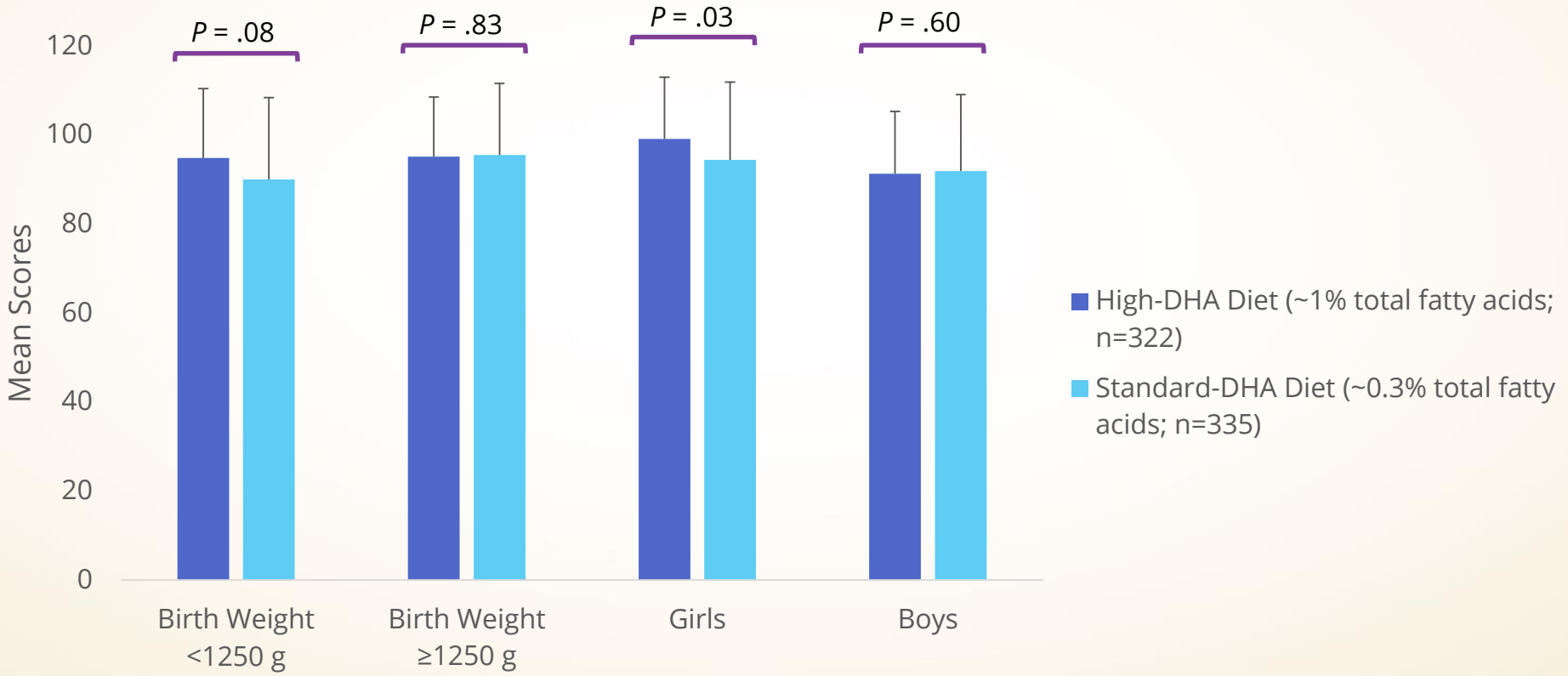


MDI, Mental Development Index; PDI, Psychomotor Development Index. *Breast-fed term > control, algal-DHA, fish-DHA ($P < .05$); †Algal-DHA > control ($P = .056$); ‡ Fish-DHA > control ($P < .05$); #Algal-DHA, fish-DHA > control ($P < .05$). Parentheses indicate number of infants per group.
Double-blinded study of 361 preterm infants. MDI and PDI assessed at 118 weeks postmenstrual age.

Clandinin MT, et al. *J Pediatr*. 2005;146(4):461-468.

Conflicting Results Regarding Benefit of DHA/ARA Supplementation in Preterm Infant Neurodevelopment: No Significant Difference†

Bayley MDI Scores at 18 Months' Corrected Age



†Randomized, double-blind controlled trial of 657 infants born at less than 33 weeks' gestation at 5 Australian tertiary hospitals with follow-up to 18 months. Standard-/high-DHA enteral feeds were given from day 2 to 4 of life until term corrected age

Makrides M, et al. *JAMA*. 2009;301(2):175-182.

Long-Chain PUFA Supplementation in Formula

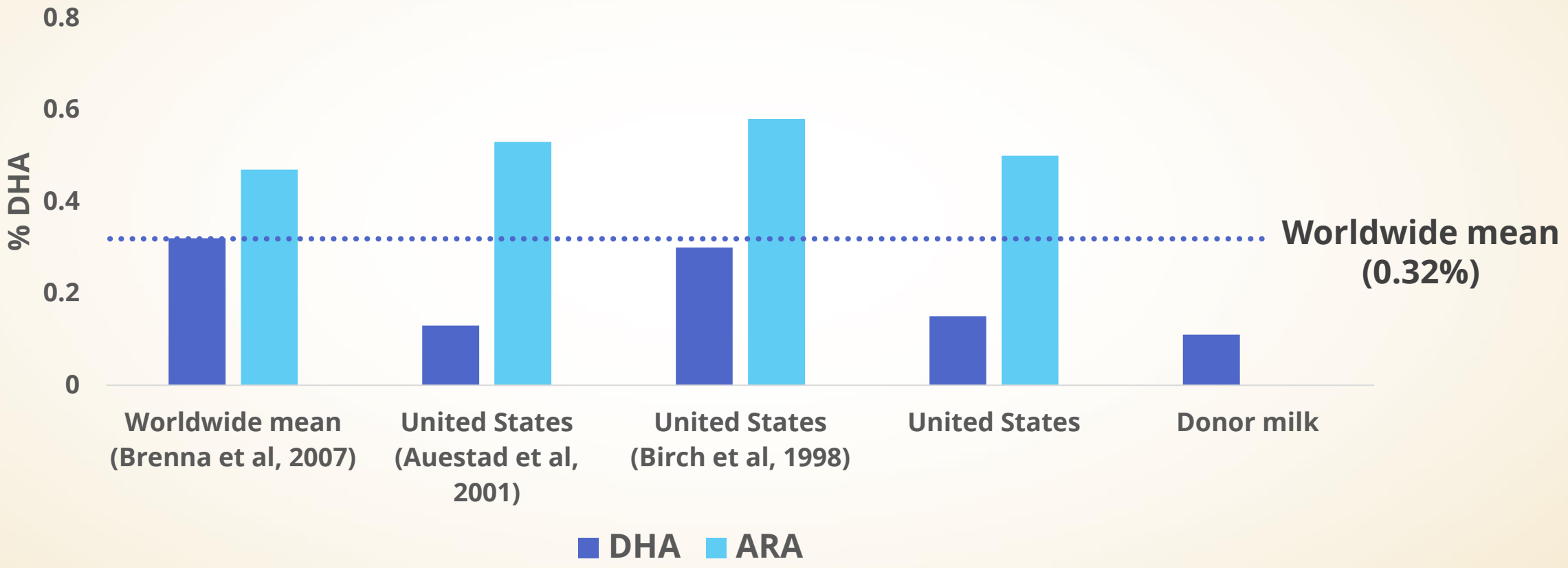
- Systematic review and meta-analysis of 17 randomized trials (13 classified as high quality) of formula supplemented with LCPUFA to assess safety and benefit to preterm infants
- Infants enrolled in the trials were relatively mature and healthy preterm infants
- Assessment schedule and methodology, dose and source of supplementation and fatty acid composition of the control formula varied between trials
- On pooling of results, **no clear long-term benefits or harms** were demonstrated for preterm infants receiving LCPUFA-supplemented formula

Schulzke SM, et al. *Cochrane Database Syst Rev*. 2011;(2):CD000375.

Enteral Strategies for Increasing DHA/ARA Intake in Preterm Infants

- Maternal supplementation
- Breast milk (mother's own)
- Structured lipids
- Pre-emulsified lipids
- Enzyme technologies

Donor Milk Levels of DHA Are Lower Than Mean Reported Levels[1†]



†Descriptive meta-analysis of 65 studies of human breast milk, including 2474 women.

1. Valentine C, et al. *J Pediatr*. 2010;157(6):906-910. 2. Auestad N, et al. *Pediatrics*. 2001;108(2):372-381. 3. Birch EE, et al. *Pediatr Res*. 1998;442:201-209. 4. Brenna JT, et al. *Am J Clin Nutr*. 2007;85(6):1457-1464.

Fatty Acid Replacement in Formula Is Challenging and Requires Standardization

- Defining target levels
- Determining dietary balance of n-3:n-6 fatty acids
- Ensuring optimal sn-position for absorption and incorporation into cellular phospholipids
- Optimizing digestion and absorption
- Achieving adequate levels at the tissue, cellular, and molecular levels

CURRENT NICU PRACTICES INVOLVING DHA/ARA IN PRETERM INFANTS

Current Practices

- Provide long chain PUFA in enteral feedings[1]
- DHA/ARA are available in breast milk and commercially available infant formula[1]
- Very premature infants do not reach full enteral feedings for several weeks[1]
  - Standard parenteral lipid emulsions do not provide DHA/ARA[1]
  - After reaching full enteral feedings, standard dietary DHA provision[2] is not adequate to alleviate deficiency of prematurity[3,4]

1. Baack ML, et al. *Lipids*. 2016;51(4):423-433. 2. Brenna JT, et al. *Am J Clin Nutr*. 2007;85(6):1457-1464. 3. Harris WS, et al. *J Perinatol*. 2015;35(1):1-7. 4. Lapillonne A, et al. *Neonatology*. 2010;98(4):397-403.

Current Parenteral Nutrition Practices†

Lipid emulsion ≤28 days (mean [SD])

	Birth (n = 17)	2 weeks (n = 14)	4 weeks (n = 17)	8 weeks (n = 17)
LA	3.6 (1.6)	8.7 (2.1)	8.8 (2.1)	7.9 (1.9)
ALA	0.03 (0.02)	0.08 (0.03)	0.07 (0.03)	0.07 (0.03)
DHA	5.3 (1.7)	3.6 (1.0)	3.7 (1.1)	4.2 (1.9)
ARA	14.8 (2.2)	12.0 (2.0)	12.7 (1.8)	11.5 (2.5)

Lipid emulsion >28 days (mean [SD])

	Birth (n = 17)	2 weeks (n = 14)	4 weeks (n = 17)	8 weeks (n = 17)
LA	3.6 (1.0)	10.1 (2.2)	11.3 (2.4)	10.1 (3.1)
ALA	0.03 (0.01)	0.09 (0.04)	0.12 (0.04)	0.12 (0.06)
DHA	5.5 (1.4)	3.0 (1.0)	3.1 (0.4)	2.7 (0.6)
ARA	15.7 (3.8)	11.7 (2.3)	11.4 (1.9)	9.4 (1.6)

- Infants showed a decline in DHA/ARA over time
- Longer exposure to intravenous lipid emulsion had a significantly greater decline in RBC DHA levels
- Infants who received intravenous lipid emulsion >28 days had longer time to start enteral feeds and reached full enteral nutrition 33 days later

†Prospective cohort study of 26 extremely low-birth-weight infants given intravenous lipid emulsion for ≤28 days or >28 days to assess change in LCPUFA
Levels reported as weight % (g/100 g).

Robinson DT, et al. *J Pediatr*. 2013;162(1):56-61.

Transition to Enteral Nutrition

Even after transitioning to full enteral feedings, premature infants cannot overcome the decline in whole blood DHA/ARA levels apparent after birth[1]

- Suggests limited activity of desaturase enzymes[2] or increased utilization of DHA/ARA due to disease or disease severity

1. Martin CR, et al. *J Pediatr*. 2011;159(5):743-749.e1-2. 2. Carnielli VP, et al. *Pediatr Res*. 1996;40(1):169-174.

The Role of Clinicians

- Help families navigate supplementation fads by sharing evidence from high-quality studies
  - Discuss problems with observational and cross-sectional findings used by companies to promote products that are not regulated directly to parents
- Consider better ways to supplement DHA/ARA in the highest risk patients

Cowden JD. *NEJM Journal Watch*. November 7, 2018. jwatch.org/na47834/2018/11/07/can-docosahexaenoic-acid-supplementation-help-toddlers.

The Role of Nurses and Dietitians

- Provide diet-related information to pregnant and lactating women to increase omega-3 fatty acid intake
- Collaborate with colleagues to determine what supplements/formulas would be appropriate to help ensure adequate DHA intake
- Continue to monitor supplement/formula developments

Brooks SL, et al. *MCN Am J Matern Child Nurs*. 2000;25(2):71-75.

The Role of Hospital Pharmacists

- Provide advice
  - Appropriate choice and correct use of formula
  - Appropriate choice of foods and drinks in weaned infants
  - Vitamin and fatty acid supplementation
- Collaborate with colleagues to ensure adequate information is provided throughout pregnancy to make informed choices about feeding
- Evaluate for and counsel on potential medication and supplement interactions

Mason P. *Pharmaceut J*. 2000;264(7089):471-475.

Future Considerations

- Define goals for fatty acid levels at specific, clinically relevant times
- Ongoing monitoring
  - Feeding advancement
  - Adverse events
  - Effects on other essential fatty acid levels
- DHA/ARA supplementation
  - Provide additional daily enteral DHA (start before full enteral feedings are reached and at a dose approximating in utero accretion rates)

Baack ML, et al. *Lipids*. 2016;51(4):423-433.

ANY Questions?