Dr. Susan Carlson

AJ Rice Professor of Nutrition
Department of Dietetics and Nutrition
University of Kansas Medical Center
A CONSEQUENCE OF THE DHA INTAKE GAP IN US PREGNANCIES: Preterm Birth
# US Dietary DHA Intake Is Low

<table>
<thead>
<tr>
<th></th>
<th>Recommended Daily DHA Intake*</th>
<th>Average Daily DHA Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant/</td>
<td>300 mg</td>
<td>54 mg</td>
</tr>
<tr>
<td>Lactating Women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult Women</td>
<td>220 mg</td>
<td>61 mg</td>
</tr>
<tr>
<td>Adult Men</td>
<td>220 mg</td>
<td>78 mg</td>
</tr>
</tbody>
</table>

*Expert panel convened by NIH/ISSFAL.
Prenatal maternal nutrition during first 1000 days includes:

- Protein
- Zinc*
- Iron*
- Choline*
- Folate*
- Copper*
- Iodine*
- Vitamins A, D, B₆, and B₁₂
- Long-chain polyunsaturated fatty acids (DHA)*

Supported by

- American Medical Association (AMA)
- American Pregnancy Association (APA)
- Academy of Nutrition and Dietetics

AAP AND AMA ADVOCACY FOR IMPROVING NUTRITION IN THE FIRST 1000 DAYS TO SUPPORT CHILDHOOD DEVELOPMENT AND ADULT HEALTH

http://americanpregnancy.org/pregnancy-health/prenatal-vitamin-ingredients/
Schwarzenberg et.al., Pediatrics. 2018 Feb;141(2)
https://jandonline.org/article/S2212-2672(14)00501-2/pdf
Schwarzenberg and Georgieff, Pediatrics 2018; 141/Issue 2
From the American Academy of Pediatrics, Policy Statement
NO OFFICIAL US REQUIREMENT FOR DHA

- Biochemical pathway to synthesize

- National Academy of Medicine does not recognize DHA as an essential nutrient at any stage of the life cycle
## DHA Dietary Sources: Fatty Fish, Meat, Eggs

<table>
<thead>
<tr>
<th>Food</th>
<th>DHA (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 oz pink salmon filet, baked/broiled</td>
<td>638</td>
</tr>
<tr>
<td>3 oz white tuna, canned in water</td>
<td>535</td>
</tr>
<tr>
<td>3 oz smoked salmon (lox)</td>
<td>227</td>
</tr>
<tr>
<td>3 oz crab, steamed</td>
<td>196</td>
</tr>
<tr>
<td>12 large shrimp, steamed</td>
<td>96</td>
</tr>
<tr>
<td>3 oz tuna salad</td>
<td>47</td>
</tr>
<tr>
<td>2 pieces chicken, fried</td>
<td>37</td>
</tr>
<tr>
<td>1 large egg, hard-boiled</td>
<td>19</td>
</tr>
</tbody>
</table>

First Studies to Suggest Omega-3 LCPUFA Reduce Early Preterm Birth (<34 weeks gestation)

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>DHA / EPA (g)</th>
<th>Subject selection</th>
<th>Delivery &lt; 34 wks (Cont vs. Supp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulstra-Ramakers 1994</td>
<td>64</td>
<td>0 / 3.0</td>
<td>IUGR +/- PIH in a previous pregnancy</td>
<td>19.3 vs. 9.4</td>
</tr>
<tr>
<td>Olsen 2000</td>
<td>797</td>
<td>0.9 / 1.3</td>
<td>Twins, preterm delivery, IUGR, PIH in a previous pregnancy</td>
<td>14.9 vs. 10.6</td>
</tr>
<tr>
<td>Makrides 2010</td>
<td>2399</td>
<td>0.8 / 0.1</td>
<td>Healthy women carrying singleton</td>
<td>2.25 vs. 1.09</td>
</tr>
<tr>
<td>Carlson 2013</td>
<td>301</td>
<td>0.6 / 0</td>
<td>Healthy women carrying singleton</td>
<td>4.8 vs. 0.6</td>
</tr>
</tbody>
</table>
### KUDOS: Very Low Birth Weight & Hospitalization
(Placebo, n=147; DHA, n=154)

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>DHA 600 mg</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early preterm birth (&lt;34 wks)*</td>
<td>4.8 %</td>
<td>0.6 %</td>
<td>P=0.025</td>
</tr>
<tr>
<td>Birth weight &lt;1500 g*</td>
<td>3.4 %</td>
<td>0 %</td>
<td>P=0.026</td>
</tr>
<tr>
<td>Neonatal Intensive Care Unit admission</td>
<td>8.3%</td>
<td>10.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Days hospitalized (mean #)**</td>
<td>40.8</td>
<td>8.9</td>
<td>P=0.026</td>
</tr>
</tbody>
</table>

*One tailed P values at $\alpha=0.05$; **if born <37 wks
Carlson et al., AJCN 2013
Public Health Significance

Evidence from KUDOS Trial (600 mg/d DHA)

• Savings of $1,652 / dyad with DHA supplementation

• Possible savings to US of up to $6 billion for hospitalization costs alone with universal supplementation

Shireman et al., PLEFA 2016
Correlation of Female Omega-3 LCPUFA Intake and Preterm Birth in 184 Countries: Benefits Found Up to 600 mg/d


Green: >600 mg/d omega-3 LCPUFA
Gold: <217 mg/d
White: 217-600 mg/d
How Much Omega-3 Supplementation is Needed to Reduce Early Preterm Birth? Weekly Capsule Intake (200 mg DHA/capsule)

600 mg DHA/day

Carlson et al., PLEFA 2018
OMEGA-3 FATTY ACIDS SUPPLEMENTATION DURING PREGNANCY: WHAT IS THE EVIDENCE FOR BENEFIT?

State of the art evidence from the November 2018 Cochrane Review

70 RCTs involving 19,927 women

Compared omega-3 interventions (supplements or food) with placebo

Middleton et al., Omega-3 fatty acid supplementation during pregnancy, Cochrane Review 2018
PRETERM BIRTH: OMEGA-3 VS NONE

<37 weeks: 27 RCTs, 10,304 participants

*High quality evidence for an 11% reduction*

<34 weeks: 9 RCTs, 5204 participants

*High quality evidence for a 42% reduction*

Middleton et al., Omega-3 fatty acid supplementation during pregnancy, Cochrane Review 2018
OTHER EFFECTS OF OMEGA-3 FATTY ACID INTAKE ON PREGNANCY OUTCOME

Low birth weight (<2500 g)
- 15 RCT, 8449 participants
- High quality evidence for a 10% reduction

Makrides 2018: ORIP (n=5544), NEJM Sept 2019
Carlson 2018: Recruiting for ADORE 200 vs 1000 mg (n=950 of 1250)
- 10 RCTs, 7026 participants
- Moderate quality evidence for a 25% reduction

NICU admissions:
- 9 RCTs, 6920 participants.
- Moderate quality evidence for an 8% reduction

Middleton et al., Omega-3 fatty acid supplementation during pregnancy, Cochrane Review 2018
Pregnancy RBC PL DHA at Baseline

*Gustafson KM et al., PLEFA 2013; 88: 331; Carlson SE et al., AJCN 2013; 97:808
SUMMARY

• Very low DHA intakes are associated with an increased risk of the most costly and devastating early births – those before 34 weeks gestation

• The 2018 Cochrane Review demonstrates strong evidence for increasing DHA intake to reduce preterm birth with most benefit for births before 34 weeks gestation

• The authors suggest a need for >500 mg/day based on their analysis of the literature

• A trial reported last week in NEJM found a 16% decrease in preterm birth (<37 weeks), but no decrease in birth before 34 weeks

• Does not refute the Cochrane Review finding that DHA can reduce early preterm and preterm birth

• DHA is a nutrient, and prenatal supplements containing DHA are now widely used in both the US and Australis such that women may be entering pregnancy with improved DHA status compared to 2006