DHA Health Benefits Overview

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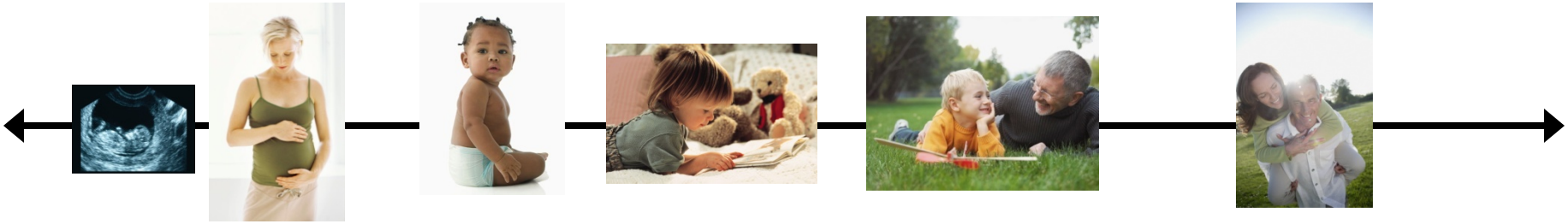
DHA is Important *Throughout Life*



Pregnancy

Maternal Health & Outcomes

Promotes maternal DHA status

Increases DHA content of breast milk

Supports normal gestation period

Promotes fetal brain and eye development

Infants & Children

Brain & Eye Development and Function

Improves visual acuity

Promotes cognitive performance

Children & Adults

Cardiovascular Heart Health

Lowers triglycerides

Increases HDL

Improves blood vessel function

Adults

Brain & Eye Health and Function

Maintains DHA blood levels which is associated with:

- less cognitive decline
- lower risk of dementia
- lower risk of age-related macular degeneration

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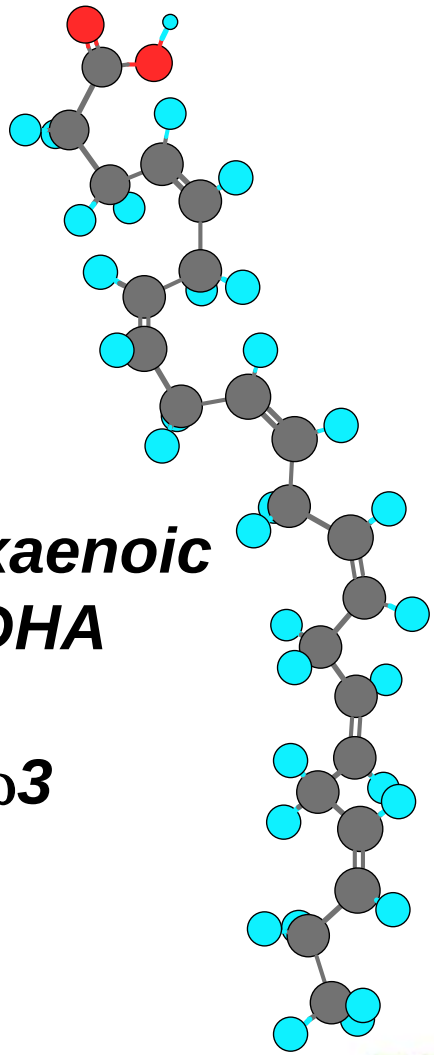
Docosahexaenoic acid (DHA)



Docosahexaenoic Acid - DHA

22:6 ω3

- Omega-3 fatty acid
- Important component of all cell membranes
- **Found in all tissues**; most abundant in **neural, retinal** and **cardiovascular conducting tissue**
  - **Brain: 97% of n-3 is DHA**
  - **Retina: 93% of n-3 is DHA**
- Facilitates synaptic transmission
- Supports myelination
  - Influences the speed that information is acquired and processed

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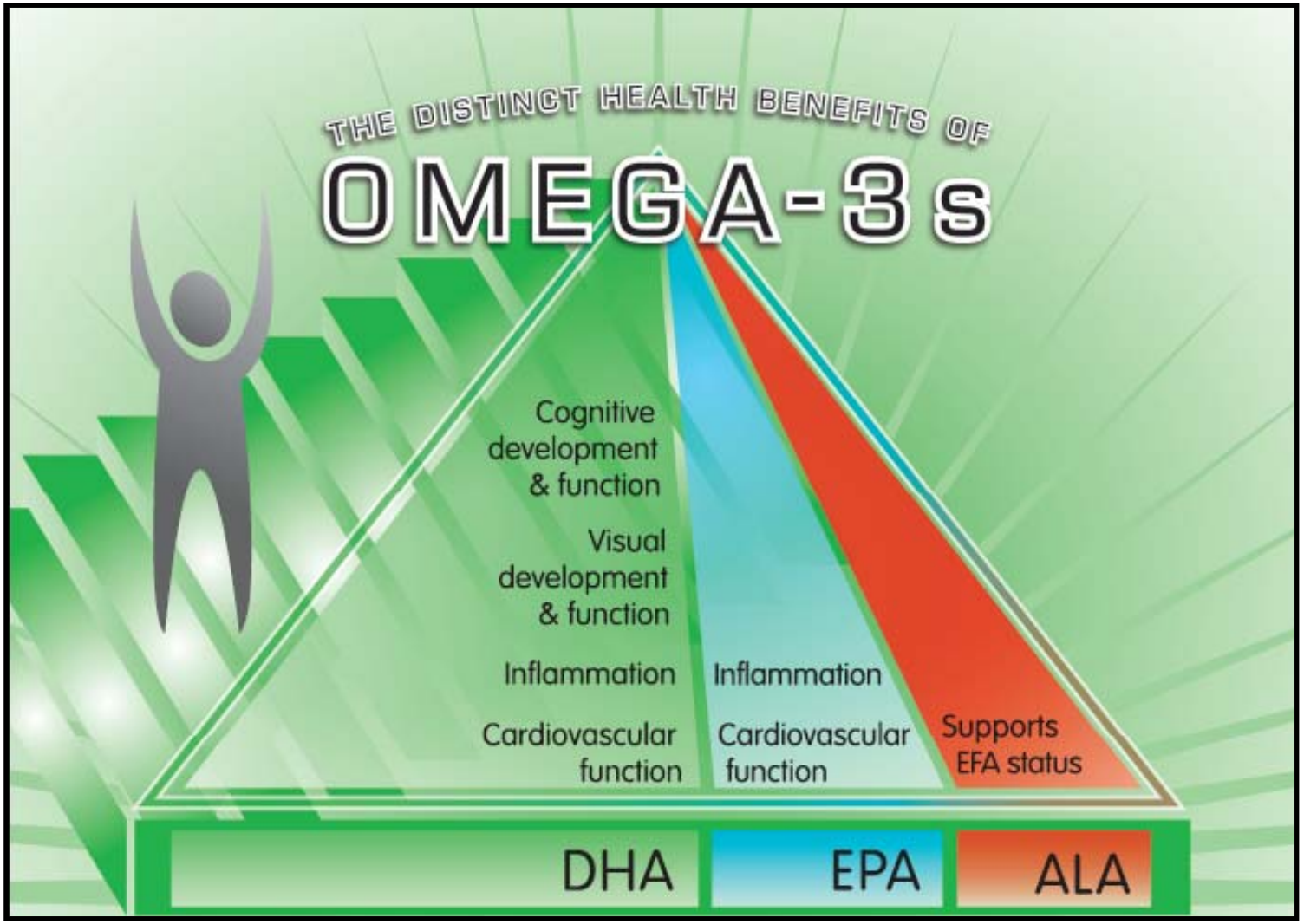
Omega-3 Fatty Acids Are Not The Same



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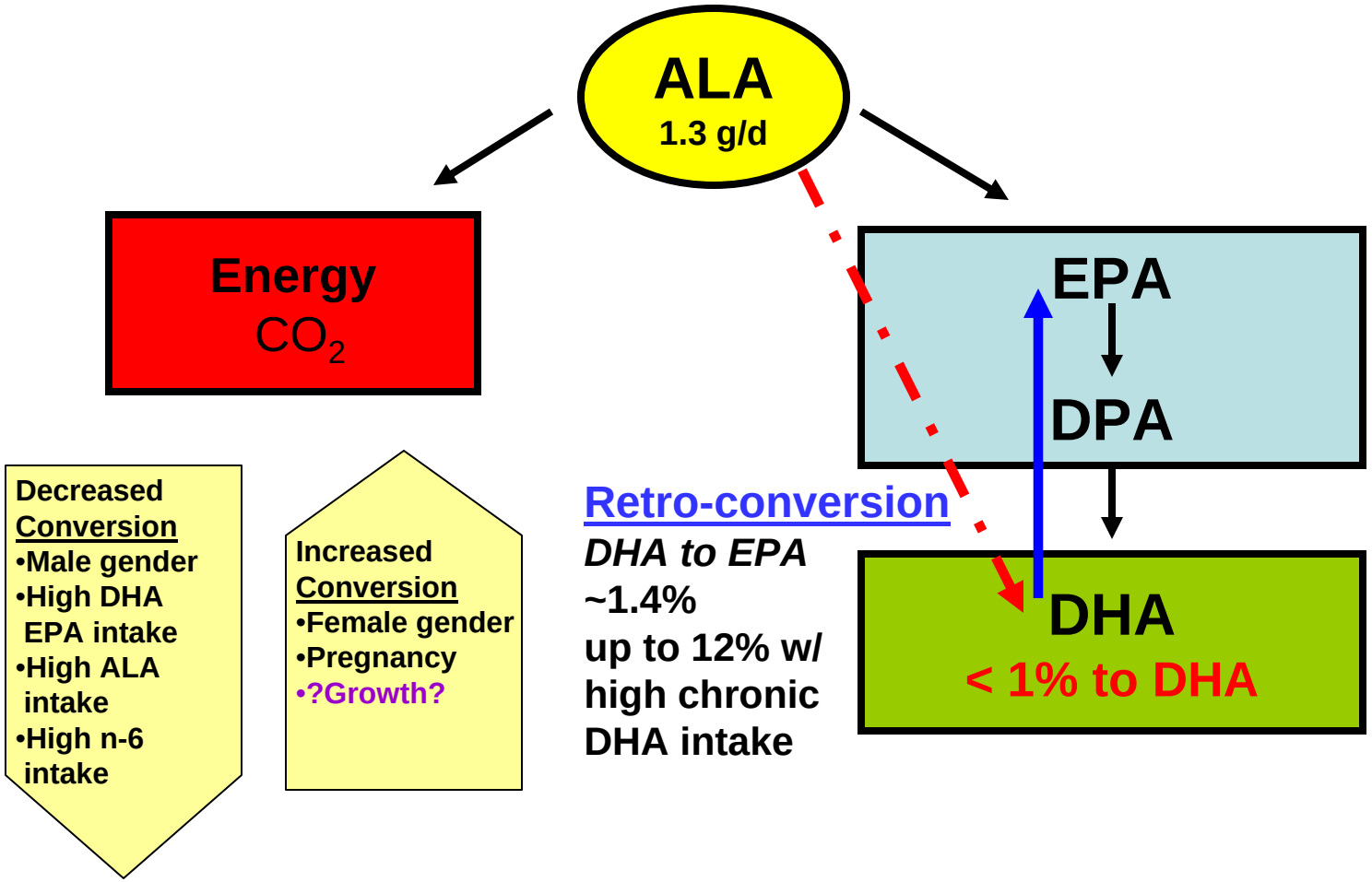
Conversion of Omega-3 Fatty Acids

Stable Isotope Studies in Humans



ISSFAL, 2007

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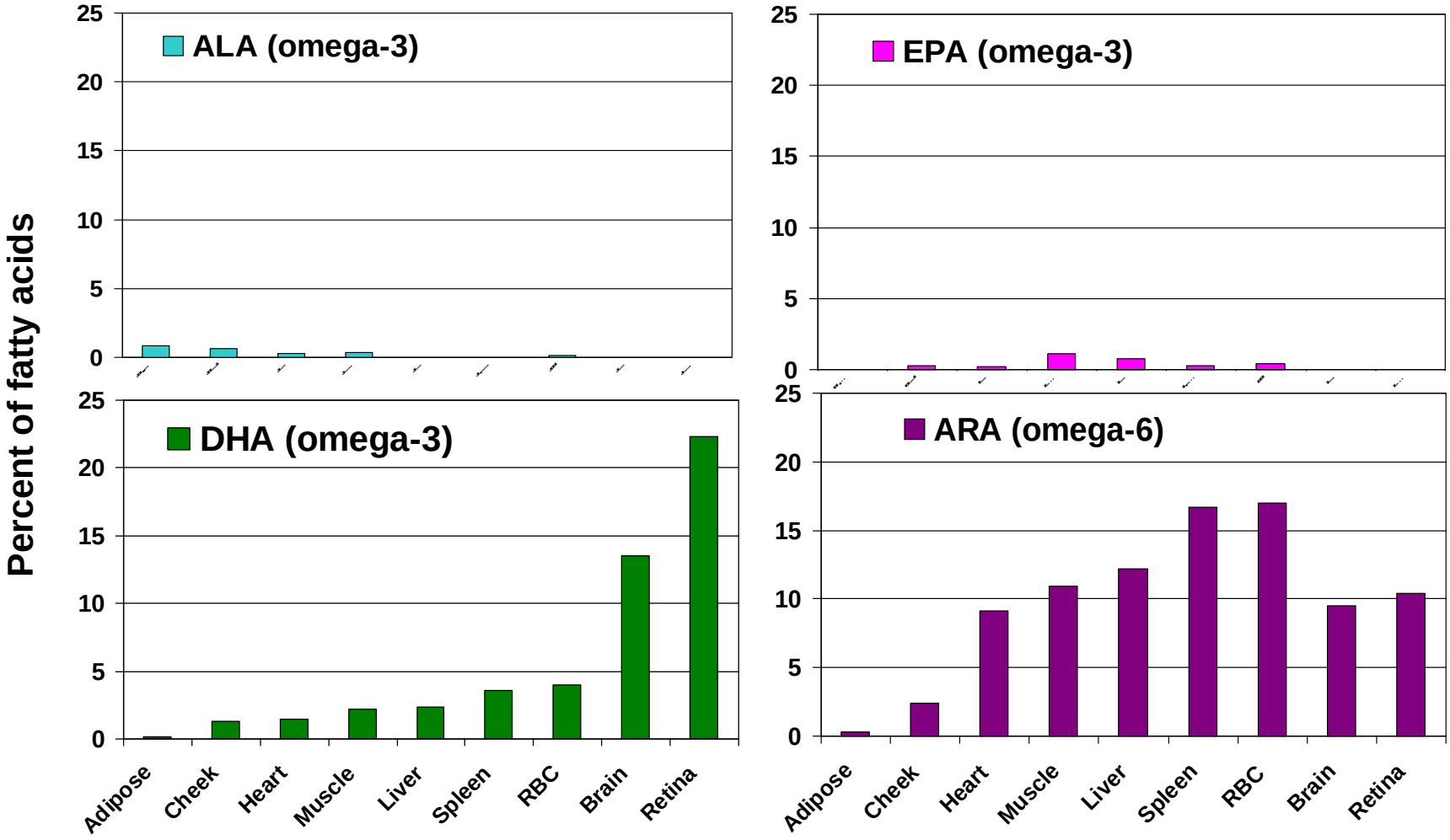
Tissue Levels of LCPUFA in Humans

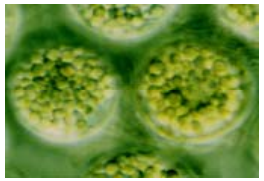


Arterburn et al., AJCN 2006, 83:1467S-76S.

Sources of DHA/Omega-3

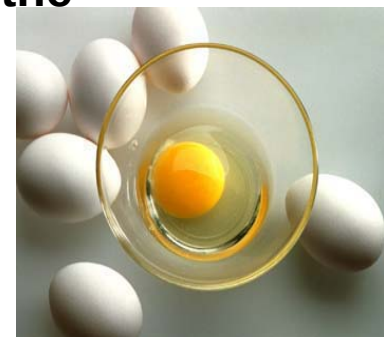
Dietary Sources of DHA and EPA:

- Algal oil
- Fatty fish including anchovies, salmon, herring, mackerel, tuna and halibut
- Organ meat such as liver
- Fish oil
- Small amounts are found in poultry and egg yolks



Dietary Sources of alpha-linolenic acid, (ALA)

- Walnuts and flaxseed oil **are not** direct sources of DHA
- **Dietary ALA does not produce sufficient DHA**
  - **The human body can convert ALA to DHA, but the process is inefficient and variable**
- No known independent benefits on brain or eye development and function



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DHA Intake
vs.
Recommendations

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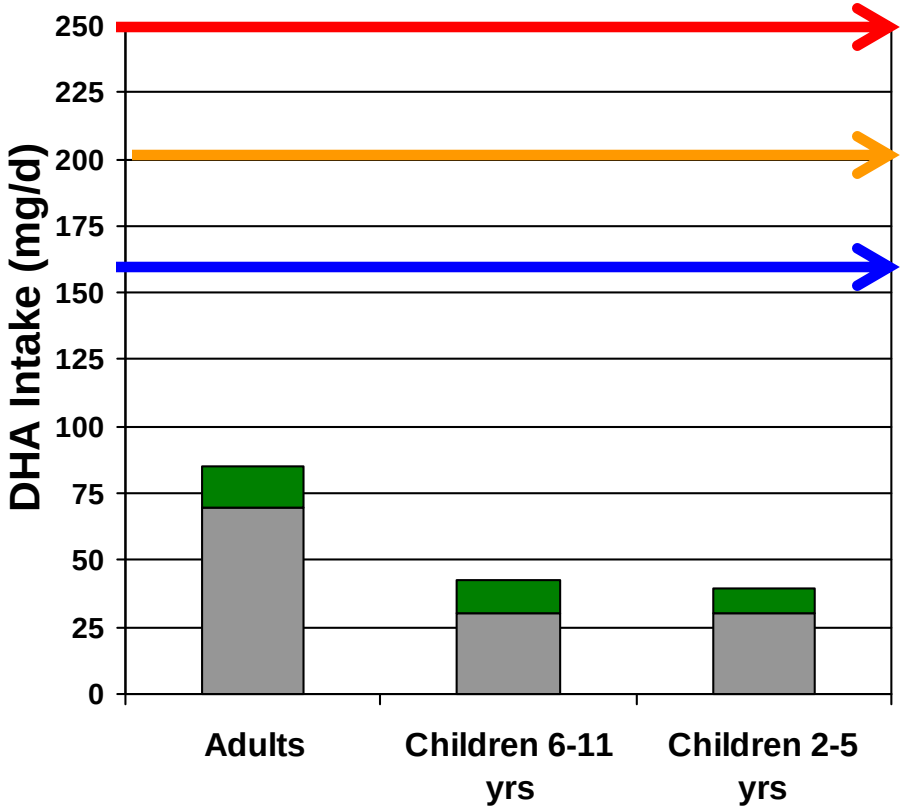
Estimated U.S. DHA Intake vs. Recommendations

Usual Daily Intake of Omega-3 PUFAs by U.S. NHANES 2003-2004



Am Diet Assoc. (500 mg/d LC-n-3)

PeriLip Recommendations (DHA only)

IOM (up to 160 mg)

Preformed DHA intake
- Adults: 70 mg/d
- Children 6-11 yrs: 30 mg/d
- Children 2-5 yrs: 30 mg/d

Conversion of ALA*
- Adults: 1.48 g/d
- Children 6-11 yrs: 1.26 g/d
- Children 2-5 yrs: 0.97 g/d

***<1.0%: ISSFAL draft statement on ALA and n-3 metabolism, 2007**

TOTAL Available DHA
- **Adults: 84 mg/d**
- **Children 6-11 yrs: 42 mg/d**
- **Children 2-5 yrs: 39 mg/d**

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Benefits of DHA Throughout Childhood

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DHA Influences Visual and Cognitive Development

DHA

Pregnant Women

- Decreased look duration (12 months)
- Reduced distractibility (24 months)

(Colombo et al. Child Dev, 2004. 75:1254-67)

- Increased IQ

(Cohen et al. Am J Prev Med, 2005, 29:366-74.)

Nursing Women

- Sustained improvements in Mental and Psychomotor Development

(Jensen et al. AJCN, 2005, 82:125-32.)

Infant Formula

- Visual Evoked Potential/Visual Acuity

(Uauy et al. J Pediatr, 2003, 143:S17-S25.)

- Improved mental and psychomotor development

(Birch et al. Dev Med Child Neurol, 2000, 42:174-181.)

- Improved "problem-solving" on means-end task

(Willatts et al. Lancet, 1996, 352:688-91.)

***Current EU expert recommendations promote at least 200 mg DHA/day during pregnancy and nursing**
Koletzko et al., Br J Nutr 2007

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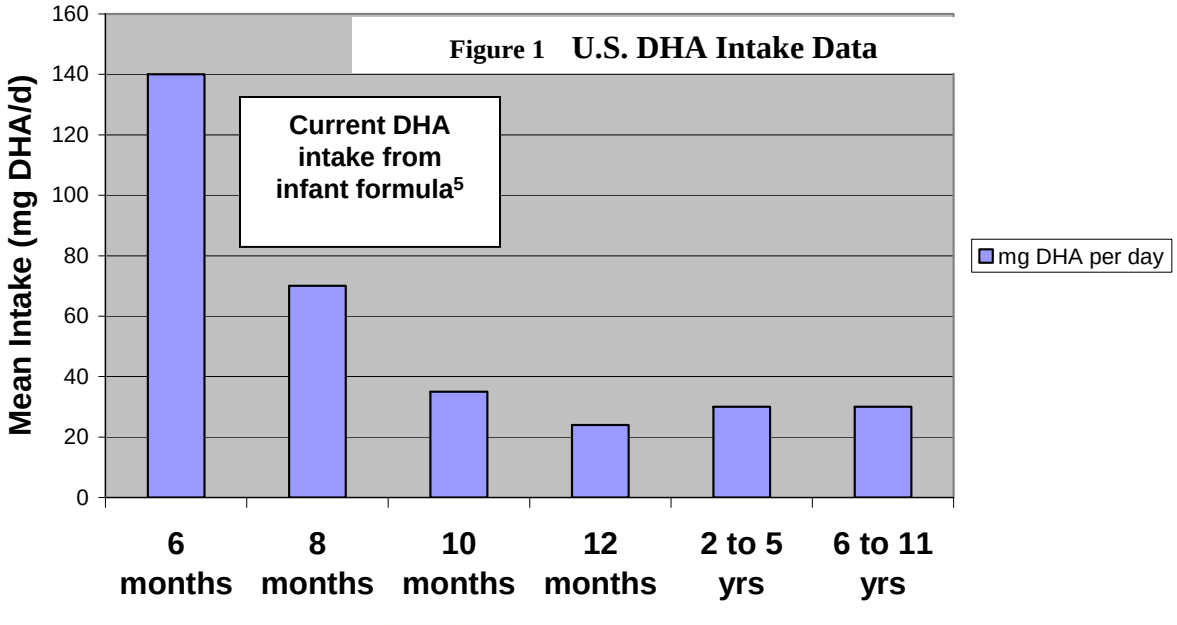
DHA Intake: Young Children

- DHA intake decreases during weaning from supplemented infant formula and breastfeeding (Figure 1).
- Estimated usual DHA intake in U.S. children 2 to 11 years of age is approximately 20 to 30 mg DHA per day**1**.
- U.S. children typically have low dietary intakes of DHA**1**.
- Typical complementary, finger, and table foods are low in DHA for children**2,3**.
- Dietary intake of alpha-linolenic acid does not lead to increased DHA blood levels4.
- Without country-specific recommendations for daily DHA intakes for young children, a minimum amount of **100 mg DHA per day i**ntake seems prudent to prevent a decrease in a child's DHA status previously supported by infant formula containing DHA and ARA.



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DHA Benefits: Adult Health

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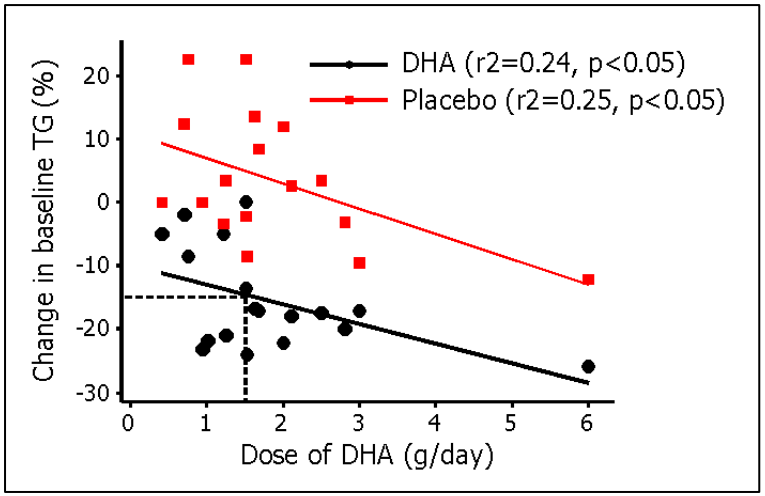
DHA Alone & Cardiovascular Health

- Favorable effects on blood lipid profile
  - Reduced triglycerides (fasting and following a meal)
    - Schwellenbach et al, AJCN, 2007
      - " Algae derived DHA products appear to be a better tolerated alternative." ($p<0.01$)
    - Keske et al, abstract 2007
    - Kelly et al, AJCN, 7/2007
  - Increased HDL (good cholesterol)
  - Improved LDL particle size
- Cardiac rhythm
  - Stabilizes heart rhythm
  - Lowers heart rate
    - Kelly et al, AJCN, 7/2007
- Modest reductions in blood pressure (higher doses)
    - Kelly et al, AJCN, 7/2007
  - Improved arterial compliance
  - Anti-thrombotic effects



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LC n-3 FA Roles in Cardiovascular Disease

Outcomes (Descending order of importance)	DHA	EPA	DHA + EPA
1. Sudden Cardiac Death (GISSI trial)			♥
2. Improves LDL Particle Size	♥	*	♥
3. Decreases High Blood Pressure	♥	♥	♥
4. Increases HDL Cholesterol	♥	*	*
5. a) Decreases Triglycerides	♥	♥	♥
5. b) Decreases postprandial TG	♥		
6. Decreases Heart Rate	♥		

Key: ♥ = Confirming evidence; * = strong evidence

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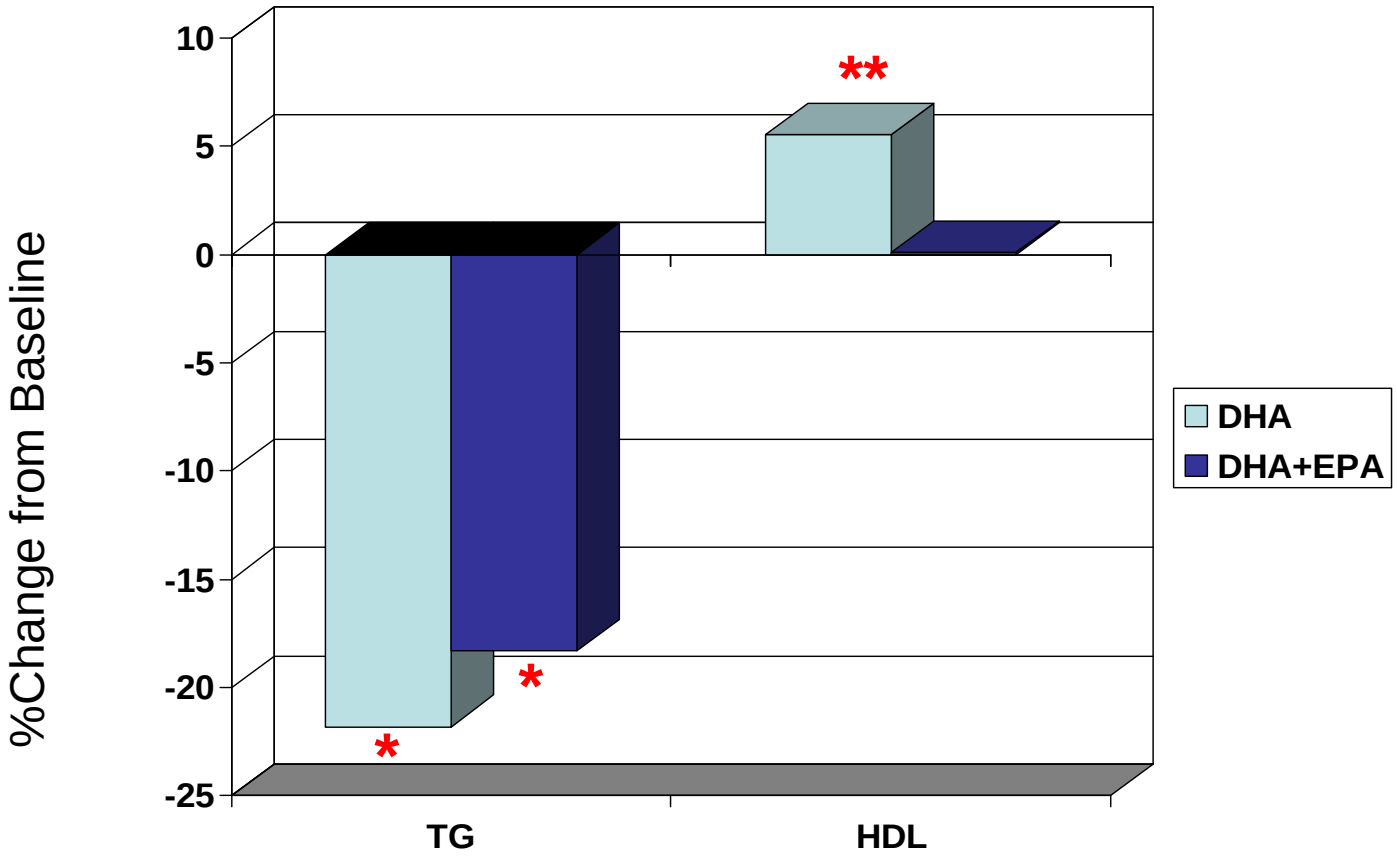
DHA Effects on Plasma Lipids Equal to or Greater Than EPA+DHA



1 g DHA vs 1.2 g EPA+DHA/d for 8 weeks
*P<.001 from baseline; **P<.05 from baseline

Schwellenbach et al., JACN 2006, 25:480-85

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TG Lowering from DHA

Study [ref number]	Martek DHA oil	Dose of DHA (g/day)	Duration (weeks)	Population	Change in baseline TG (%) with DHA supplementation
[1]	C	0.4	192	normal	~ -5.0
[2]	C	0.7	12	normal	-1.9
[3]	C	0.75 or 1.5	6	normal	-8.5 or -0.06
[4]	U	0.94	8	normal	-23.1
[5]	S	1.5	4	normal	-13.5
[6]	S	1.52	6	normal	-24.0
[7]	C	1.6	6	normal	-16.7
[8]	C	1.68	15	normal	-17.1
[9]	S	2.14	6	normal	-17.9
[10]	C	6.0	12	normal	-12.1
[11]	C	1.2	6	normal	-5.0
[12]	C	2.8	4	normal	-19.9
[13]	C	1.25 or 2.5	6	hyper	-20.9 or -17.6
[14]	C	3.0	12	hyper	-17.2
[15]	S	1.0	8	Hyper + statin therapy	-21.8
[16]	C	2.0	6	Hyper + statin therapy	-22.0

C=Crypthecodinium cohnii; S=Schizochytrium sp.; U=Ulkenia sp., hyper = hypertriglyceridemic (mean TG >150 mg/dL). Data from ref [1] estimated from graph and not raw data.

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Martek Review Abstract: TG lowering from DHA– October 2007 NYC Lipid conference

DHA & Normal Adult Cognitive Function

- Strong data from a **US cohort** (n=3718) supports a relationship between decreased cognitive decline and fish intake
  - 10% slower decline among subjects reporting 1 fish meal per week (about 80 mg DHA); 13% slower with 2 fish meals per week

Morris et al. Arch Neruol, 2005, 62:1-5.

- Data from **EU cohorts** suggest a relationship between DHA and cognitive function
  - Whalley and coworkers studied 364 non-demented elderly from a cohort of 2,000 studied for childhood IQ
  - Plasma DHA significant predictor of IQ at age 64

Kalmijn et al. Neurology, 2004, 62:275-80.
Whalley et al. AJCN, 2004, 80:1650-7.

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DHA in Alzheimer's and Dementia

- **Morris 2003 (Archives of Neurology)**
  - Increased DHA intake from fish consumption reduced risk of AD
  - No relationship with ALA/EPA and reduced risk of AD
- **Schaefer 2006 (Archives of Neurology)**
  - Highest plasma PC-DHA correlated with 47% reduced risk of all-cause dementia among 899 subjects
  - No benefit from plasma PC-EPA or ALA
  - Beneficial DHA intake estimated at 180 mg
- **Calon 2004; Lim 2005 (Journal of Neuroscience)**
  - Dietary DHA supplementation of transgenic Alzheimer's mice:
    - 70% reduction in insoluble plaque
    - 25% reduction in amyloid plaque burden
    - Improvement in learning and memory

AHRQ review of LCPUFA and Cognitive Function

(MacLean, 2005)

"Total omega-3 fatty acid consumption and consumption of **DHA (but not ALA or EPA)** are associated with a significant reduction in the incidence of Alzheimer's."

Martek's DHA selected for NIH Clinical Trial

DHA (Docosahexaenoic Acid), an Omega 3 Fatty Acid, in Slowing the Progression of Alzheimer's Disease

www.clinicaltrials.gov

Morris et al. Archives of Neurology, 2003, 60:940-46; Schaefer et al. Archives of Neurology, 2006, 63:1545-50; Calon et al. Neuron, 2004, 43:633-45. Lim et al. J Neurosci, 2005, 23:3032-40.

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