Is Fat Where It’s At?

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Fats Through the Ages
Fatty Acids

- Dietary Fats are Used to Build Every Cell in the Body
- Cell Membranes are Made From a Variety of Individual Fatty Acids
- Cell Membrane Fatty Acids
  - Protect the Cell from its Surroundings
  - Facilitate Cell-to-Cell Communication
  - Serve as a Reservoir of Fatty Acids that are Precursors to Powerful Hormone-Like Molecules that Drive the Body’s Immune Response and Can Promote Anti-inflammatory Activity
Fatty Acids 101

• **A Fatty Acid:** A hydrocarbon chain with a methyl group at one end and a carboxyl group at the other

• **Saturated Fatty Acids:** fatty acids containing the maximum number of hydrogen atoms

• **Steric Acid (18:0)** Found in Animal fat
Fluidity of Fats

- **Saturated**: Solid at room temperature
- **Monounsaturated**: Liquid at room temperature, cloudy in the refrigerator
- **Polyunsaturated**: Liquid in refrigerator, more double bonds, more fluid, more unstable, easily oxidized
Where Trans Fats Come In

- C=C introduced into fatty acid chain
  - Remaining hydrogen molecules can either be on the same side of the chain (cis)
  - or opposite sides of the chain (trans).

- A cis bond in a fatty acid causes the chain to fold back on itself.
Where Trans Fats Come In

- A **trans** bond is rigid and the properties more closely resemble those of a saturated fatty acid.
- Like saturated fatty acids, **trans** fatty acids are able to pack together more closely and so have a higher temperature of melting.

- **Trans fatty acids raise LDL and lower HDL more than saturated fats**
- **Lack of fluidity due to rigid structure**
- **Solid at room temperature**
Trans Fatty Acids (TFA) and Inflammation

• TFA intake is positively associated with markers of systemic inflammation in women

• TFAs raise C-reactive protein, IL-6, TNF-alpha, especially in women, and especially in those who are overweight.
Trans Fats & Cardiovascular Disease

- TFA have no intrinsic value, and even consumption of 20-60 calories per day (2-7g) is associated with a dramatically increased risk of CVD.
- Eliminating TFAs would conservatively prevent 12-22% of the 1.2 million annual ‘heart attacks’ and deaths from coronary heart disease in the U.S.
- This translates to between 144,000 (12%) to 264,000 (22%) events per year in the United States alone, but does not come close to estimating for all the other forms of disease caused by CVD and increased systemic inflammation due solely to TFAs.
  – The FDA
Naturally Occurring Fat Structures

• **Monounsaturated fatty acids (MUFA)** contain one carbon=carbon double bond.
  – Avocados
  – Extra-virgin olive oil
  – Almonds
  – Macadamia nuts

• **Oleic acid (18:1 n-9)**
Naturally Occurring Fat Structures

- Polyunsaturated fatty acids (PUFAs)
  - Contain 2 or more carbon=carbon double bonds
- Plant (short chain) and marine (long chain) sources
- n-6 and n-3 series
- Linolenic acid (18:3 n-3)
Fatty Acid Nomenclature

• Fatty acids can be identified by 3 important characteristics (in this order).
  1. Chain length (number of carbons)
  2. The number of carbon-carbon double bonds.
  3. The location (starting from the methyl end) of the first double bond.

• 18:3 n-3 (or w3) for linolenic acid
Cell Membrane – Lipid Bilayer
The Fluid Mosaic Model
Diet High in Essential Fatty Acids

• Essential Fatty Acids (EFAs) are *essential* because they cannot be produced in the human body and therefore they must be obtained from the diet.

• Omega-3 fatty acids from fish are a direct source of EPA and DHA, two fatty acids vital for proper cellular function.

• EPA and DHA are precursors to immune molecules that promote a positive immune response and are the body’s strongest inflammation-reducing compounds.
Rich in OMEGA-3 and GLA
DHA (C22:6n-3)
Omega 3 vs. Omega 6

- Position of the double bond determines the 3 dimensional structure
- This determines reactions with receptors
Eicosanoids

Derivation of the term “Eicosanoid”

Arachidonic Acid = Eicosatetraenoic Acid

\[
\begin{align*}
Eicosa &= 20 \text{ carbons} \\
\text{tетраен...} &= 4 \text{ double bonds at C-5, C-8, C-11, C-14}
\end{align*}
\]
Eicosanoids

Sir John Vane – Nobel Prize 1982
– Aspirin, Eicosanoids prostaglandins, leucotrienes

• Earliest hormones in evolution
• Autocrine hormones produced by every cell in the body
Eicosanoids

- Chronic Disease – imbalance of eicosanoids
  - Heart disease, cancer, diabetes, arthritis, depression
- Inflammation – imbalance of eicosanoids
- Corticosteroids
  - Inhibit release of fatty acids from cell membrane
- Suppress favorable + unfavorable eicosanoids
Favorable Eicosanoid Effects

- Vasodilatation
- Decrease platelet aggregation
- Decrease inflammation
- Decrease cell division/Cause apoptosis
- Enhance immune function
- Improve cognitive function
- Antiarrhythmic
- Prevent atherosclerosis
Unfavorable Eicosanoid Effects

- Vasoconstriction
- Increase platelet aggregation
- Increase inflammation
- Promote cell division/Promote Cancer
- Depress immune function
- Depress cognitive function
- Pro-arrhythmic
- Promote atherosclerosis
n-3, n-6 and Inflammation

- EPA and DHA inversely associated with TNF and CRP
- Alpha-Linolenic Acid not associated with inflammatory markers
- The higher the intake of n-6, the more important n-3 for anti-inflammation

BLOOD LEVELS OF LONG-CHAIN n–3 FATTY ACIDS AND THE RISK OF SUDDEN DEATH

• Long chain n-3 PUFA (Omega 3) have anti-arrhythmic properties
• Dietary supplements of Omega 3’s reduce risk of sudden death in MI survivors
• Do Omega 3s reduce sudden death in patients without history of CV Disease?

BLOOD LEVELS OF LONG-CHAIN n–3 FATTY ACIDS AND THE RISK OF SUDDEN DEATH
A Prospective study

• 22,000 male physicians
• Followed 17 years
• Fatty acid content of blood of men with sudden death as first manifestation of cardiovascular disease vs. matched controls
Study Results:

• Baseline blood levels of long chain n-3 were inversely related to risk of sudden death.
  – $P = .007$

• Comparing risk of sudden death in highest to lowest quartile: 81% reduction of risk

• That’s significant!
Study Results:

• n-3 fatty acids are antiarrhythmic
• > ½ of sudden death from cardiac causes have no history of c-v disease
• This study was prospective, controlled and in men without hx of c-v disease
• Of all the fatty acids in the blood including saturated, monounsaturated, and polyunsaturated, only percentage of long chain **omega 3** predicted less sudden death. P =0.01
Sudden Cardiac Death and Whole Blood Cell Omega-3 Levels

90% Risk Reduction
*p = 0.001

Physicians' Health Study
Correlation with Omega-3 Fatty Acid and SCD

Quartile of Omega-3 Fatty Acids

<table>
<thead>
<tr>
<th>Quartile</th>
<th>RR SCD</th>
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<tbody>
<tr>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>2</td>
<td>0.54</td>
</tr>
<tr>
<td>3</td>
<td>0.18</td>
</tr>
<tr>
<td>4</td>
<td>0.1</td>
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P < 0.001

Physicians' Health Study
Omega 3 and Triglycerides

![Graph showing the relationship between dose of n-3 PUFA (g/d) and plasma TAG change (%Baseline concentration). The equation T = -7.6736 - 3.0475 (P) is also shown.]
• “n-6 AA...unbalanced by n-3 EPA and DHA may increase coronary atherosclerosis and sudden cardiac arrhythmic deaths”
• N-6/n-3 ratio in US is 20:1
• Optimal ratio 1:1 (Paleolithic diet)
Fish and Omega 3 fatty acid intake and risk of Coronary Heart Disease in Women

- Hu, F et al. *JAMA* 2002;287: 1815-1821
- All previous fish and CHD studies – men
- 84,688 female nurses followed 16 years
- Highest fish intake 34% less CHD p < .001
- Highest omega 3 intake 33% less CHD p < .001
- Highest fish or omega 3 intake – 45% less CHD deaths p < .001
Omega 3s Decrease Inflammation in Arterial Wall

N-3 PUFA decrease inflammation in the arterial wall and decrease atherogenesis and plaque rupture

Omega 3 and Atherosclerosis

• Decrease Cytokines IL-6, TNF etc
• Decrease CRP, Improve Endothelial function
• Decrease adhesion molecules VCAM ICAM
• Decrease LDL oxidation
• Decrease monocyte infiltration
• Increase Plaque stability
• Reverse Endothelial Dysfunction
Omega 3 and Cancer


- Fatty Acids composition in biopsy of adipose tissue in breast carcinoma and benign breast disease
- Inverse association between breast cancer risk and n-3 fatty acid levels
- Highest vs. lowest tertile
- ALA (18:3 n-3) Odds ratio 0.39
- DHA (22:6 n-3) Odds ratio 0.31
- Ratio Long chain n-3/n-6 Odds ratio 0.33
- N-6 positively associated with increased breast cancer risk
- LA (18:2 n-6) Odds ratio 2.31
Fatty Fish and Endometrial Cancer

• Consumption of fatty fish, but not other types of fish, may decrease the risk of endometrial cancer.

• 40% decreased risk

Omega 3 and Breast Cancer

• Long-chain n-3 consistently inhibit the growth of human breast cancer (BC) cells both in culture and in grafts in immunosuppressed mice
• EPA and DHA inhibit cyclooxygenase 2 which promotes mammary carcinogenesis

Omega 3 and Colon Cancer

“These data indicate that dietary omega-3 fatty acids prevent colon cancer, at least in part, through inhibition of colonic PKCbetaII signaling and restoration of TGF-beta responsiveness.”

Omega 3 and Prostate Cancer

• Multivariate relative risk analysis: highest fatty fish consumption group had approx $\frac{1}{4}$ rate of death from prostate cancer
  • Terry P. et al. Fatty fish consumption and risk of prostate cancer The Lancet Volume 357 Issue 9270 June 2001 Page 1764

• EPA and DHA in diet lowered risk

• ALA increased risk of advanced PC
Dysmenorrhea

• 1.8 g EPA+DHA x 2 months
• After 2 months of treatment with fish oil there was a marked reduction in the Cox Menstrual Symptom Scale from a baseline mean value of 69.9 to 44.0 (p < 0.0004)

Fatty Acids and Major Depressive Disorder

• Overall incidence of depression has increased in Western countries.
• Epidemiological studies support a connection between dietary fish/seafood consumption and a lower prevalence of depression.
• Clinical symptoms of depression have been found to decrease at higher levels of EPA.
Fatty Acids and Major Depressive Disorder

• The omega-6 arachidonic acid to EPA ratio (AA/EPA) has been found to positively correlate with the clinical symptoms of depression.

• A 1% increase in plasma DHA was associated with a 59% reduction in the reporting of depressive symptoms.

• Suicide attempts have also been associated with low levels of RBC EPA.
Omega 3 and Children’s Depression

![Graph showing the effect of omega-3 fatty acids and placebo on children's depression rating scale over 16 weeks. The graph indicates a decrease in depression scores over time for both groups, with omega-3 fatty acid group showing a more significant decrease.]
## Avg. Daily Intake of Omega 3

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Inuit (Eskimos)</td>
<td>7-10 g/day</td>
</tr>
<tr>
<td>Neo-Paleolithic hunters</td>
<td>3</td>
</tr>
<tr>
<td>One tablespoon cod liver oil</td>
<td>2.5</td>
</tr>
<tr>
<td>Current American intake</td>
<td>0.12</td>
</tr>
<tr>
<td>AHA recommendation</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>2 servings of fish per week</td>
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</table>
The Many Benefits of Omega 3

- Heart
- Brain
- Cancer
- Autoimmune
- Pain and inflammation
- Skin
- Quality of Life
- Can control Insulin levels through diet of adequate protein, adequate fat and carbs mostly from vegetables
# How Much Omega 3 Do You Need?

<table>
<thead>
<tr>
<th>Goal</th>
<th>Grams per Day</th>
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<tbody>
<tr>
<td>Maintaining Good Health</td>
<td>2.4</td>
</tr>
<tr>
<td>Improved Cardiovascular Health</td>
<td>2.4 - 4.8</td>
</tr>
<tr>
<td>Improved Brain Function</td>
<td>4.8 – 9.6</td>
</tr>
<tr>
<td>Inflammation Reduction</td>
<td>4.8 – 9.6</td>
</tr>
<tr>
<td>Optimal Health</td>
<td>4.8 – 9.6</td>
</tr>
<tr>
<td>Treating Neuro Disease</td>
<td>9.6 +</td>
</tr>
</tbody>
</table>
Long Chain Omega 3 per 4oz Serving

• 2 or more grams of Omega 3
  – Herring  2.4 g
  – Mackerel  2.1 g
  – Atlantic Salmon  2.1 g
1-2 g of Omega 3 per 4oz Serving

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<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Pacific Oysters</td>
<td>1.6g</td>
</tr>
<tr>
<td>Pacific Salmon</td>
<td>1.5</td>
</tr>
<tr>
<td>Atlantic Mackerel</td>
<td>1.4</td>
</tr>
<tr>
<td>Bluefish</td>
<td>1.1</td>
</tr>
<tr>
<td>Trout</td>
<td>1.1</td>
</tr>
</tbody>
</table>
Less Than 1 Gram of Omega 3

- Freshwater bass 0.9 g
- Swordfish 0.9 g
- Canned tuna 0.8g
- Halibut 0.5g
- Shrimp 0.4g
- Snapper 0.4g
- Clams 0.3g
- Yellowfin tuna 0.3g
- Catfish 0.1g
Low or No Omega 3

- Fast food fish sandwiches
- Fish sticks
- Imitation crab (made from low fat Pollack)
Beef

• Grain feed cattle:
  – 33-74% fat, mostly saturated
  – Omega 3: < 1% of fat
  – Omega 6/Omega 3 ratio is 20:1

• Grass feed cattle
  – Omega 3: 7% of fat
  – Omega 6/Omega 3 ratio is 3:1
Meat From Grass-Fed Animals Have Two to Four Times More Omega-3 Fatty Acids than Meat from Grain-Fed Animals

http://www.eatwild.com/IMAGES/gr_fatty_acid_ratio.gif
Omega-3s Vanish in the Feedlot

Percentage of Total Fat vs. Days being grainfed in the feedlot

Omega-3 Decreases in Feedlots
Other Sources of Fats
ONLY Organic

• Dairy: Milk, Yogurts, Cheeses– preferably RAW

• Coconut oil, ghee (organic, organic)

• Nuts & Seeds (organic & organic)

• Do NOT cook with Nut or Seed oils, as the polyunsaturated fats become trans fats with heat!
This does NOT qualify:

Nonfat yogurt (cultured grade A non fat milk, modified food starch, fructose, kosher gelatin, vitamin A palmitate, vitamin D3), water, blueberry puree, fructose, contains less than 1% of modified corn starch, natural flavor, blue 1, red 40, aspartame, potassium sorbate (to maintain freshness), acesulfame potassium, sucralose, malic acid, sodium citrate.
How to Read This Label:

### Nutrition Facts

- **Serving Size**: 1 oz (28g/about 28 nuts)
- **Servings per Can**: 6
- **Calories**: 170
- **Calories from Fat**: 140

<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>% DV*</th>
<th>Amount Per Serving</th>
<th>% DV*</th>
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</thead>
<tbody>
<tr>
<td>Total Fat</td>
<td>15g</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Sat. Fat</td>
<td>1g</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Trans Fat</td>
<td>0g</td>
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</tr>
<tr>
<td>Cholest.</td>
<td>0mg</td>
<td>0%</td>
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</tr>
<tr>
<td>Sodium</td>
<td>115mg</td>
<td>5%</td>
<td>Protein 6g</td>
</tr>
<tr>
<td>Potassium</td>
<td>180mg</td>
<td>5%</td>
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</tr>
<tr>
<td>Total Carb.</td>
<td>6g</td>
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<tr>
<td>Dietary Fiber</td>
<td>3g</td>
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</tr>
<tr>
<td>Sugars</td>
<td>2g</td>
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*Percent Daily Values are based on a 2,000 calorie diet.*

**Ingredients:** ALMONDS, VEGETABLE OIL (CANOLA, SAFFLOWER AND/OR SUNFLOWER), SUGAR MODIFIED, STARCH, SALT, SOY SAUCE (SOYBEAN, WHEAT, SALT), HORSE RADISH, ONION, SPICE FRACTIONS, CITRIC ACID, LACTATE, SODIUM NITRITE AND SODIUM PEROXIDE. PEANUT FREE. MAY CONTAIN OTHER TREE NUTS FROM CALIFORNIA. PACKED BY: BLUE DIAMOND GROWERS, SACRAMENTO, CA. 95812 U.S.A.
References

• “Omega 3 Poly Unsaturated Fatty Acids: What you need to know to save your (and your patient’s) life”
  Slides from Ron Rothenberg, M.D.

• “Fatty Acids, Genomic Analysis, Porphyrin Testing”
  Slides from Todd R. LePine, M.D.