

OMEGA-3 FISH OILS

APPLICATIONS AND EMERGING RESEARCH

Dr Kamal Karl, FRNZCGP, FACNEM

Hawke's Bay Wellness Centre

Napier – Auckland – Christchurch

reception@wellnesscentre.co.nz

www.wellnesscentre.co.nz

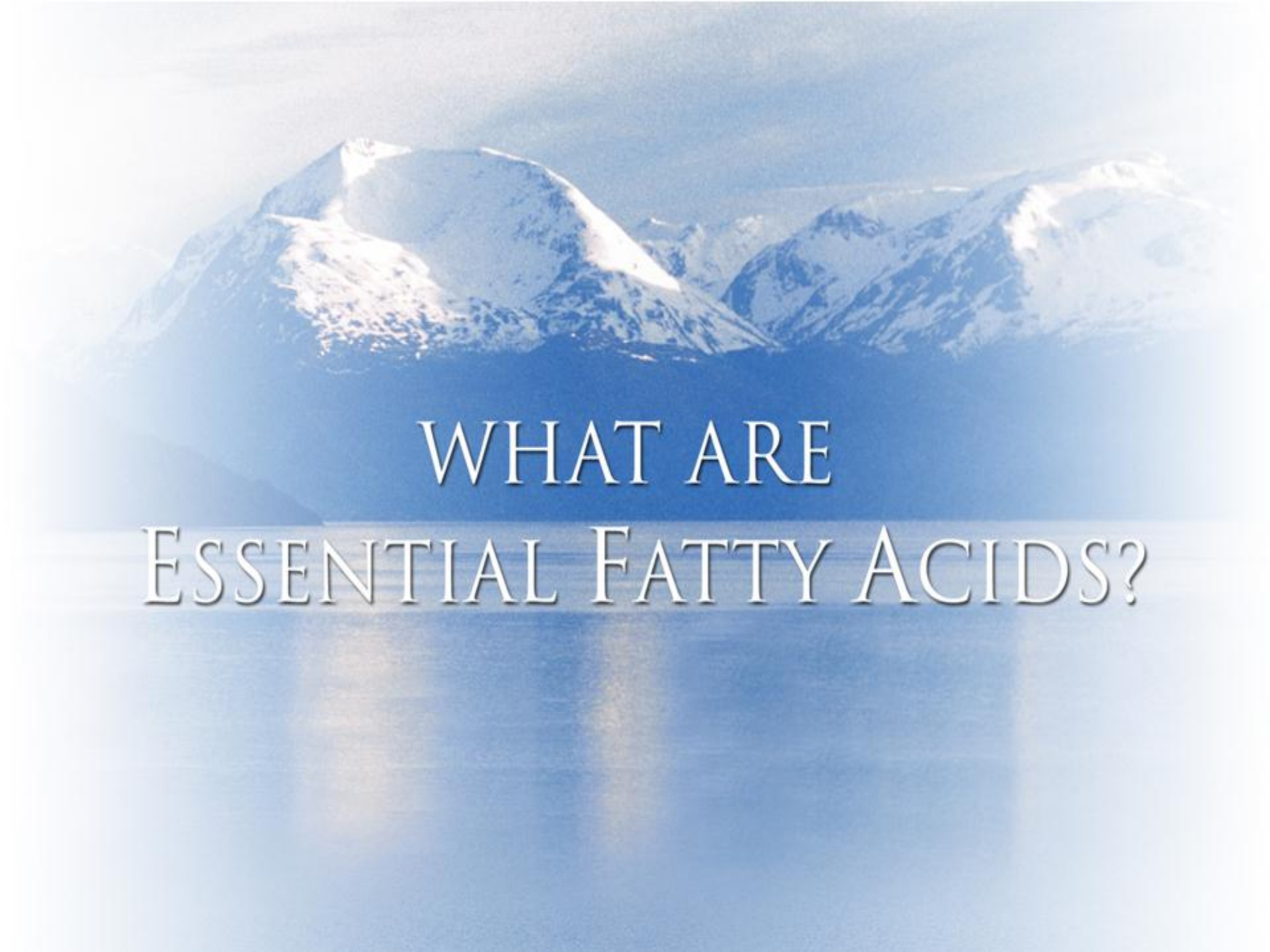
GPCME Conference – June 2012 – Rotorua



What We Will Cover

- ◆ What are Essential Fatty Acids?
- ◆ The emerging science that explains how EFA's work at a cellular level
- ◆ Omega-6 intake increases need for omega-3s
- ◆ Proven Benefits of Fish Oil
 - ◆ Heart health
 - ◆ Mental health
 - ◆ Joint health
 - ◆ Exercise and recovery
 - ◆ Infant development
 - ◆ Maternal health
 - ◆ Children and behavior
- ◆ How to choose a fish oil supplement
- ◆ Dosing Guidelines

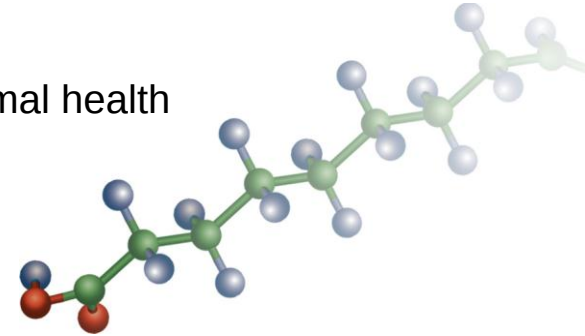




WHAT ARE ESSENTIAL FATTY ACIDS?

What are Essential Fatty Acids?

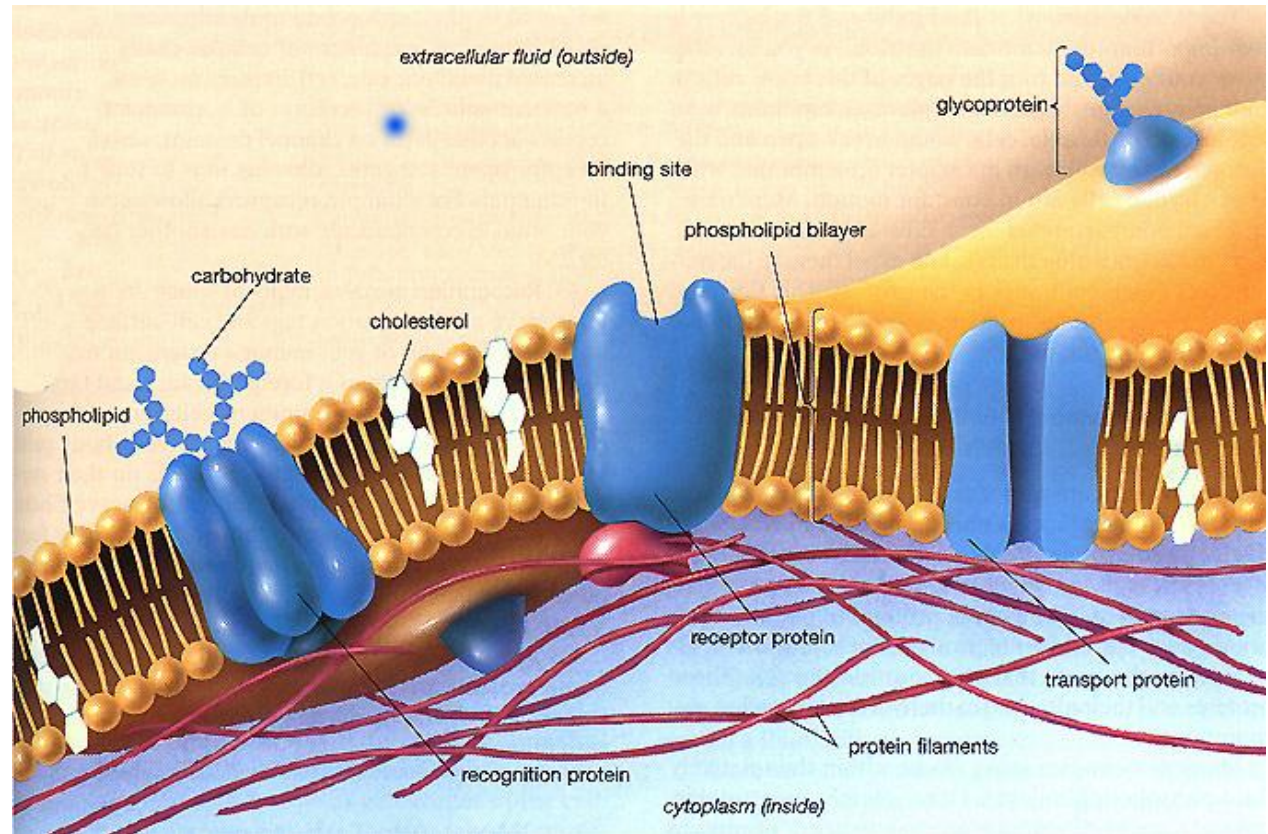
- ◆ Essential Fatty Acids are:
 - ◆ Polyunsaturated long chain fatty acids that are essential for optimal health
 - ◆ Essential because the human body cannot make them; they must be consumed through diet or supplementation
 - ◆ Required for proper functioning of all living cells
- ◆ Essential Fatty Acids reside in cell membranes
 - ◆ They impact every biological process in the body, including cell communication, the inflammatory response, and immune function.
- ◆ In the cell, EPA and DHA have metabolic, regulatory, and structural functions
 - ◆ Cells become less flexible, less permeable, and functionally compromised when Omega-3 intake is inadequate
- ◆ Fish oil is the best source of the omega-3 essential fatty acids EPA and DHA



Stillwell W et al, *Chem Phys Lipids* 2003
Cordain L, *AJCN* 2005
Linus Pauling Institute, Corvallis OR 2006

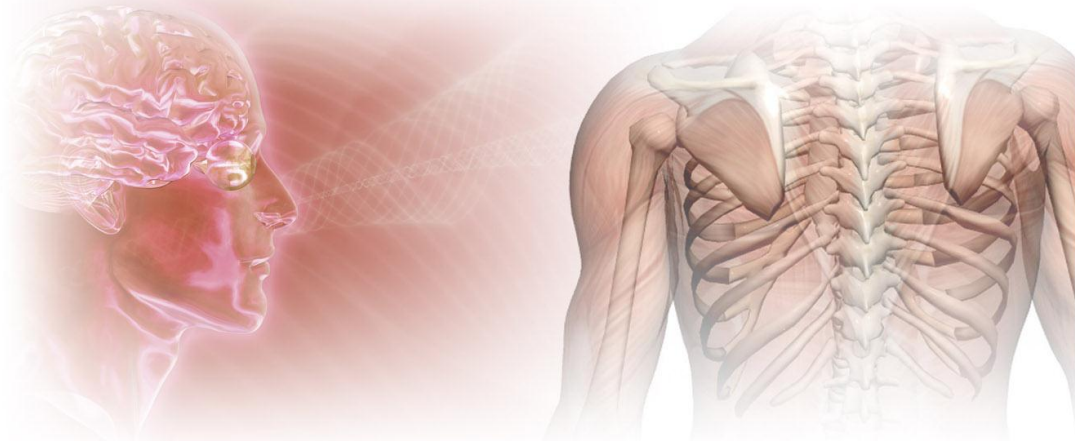
Cell Membrane – Lipid Bilayer

- ◆ EPA and DHA are structural components of every cell and therefore influence:
- ◆ cell membrane stability and fluidity
- ◆ receptor action
- ◆ membrane-bound enzyme activity
- ◆ hormone binding
- ◆ signal transduction
- ◆ action potentials



Effects of Reduced Membrane Fluidity

- ◆ Plays havoc with hormonal regulation of cells, exaggerating some effects and dampening others:
 - ◆ Exaggerated effect (oestrogen, progestins etc.)
 - ◆ Diminished effect (insulin, serotonin)
- ◆ This dysregulation is why PMS, depression, insulin resistance, hypertension (to name a few) results



Changes in Membrane Fluidity May Result in Accelerated Rates of Neuro Dysfunction/Death, Resulting in Pre-mature Senility & Dementia

1. Exaggerated effect of cortisol → hyperstimulation → loss of dendritic spines (cell-cell communication)
2. Diminished effect of insulin → glucose dysregulation & energy dysfunction
3. Diminished production of L-Dopa and decreased serotonin sensitivity



Nutrition and Genetics are Interconnected

- ◆ Omega-3s EPA and DHA
- ◆ Modulate (turn on and off) DNA and gene function
- ◆ Promote the resolution of inflammation

Diet,
adipose tissue

Lipoxygenases,
Cyclooxygenases

Cell Membrane

Fatty acids

PPAR α

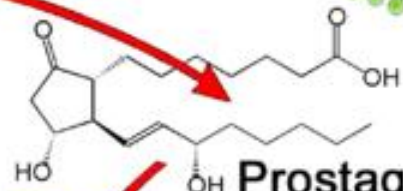
Cell Nucleus

PPAR α

RXR

PPAR γ

RXR

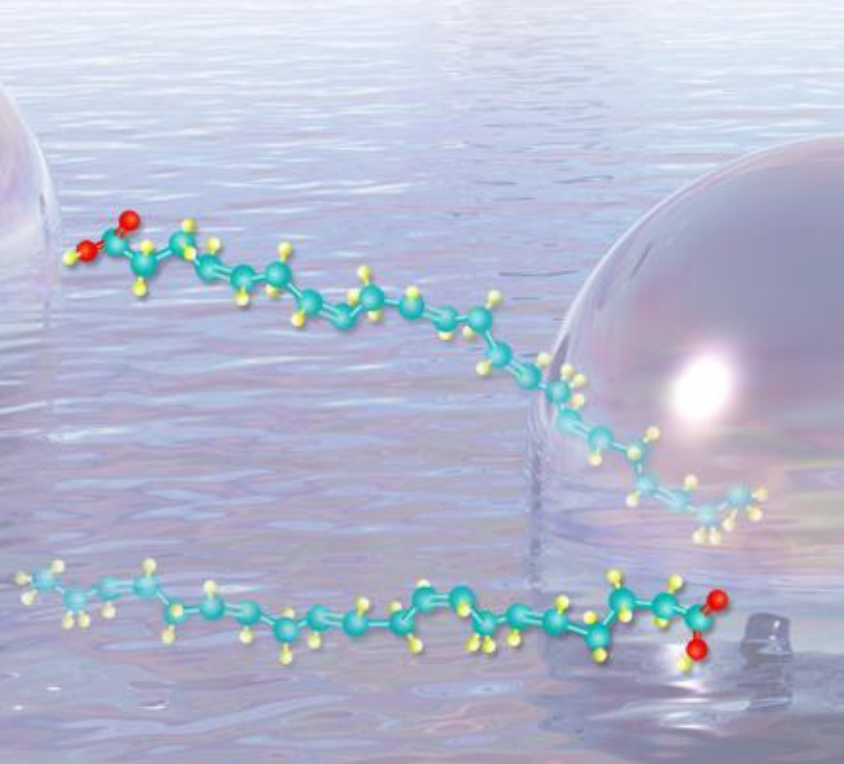


Prostaglandins,
Leukotrienes

Newly Discovered Lipid Mediators

- ◆ Resolvins and Protectins=EPA and DHA derived mediators
- ◆ These mediators have both anti-inflammatory and proresolution properties, thereby:
 - ◆ Protecting organs from collateral damage
 - ◆ Stimulating the clearance of inflammatory debris
 - ◆ Promoting mucosal antimicrobial defense

Serhan C. Nature Immunology 2008.



Tissue Regeneration



Dental Plaque

Tartar

“This report is the first to show that resolution of inflammation by a naturally occurring endogenous lipid mediator results in complete regeneration of pathologically lost tissues, including bone.”

Resolvin E1 regulates inflammation at the cellular and tissue level and restores tissue homeostasis in vivo. *J Immunol* 2007;179:7021–7029.

Sources of Essential Fatty Acids

◆ Omega-3

- ◆ EPA and DHA are found primarily in oily cold-water fish such as herring, tuna, sardines, anchovies and salmon (*Fish-form Omega-3's*)
- ◆ ALA (alpha linolenic acid) is found primarily in flaxseed oils, certain vegetable oils and some green leafy vegetables (*Plant-form Omega-3's*)



ALA is not a reliable source of EPA and DHA for humans

Pawlosky RJ et al, AJCN 2003; Davis BC et al, AJCN 2003

◆ Omega-6

- ◆ Linoleic acid is found primarily in seeds, nuts, grains and legumes and is heavily present in our diet as vegetable oils (e.g. corn and soy oils) and seed oils (e.g. sunflower and safflower oils)

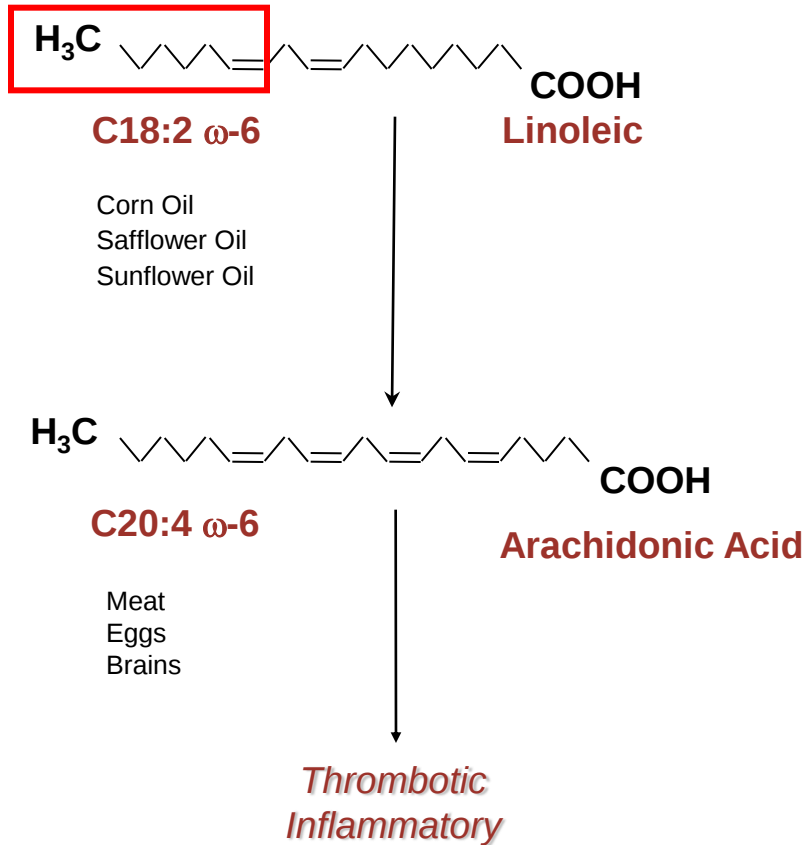


What about Omega-9?

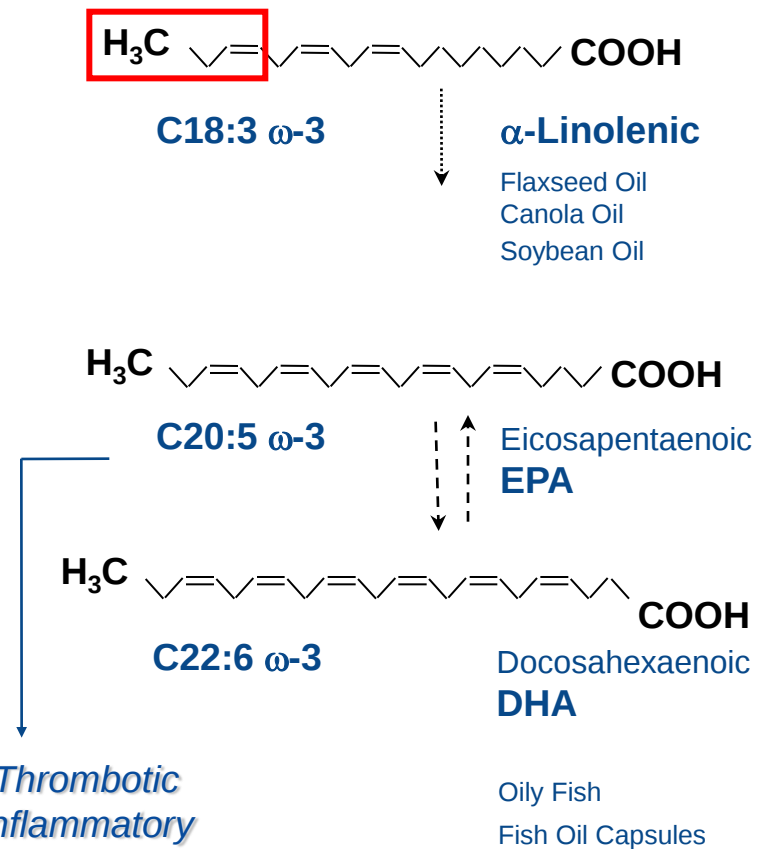
Omega-9 is an important, but not essential fatty acid. It naturally occurs in small amounts in fish oil and borage oils.

Essential Fatty Acid Families

ω -6 family



ω -3 family



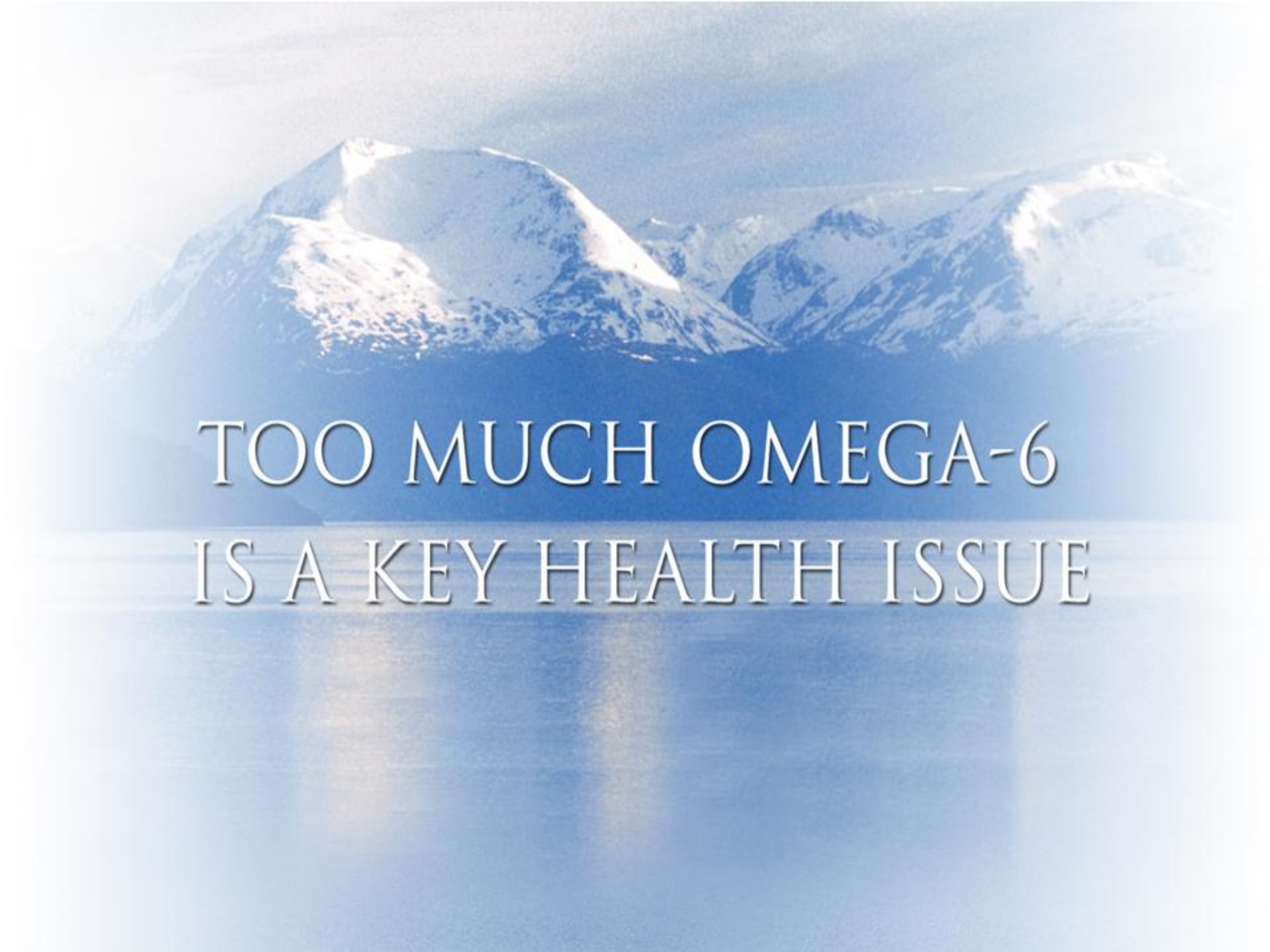
Clinical Signs & Sx of Omega-6 Deficiency

- ◆ Bumps on backs of upper arms (“chicken skin”)
- ◆ Red, scaly eczematoid dermatitis
- ◆ Excess thirst with/without excess urination
- ◆ Coarse, dry hair, alopecia
- ◆ Brittle nails
- ◆ Slow wound healing

Clinical Signs & Sx of Omega-3 Deficiency

- ◆ Numbness & tingling of the extremities
- ◆ Impaired immune system function
- ◆ Frequent infections
- ◆ Labile mood swings; depression
- ◆ Senile dementia





TOO MUCH OMEGA-6
IS A KEY HEALTH ISSUE

The problem with too much Omega-6

An imbalance of **too much** Omega-6 (linoleic acid) forms a type of eicosanoid that promotes unhealthy conditions, such as:

- ◆ Heart conditions
- ◆ Inflexible joints and swelling
- ◆ Poor memory, unclear thinking
- ◆ Aggression and violence
- ◆ Acute immune conditions
- ◆ Inconsistent mood and behaviors

Important fact: Eicosanoids “direct traffic” in cell walls

Simopoulos AP, Biomed Pharm 2002

Cordain L, AJCN 2005

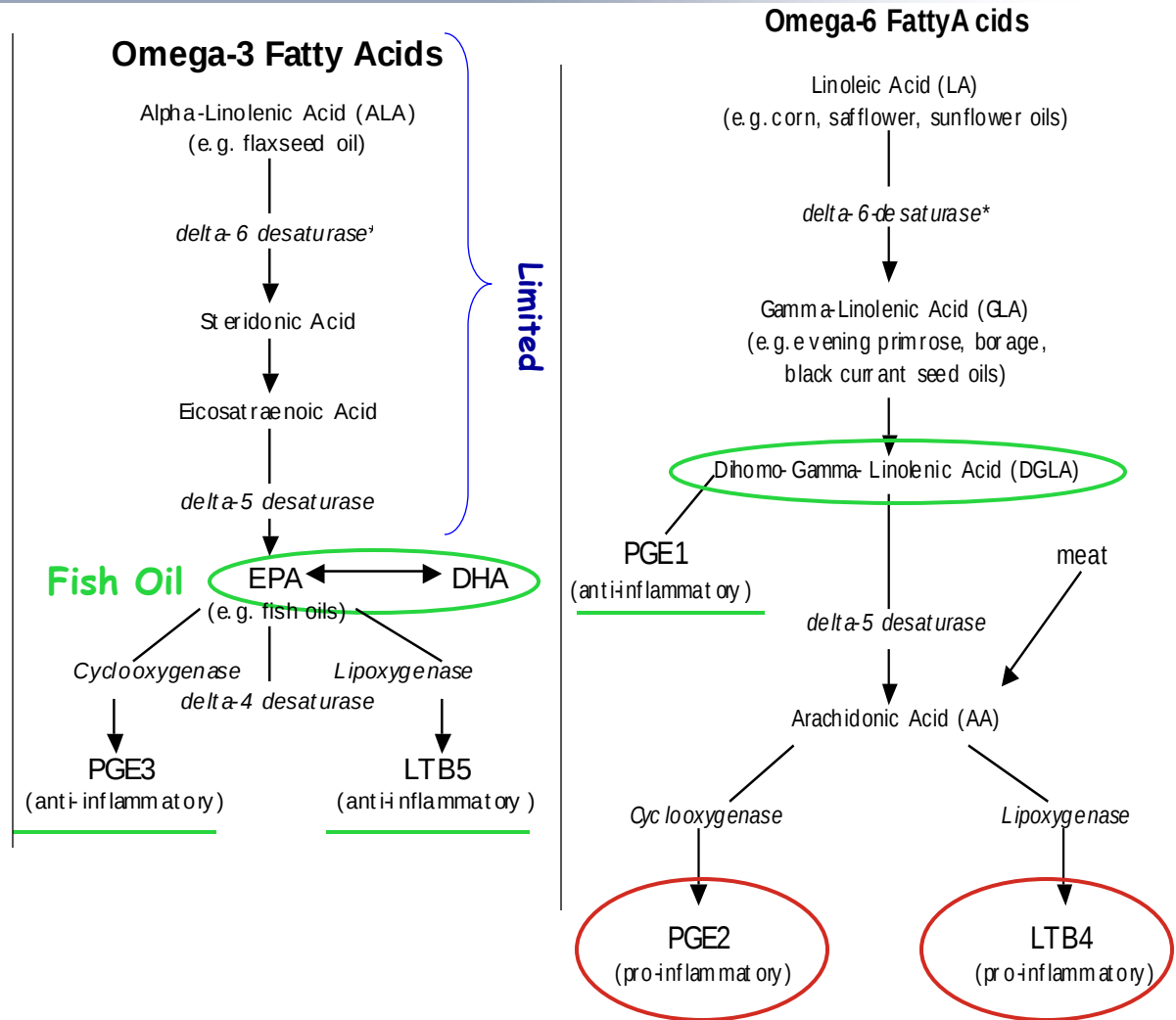
Hughes-Fulford M, Ca Res 2006

Hibbeln J, et al. Lipids, 2004



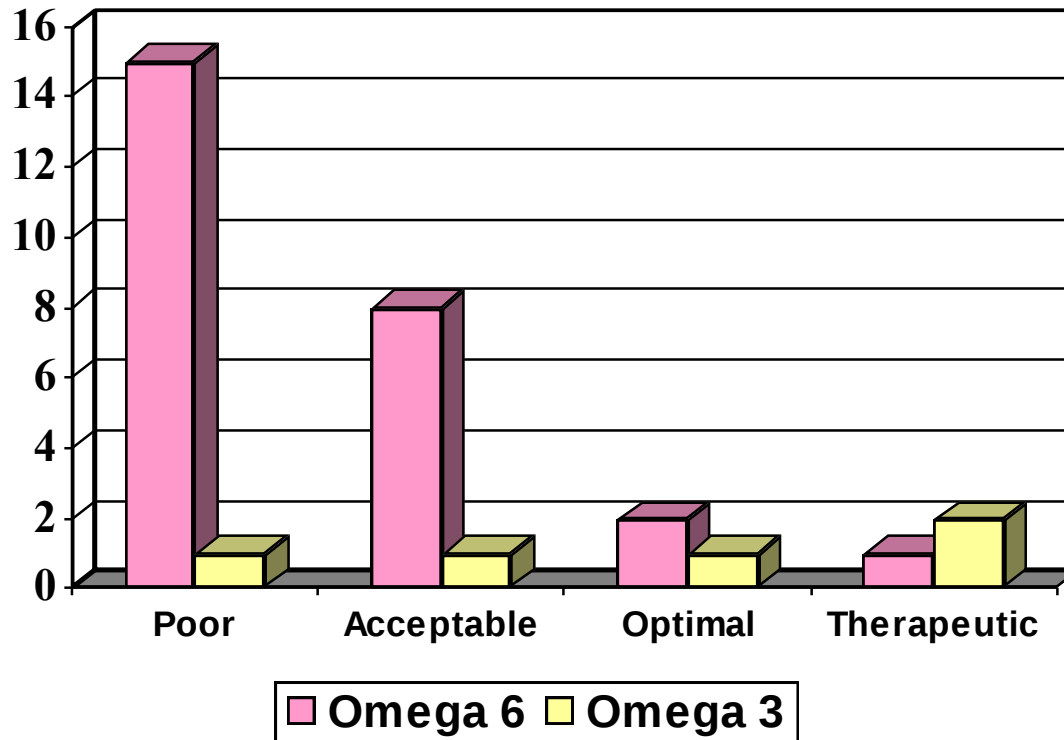
EFAs Influence Eicosanoid Production

- EFAs are precursors to eicosanoids, including prostaglandins (PG), thromboxanes (TX), and leukotrienes (LT)
- The ratio of omega-6 to omega-3 intake has increased from 3:1 to over 15:1 in the western world over the last century, dramatically increasing production of pro-inflammatory prostaglandins
- Omega-3s support the body's natural anti-inflammation response and inhibit Omega-6 (AA) conversion



A Key Issue in the Western World

Omega-6 intake is too high, Omega-3 intake is too low. This imbalance is not healthy.



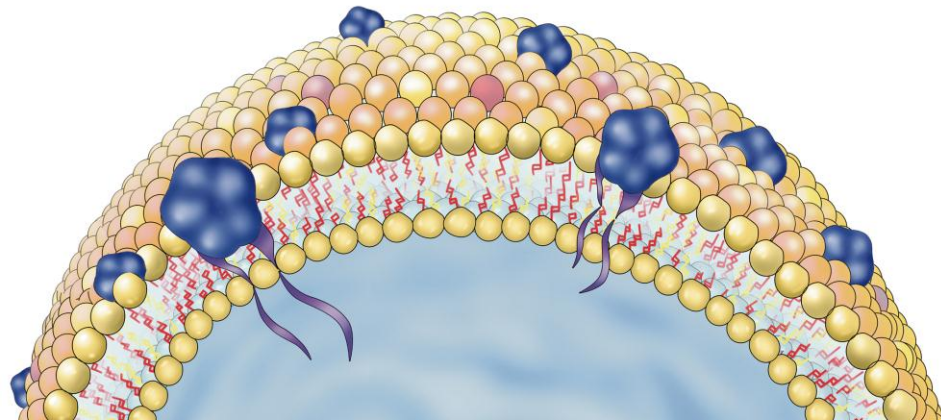
Recent studies have shown that up to 25% of Americans do not eat fish at all. Even fish lovers find it hard to regularly consume two servings of oily fish every week, as recommended by the *American Heart Association*¹ and the *United States Department of Agriculture*.

1. Kris-Etherton P, Harris W, Appel L, for the AHA Nutrition Committee. Omega-3 Fatty Acids and Cardiovascular Disease: New Recommendations from the American Heart Association. *Arterioscler Thromb Vasc Biol* 2004;23:151-152.

Diet High in Omega-3 Essential Fatty Acids



- ◆ Rich in omega-3 and GLA
- ◆ **EPA and DHA are precursors to immune molecules that promote a positive immune response and supports the body's natural anti-inflammatory response.**
- ◆ Omega-3 fatty acids from fish and fish oil are a direct source of EPA and DHA, **two essential fatty acids vital for proper cellular function.**

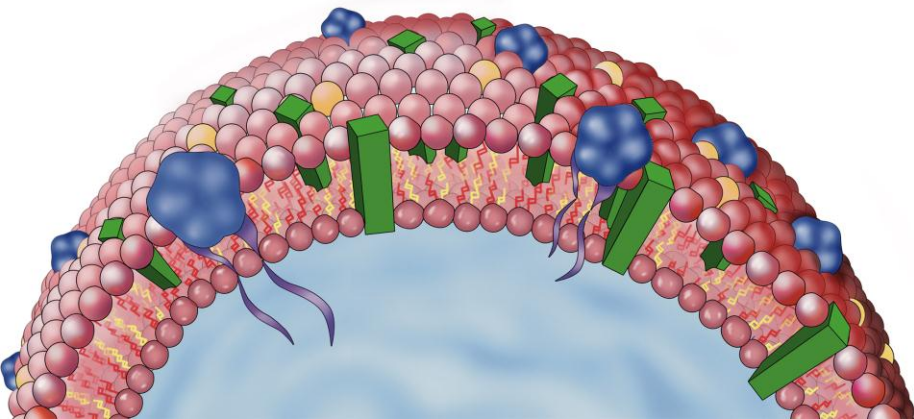


Diet High in Omega-6, Saturates, and Trans Fats



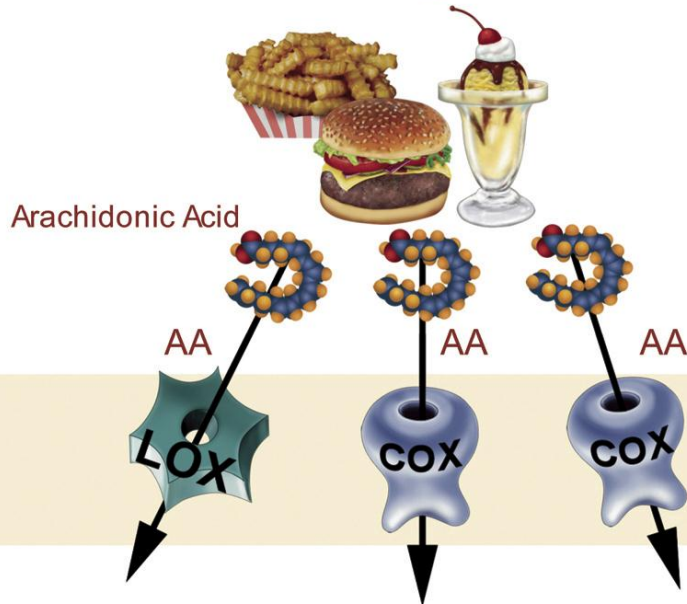
High in **Omega-6** – linoleic and arachidonic acid, as well as **saturated** fats and **trans** fatty acids

- ◆ Saturated fats and trans fatty acids result in stiffer, non-permeable cell membranes
- ◆ Stiff, non-permeable cell membranes reduce cell communication and limit adequate transport of nutrients into cells and metabolic waste out of cells
- ◆ Arachidonic acid is the precursor to pro-inflammatory eicosanoids



Cellular Structure Supported by EFAs

Omega-6



LTB-4

Leukotrienes-4 series

- Promotes inflammation
- Constricts airways
- Prolongs duration of inflammation

TXA-2

Thromboxane-A2

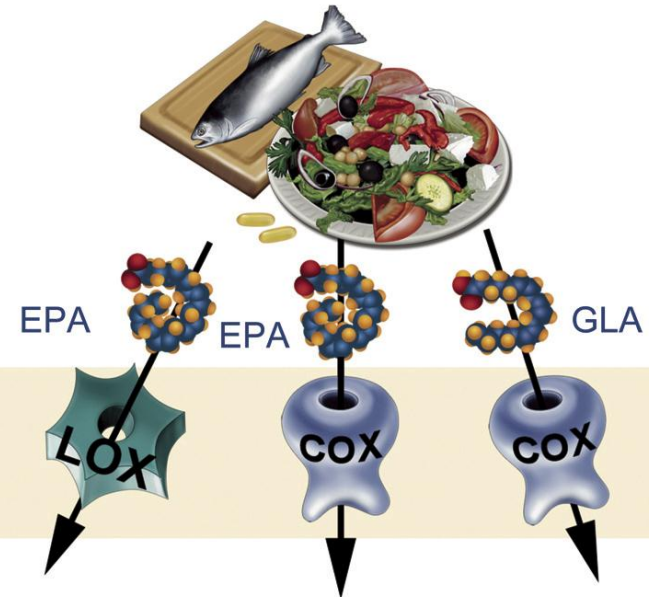
- Constricts blood vessels
- Constricts airways
- Increases blood clotting
- Reduces circulation

PGE-2

Prostaglandin-E2

- Increases sensitivity to pain
- Increases swelling
- Induces fever
- Constricts blood vessels

Omega-3 and GLA



LTB-5

Leukotriene-5 series

- Relaxes blood vessels
- Increases circulation
- Relaxes airways
- Promotes anti-inflammatory response

PGE-3

Prostaglandin-E3

- Improves circulation
- Decreases sensitivity to pain
- Relaxes blood vessels
- Promotes anti-inflammatory response

PGE-1

Prostaglandin-E1

- Relaxes muscles spasms
- Reduces blood clotting
- Increases protective stomach secretions
- Improves circulation

PROINFLAMMATORY

ANTI-INFLAMMATORY

Striking the Right Balance

- ◆ Similar metabolism of omega-3 and omega-6 fats causes **competition between them** for space within cell membranes
- ◆ Consuming too little omega-3 allows for an abundant production of omega-6 eicosanoids; this leads to inflexible, non-permeable cell membranes
- ◆ With a **high omega-6 to omega-3** ratio, the progression to compromised cell function begins
- ◆ Increasing intake of omega-3s can have significant health benefits



EPA & DHA work together

EPA and DHA **occur together** in foods, **work together** in the body, and **contribute** unique benefits

EPA (*eicosapentaenoic acid*)

- ◆ Heart
 - ◆ Supports healthy lipid levels
 - ◆ Maintains healthy blood vessels
 - ◆ Enhances overall cardiovascular function
- ◆ Joints
 - ◆ Supports joint flexibility and mobility
 - ◆ Supports the body's natural anti-inflammatory response
- ◆ Immune
 - ◆ Promotes healthy cell functioning
 - ◆ Supports healthy immune response
- ◆ Fitness
 - ◆ Supports healthy metabolism

DHA (*docosahexaenoic acid*)

- ◆ Brain
 - ◆ Supports health mood & behavior
 - ◆ Supports healthy nervous system
 - ◆ Enhances memory and focus
- ◆ Eyes
 - ◆ Supports healthy tissue moisture
 - ◆ Protects against age-related oxidative stress
- ◆ Mother and Child
 - ◆ Essential for brain and visual development
 - ◆ Promotes healthy birth weights
 - ◆ Supports healthy mood

GLA (*gamma linolenic acid*)

GLA is a beneficial Omega-6 found in borage and evening primrose oils

- ◆ Cellular health
 - ◆ Promotes healthy skin, hair, and nails
 - ◆ Supports hormonal balance
 - ◆ Supports healthy metabolism
- ◆ Immune
 - ◆ Supports healthy immune system function
- ◆ GLA and fish oil work well together



PROVEN BENEFITS
OF FISH OIL

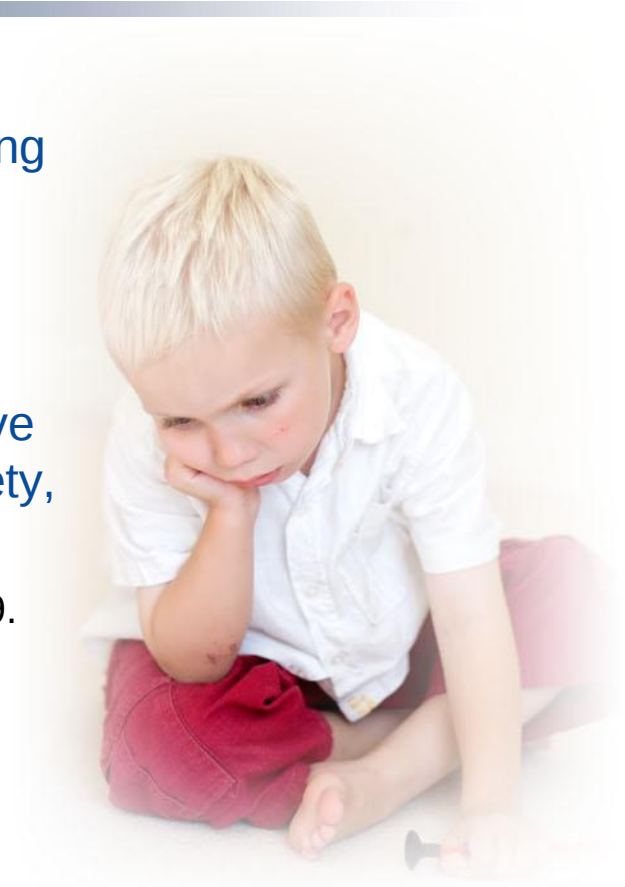
Omega-3 Benefits: Infant Development

- ◆ DHA is an essential fat for healthy infant development
 - ◆ DHA is necessary for normal development of visual, immune, brain, and nervous systems
 - ◆ DHA is the predominant fat in brain cell membranes
 - ◆ Research shows that omega-3 intake during infancy may promote health in adulthood
- ◆ Fetus depends on mother for Omega-3s
 - ◆ The developing fetus is completely dependent on mother for Omega-3 essential fatty acids
 - ◆ Fish oil supplementation improves Omega-3 levels
- ◆ The fetus is unable to make DHA from short chain fats (vegetable or flax)
 - ◆ Pre-formed DHA (fish oil) is the preferred and best-used form
 - ◆ Fish oil has an excellent safety profile
 - Holman, RT, et al, NAS, 1991
 - Salem, N, et al, ADA, 2004
 - Dunstan J, et al, EJCN, 2004



Fish Oil supports a child's future

- ◆ A Scandinavian study found that children born to mothers who had taken cod liver oil (2 tsp/day) during pregnancy and lactation had **higher IQs** than those born to mothers who had taken the corn oil placebo
Pediatrics 2003;111:39-44.
- ◆ Lower brain DHA levels are associated with cognitive deficits and increased behavioral indicators of anxiety, aggression, and depression in children
Prostaglandins Leukot Essent Fatty Acids 2006;75:329–349.



Omega-3 Benefits: Maternal Health

- ◆ Babies benefit when mom takes cod liver oil during pregnancy
 - ◆ Supports healthy delivery
 - ◆ May result in improved achievement test scores
- ◆ Moms benefit before & after delivery
 - ◆ The demand for DHA increases during pregnancy
 - ◆ *Mom's reserves will remain low up to one year after delivery without supplementation*
 - ◆ Supports mom's moods after delivery
 - ◆ In the US, women bearing children have the 3rd lowest level of DHA in the world

Helland, IB, et al. Peds, 2001

Lauritzen, L, et al. Ped Res, 2005

Olafsdottir AS, et al. BJOG, 2005

Helland, IB et al. Peds, 2003

Carlson SE, Bethesda, MD 2004



Are expecting mothers getting enough DHA?

- ◆ National nutritional surveys have shown that the **average intake of DHA** during the last trimester of pregnancy is **between zero and 100 mg**
J Lipid Res Mar 2005;46:516–525.
- ◆ **90%** of women surveyed were **well below the minimum** recommendation of 300 mg daily
- ◆ Pregnant women in the United States reportedly have the **third lowest intake** of DHA in the world

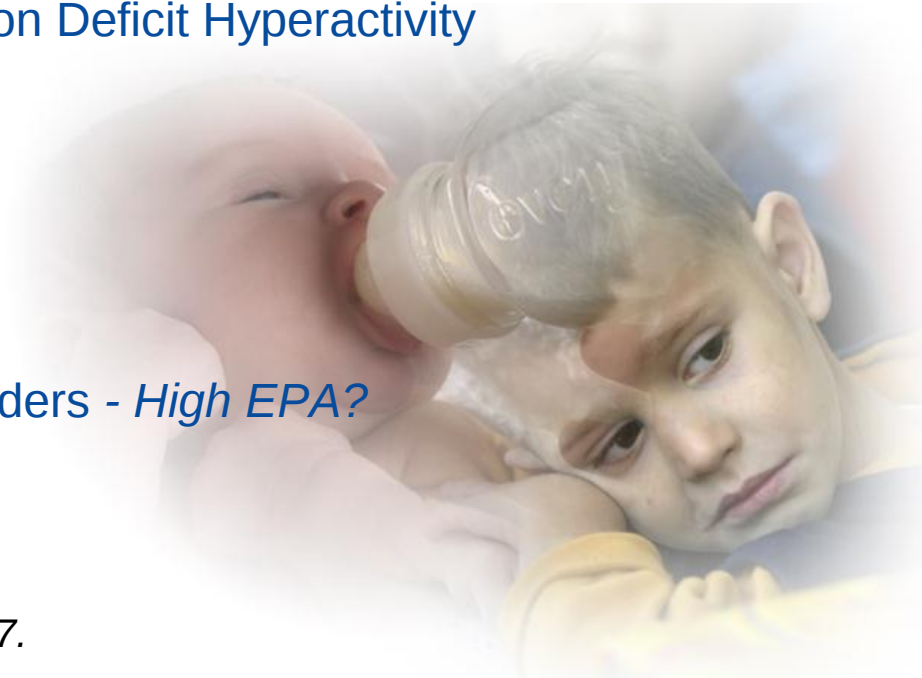
International Conference on Fatty Acids. Bethesda, MD;2004.



Omega-3 Deficiency

In children, a lack of omega-3 has been linked to such disorders as:

- ◆ Attention Deficit Disorder and Attention Deficit Hyperactivity Disorder- *High EPA?*
 - ◆ *Nutr Neurosci.* 2007;10(1-2):1-9.
- ◆ Childhood Depression - *High EPA?*
 - ◆ *Am J Psychiatry.* 2006;163:1098-100.
- ◆ Developmental and Educational disorders - *High EPA?*
 - ◆ *Pediatrics.* 2005;115:1360-6.
- ◆ Bipolar Disorder - *High EPA?*
 - ◆ *Eur Neuropsychopharmacol.* 2007;17:440-7.
- ◆ Autism- *EPA/DHA/GLA?*
 - ◆ *Biol Psychiatry.* 2007;61(4):551-3

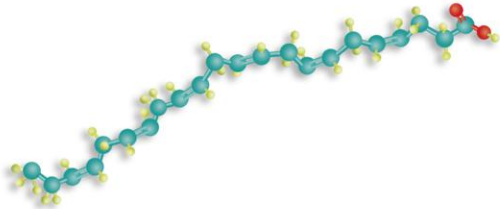


Omega-3 Recommendations

International experts have concluded that a healthy intake of EPA + DHA for children is approximately...

Pregnancy	300 mg DHA daily
Infants 1–18 months	32 mg/lb EPA+DHA
Children 1.5–15 yrs	15 mg/lb EPA+DHA

These are not therapeutic levels only to prevent deficiency



Therapeutic Levels of Omega-3

- ◆ Behavioral disorders

- ◆ ADHD, Depression, Bipolar, etc -
- ◆ 2 grams EPA

- ◆ Childhood Rheumatoid Arthritis

- ◆ 3 grams EPA + DHA to achieve anti-inflammatory response

- ◆ Metabolic Support -

- ◆ Overweight and Obese
- ◆ Blood Sugar
- ◆ Cardio
- ◆ 1 gram EPA + DHA

- ◆ Autism

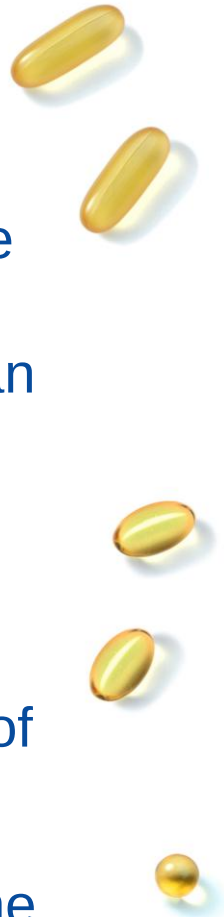
- ◆ Many differing opinions here
- ◆ 1 -2 tsp Complete Omega 369 liquid (1-2 grams EPA/DHA + 165 - 330 mg GLA)



Fish Oils and Atherosclerosis

[von Schacky, Clemens, et al. *Annals of Internal Medicine*, 1999;130: 554-562]

- ◆ A randomised, double-blind, placebo-controlled clinical trial involved 162 patients with confirmed atherosclerosis
- ◆ Half the patients were given 6g/day of fish oil for 3 months, the other half were given 6g/day of placebo capsules containing a fatty acid composition resembling that of the average European diet
- ◆ After 3 months the dosages were reduced to 3g/day for a further 21 months
- ◆ Angiograms were taken at the start of the trial and at the end of the 2-year study period
- ◆ At the end of the treatment, twice as many of the patients in the fish oil group (16) showed regression of their atherosclerotic deposits when compared to the placebo group



Fish Oils Can Regulate Heart Beat

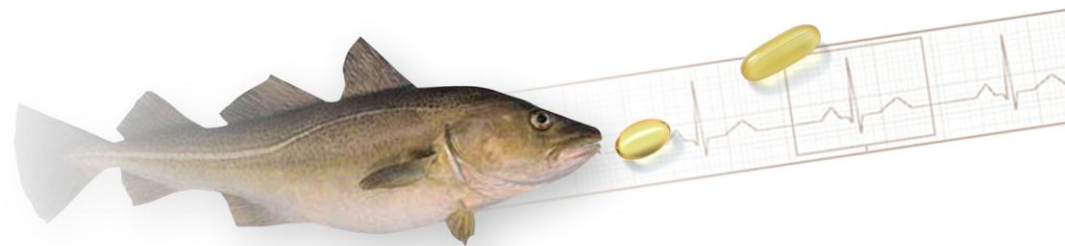
[Circulation, 2004. Prosto Leuko Ess Fatty Acids, 2004]

- ◆ 65 people with arrhythmia were randomly assigned to receive either 3g/day of fish oil (providing 1g of omega-3 fatty acids), or placebo, for 6 months
- ◆ Blood tests were then performed and heart rhythms were assessed during the 6-month trial and for 6 months after stopping the supplements
- ◆ Compared to the beginning of the study, people receiving fish oil had significantly fewer, and less severe, arrhythmia
- ◆ People taking fish oil had 46.9%, 67.8%, 71.8% and 100% fewer occurrences of the 4 types of arrhythmia monitored in the study, namely atrial premature complexes, ventricular premature complexes, couplets and triplets
- ◆ 6 months after the patients stopped taking the fish oil, these improvements were reversed and all measurements were similar to those from the beginning of the study
- ◆ People receiving the placebo experienced no significant changes in arrhythmia frequency during the study

Fish Oil Reduces Heart Disease Risk in Menopausal Women – HRT or Not

[Stark KD, Park EJ, Maines VA, Holub BJ. American Journal Clinical Nutrition 2000; 72(2):389-394]

- ◆ Effect of a fish oil concentrate on serum lipids in postmenopausal women receiving, and not receiving, hormone replacement therapy in a placebo-controlled, double-blind trial
- ◆ These results showed that supplementation with a fish-oil derived concentrate can favourably influence selected cardiovascular disease risk factors, particularly by achieving marked reductions in serum triacylglycerol concentrations and triacylglycerol/HDL cholesterol in postmenopausal women receiving, and not receiving, HRT (28% reduction)
- ◆ This approach could potentially reduce the risk of coronary heart disease by 27% in postmenopausal women



Heart - Fish Oil and Statin Meds in CHD

[Durrington P, Bhatnagar D, et al. *Heart* 2001; 85 (5):544-548]

- ◆ An omega-3 polyunsaturated fatty acid concentrate administered for 1 year decreased triglycerides in simvastatin-treated patients with coronary heart disease
- ◆ 59 patients with CHD receiving simvastatin 10-40mg daily with serum triglycerides > 2.3 mmol/l were randomised to receive Omacor 2g twice daily, or placebo, for 24 weeks in a double-blind trial
- ◆ 46 patients accepted the offer of active treatment for a further 24 weeks in an open phase of the trial
- ◆ There was a sustained significant decrease in serum triglycerides by 20-30% ($p < 0.005$) and in very low density lipoprotein (VLDL) cholesterol by 30-40% ($p < 0.005$) in patients receiving active Omacor at 3, 6 and 12 months compared to baseline or placebo
- ◆ Omacor did not have any deleterious effect on low density or high density lipoprotein cholesterol or on biochemical and haematological safety tests



Omega-3 Fatty Acids Improve Function in Nonischemic Heart-Failure Patients

Treatment with a high dose of n-3 PUFAs improved ejection fraction, peak VO₂, exercise duration, and mean NYHA functional class, as well as reduced hospitalizations for heart failure

Abstract

Vitamin K, an essential associated with the clotting the focus of consideration demonstrating an anticancer of this research has focused through vitamins K2 and K shown to have anticancer effect of vitamin K3 employed and explain the anticancer effect *vitro* and *in vivo* studies; however does not adequately address vitamins K1 and K2. Research demonstrated the anticancer K may act at the level of tyrosine phosphatases, modulating transcription factors such as Myc kinases associated with cyclins shown to be affected by vitamin led to cell cycle arrest and (Altern Med Rev 2003;8(2):26)

Introduction

After earlier research, vitamin K, phyloquinone, was isolated from plants in 1939 and used to treat a nutritional deficiency characterized by decreased prothrombin levels. Henrik Dam received the Nobel Prize in 1943 for his discovery of vitamin K (the "coagulation" vitamin). The role of vitamin K as a cofactor in normal blood coagulation stems from the post-translational modification of a number of plasma proteins such as factors II (prothrombin), VII, IX, X, as well as proteins C, S, and Z. Vita-

CONCLUSION: Both peak VO₂ and NYHA functional class appear to be favourably affected by the treatment. These benefits are consistent with the decrease of the mean furosemide dose needed to maintain a congestion-free clinical status observed in the n-3 PUFA group and may account for the lower number of cardiovascular hospitalizations for heart failure recorded during the 12-month follow-up period in these patients compared with those receiving placebo.

Davis W. Lamson, MS, ND - Coordinator of Oncology, Bastyr University, Kenmore, WA; Private practice, Tahoma Clinic, Renton, WA. Product consultant, Thorne Research. Correspondence address: 9803 17th Ave NE, Seattle, WA 98115
E-mail: davisl@seanet.com

Steve Plaza, ND, LAc - Faculty member of Oncology department, Bastyr University, Kenmore, WA; Private practice, Northwest Center for Natural Medicine, Olympia, WA.

Dr Savina Nodari, University of Brescia, Italy

Omega-3 Fatty Acids and CVD

- ◆ Reduction of arrhythmia susceptibility
- ◆ Antithrombotic
- ◆ Anti-inflammatory
- ◆ Antioxidant effects
- ◆ Improvement of endothelial function
- ◆ Delayed atherosclerosis development
 - ◆ Atherosclerosis. 2012 Jan 20.
 - ◆ Curr Vasc Pharmacol. 2012 Feb 20.

High Concentrate Fish Oil Benefits Individuals With Non-Surgical Back and Neck Pain, many are able to discontinue pain medication

[Maroon J, Bost J, Baugham J, Wert M. Department of Neurosurgery, University of Pittsburgh, Pittsburgh, PA. Presented at the American Association Neurological Surgeons annual meeting, New Orleans, LA]

- ◆ From March-June 2004 250 patients who had been seen by a neurosurgeon, and were found to have non-surgical neck or back pain, were asked to take a total of 1200mg of omega-3 essential fatty acids (EPA and DHA) found in fish oil
- ◆ A questionnaire was then forwarded to these patients approximately 1 month after taking the supplement
- ◆ Of the 250 patients, 125 returned the questionnaire, at an average of 75 days on fish oil
- ◆ 78% were taking the 1200mg and 22% 2400mg of EFAs
- ◆ 59% have since discontinued taking other prescription medications for pain, 60% stated their overall pain was improved and 60% stated specifically that their joint pain had improved
- ◆ 80% stated they were satisfied with their improvement and 88% stated they would continue to take the fish oil
- ◆ There were no significant side effects reported



Omega-3 Fatty Acids in Bipolar Disorder: a preliminary double-blind, placebo-controlled trial

[Andrew L, Stoll W, Severus E, et al. *Arch Gen Psychiatry* 1999; 56: 407-412]

- ◆ A 4-month, double-blind, placebo-controlled study comparing omega-3 fatty acids (9.6g/d) vs. placebo (olive oil) in addition to usual treatment, in 30 patients with bipolar disorder
- ◆ The omega-3 fatty acid patient group had a significantly longer period of remission than the placebo group
- ◆ In addition, for nearly every other outcome measure, the omega-3 fatty acid group performed better than the placebo group



Fish Oil May be Used to Combat Diabetes & Cancer

Are fish oil omega-3 long-chain fatty acids and their derivatives peroxisome proliferator-activated receptor agonists?

Abstract

Vitamin K₁, an essential associated with the clotting the focus of consider demonstrating an anticancer of this research has focused although vitamins K₂ and K₃ shown to have anticancer effect of vitamin K₃ employed and explain the anticancer effect *vitro* and *in vivo* studies; however does not adequately address vitamins K₁ and K₂. Recent demonstrated the anticancer K₁ may act at the level of tyrosine phosphatases, modulating transcription factors such as Myc kinases associated with cell cycle shown to be affected by vitamin lead to cell cycle arrest and (Altern Med Rev 2003;8(2):26)

Introduction

After earlier research, vitamin K₁, phyloquinone, was isolated from plants in 1939 and used to treat a nutritional deficiency characterized by decreased prothrombin levels. Henrik Dam received the Nobel Prize in 1943 for his discovery of vitamin K (the "coagulation" vitamin). The role of vitamin K as a cofactor in normal blood coagulation stems from the post-translational modification of a number of plasma proteins such as factors II (prothrombin), VII, IX, X, as well as proteins C, S, and Z. Vita-

CONCLUSION: Docosahexaenoic acid and eicosapentaenoic acid, which are the fatty acids abundant in fish oil, are traditionally used against metabolic diseases. These fatty acids act as PPAR agonists that transcribe the genes involved in glucose and lipid homeostasis.

Davis W. Lamson, MS, ND - Coordinator of Oncology, Bastyr University, Kenmore, WA; Private practice, Tahoma Clinic, Renton, WA. Product consultant, Thorne Research. Correspondence address: 9803 17th Ave NE, Seattle, WA 98115
E-mail: davisl@seanet.com

Steve Plaza, ND, LAc - Faculty member of Oncology department, Bastyr University, Kenmore, WA; Private practice, Northwest Center for Natural Medicine, Olympia, WA.

Cardiovasc Diabetol. 2008
Mar 20;7:6

EPA and DHA May Postpone Cognitive Decline in Elderly men

Fish consumption, n-3 fatty acids, and subsequent 5-y cognitive decline in elderly men: the Zutphen Elderly Study

Abstract

Vitamin K, an essential nutrient often associated with the clotting cascade, has been the focus of considerable research demonstrating an anticancer potential. Much of this research has focused on vitamin K₂ and K₁, although vitamin K₃ employed in *vitro* and *in vivo* studies; however, does not adequately address the role of vitamins K₁ and K₂. Research has demonstrated the anticancer potential of K₂ may act at the level of tyrosine phosphatases, modulating transcription factors such as Myc and Ras, which are associated with cell cycle arrest and apoptosis. (Altern Med Rev 2003;8(2):20)

Introduction

After earlier research on vitamin K, phyloquinone, was isolated from plants in 1939 and used to treat a nutritional deficiency characterized by decreased prothrombin levels. Henrik Dam received the Nobel Prize in 1943 for his discovery of vitamin K (the "coagulation" vitamin). The role of vitamin K as a cofactor in normal blood coagulation stems from the post-translational modification of a number of plasma proteins such as factors II (prothrombin), VII, IX, X, as well as proteins C, S, and Z. Vita-

min K, in its reduced hydroquinone form, acts as a cofactor in the enzymatic carboxylation of gamma-glutamyl-carboxylase of glutamic acid residues forming gamma-carboxyglutamic acid in plasma proteins. In the process of carboxylation,

CONCLUSION: Fish consumers had significantly (P = 0.01) less 5-y subsequent cognitive decline than did nonconsumers. A linear trend was observed for the relation between the intake of EPA+DHA and cognitive decline.

Davis W. Lamson, MS, ND - Coordinator of Oncology, Bastyr University, Kenmore, WA; Private practice, Tahoma Clinic, Renton, WA. Product consultant, Thorne Research. Correspondence address: 9803 17th Ave NE, Seattle, WA 98115. E-mail: davisl@seanet.com

Steve Plaza, ND, LAc - Faculty member of Oncology department, Bastyr University, Kenmore, WA; Private practice, Northwest Center for Natural Medicine, Olympia, WA.

van Gelder B, Tijhuis M, Kalmijn Journal of Clinical Nutrition 2007

High Fish Intake Associated With Better Cognitive Performance In Elderly

Cognitive performance among the elderly and dietary fish intake: the Hordaland Health Study

Abstract

Vitamin K, an essential nutrient often associated with the clotting cascade, has been the focus of considerable research

demonstrating an anticancer effect. The focus of this research has focused on vitamin K₂ and K₁, although vitamins K₂ and K₁ have been shown to have anticancer effects. Vitamin K₃ employed in this study to explain the anticancer effect in *vitro* and *in vivo* studies; however, it does not adequately address the role of vitamins K₁ and K₂. Research has demonstrated the anticancer effect of K₃ may act at the level of tyrosine phosphatases, modulating transcription factors such as Myc and c-Jun, which are associated with cell cycle arrest and apoptosis. (Altern Med Rev 2003;8(2):20)

Introduction

After earlier research, vitamin K, phylloquinone, was isolated from plants in 1939 and used to treat a nutritional deficiency characterized by decreased prothrombin levels. Henrik Dam received the Nobel Prize in 1943 for his discovery of vitamin K (the "coagulation" vitamin). The role of vitamin K as a cofactor in normal blood coagulation stems from the post-translational modification of a number of plasma proteins such as factors II (prothrombin), VII, IX, X, as well as proteins C, S, and Z. Vita-

min K, in its reduced hydroquinone form, acts as a cofactor in the enzymatic carboxylation by gamma-glutamyl-carboxylase of glutamic acid residues forming gamma-carboxyglutamic acid in

CONCLUSION: In the elderly, a diet high in fish and fish products is associated with better cognitive performance in a dose-dependent manner.

Davis W. Lamson, MS, ND - Coordinator of Oncology, Bastyr University, Kenmore, WA; Private practice, Tahoma Clinic, Renton, WA. Product consultant, Thorne Research. Correspondence address: 9803 17th Ave NE, Seattle, WA 98115
E-mail: davisl@seanet.com

Steve Plaza, ND, LAc - Faculty member of Oncology department, Bastyr University, Kenmore, WA; Private practice, Northwest Center for Natural Medicine, Olympia, WA.

Nurk E, Dreven C, Refsum H, American Journal of Clinical Nutrition 2007

Omega-3 Fatty Acids and the Rate of Telomere Shortening

Association of Marine Omega-3 Fatty Acid Levels with Telomeric Aging in Patients With Coronary Heart Disease

Ramin Farzaneh-Far, MD

Jue Lin, PhD

Elissa S. Epel, PhD

William S. Harris, PhD

Elizabeth H. Blackburn, PhD

Mary A. Whooley, MD

MULTIPLE EPIDEMIOLOGIC studies, including several large randomized controlled trials, have demonstrated higher survival rates among individuals with high dietary intake of marine omega-3 fatty acids and established cardiovascular disease.¹⁻⁴ On this basis, the American Heart Association recommends increased oily fish intake and the use of omega-3 fatty acid supplements for the primary and secondary prevention of coronary heart disease. The mechanisms underlying the protective effect are poorly understood but are thought to include anti-inflammatory, antiplatelet, antihypertensive, antiarrhythmic, and triglyceride-lowering effects.⁶ There is ongoing interest in the identification of novel mechanisms of cardiovascular benefit from omega-3 fatty acids.

Telomeres are tandem repeat DNA sequences (TTAGGG)_n that form a protective cap at the ends of eukaryotic chromosomes.⁷ During somatic cell division, DNA polymerase cannot fully replicate the 3' end of linear DNA, resulting in an obligate and progressive

Context Increased dietary intake of marine omega-3 fatty acids is associated with prolonged survival in patients with coronary heart disease. However, the mechanisms underlying this protective effect are poorly understood.

Objective To investigate the association of omega-3 fatty acid blood levels with temporal changes in telomere length, an emerging marker of biological age.

Design, Setting, and Participants Prospective cohort study of 608 ambulatory outpatients in California with stable coronary artery disease recruited from the Heart and Soul Study between September 2000 and December 2002 and followed up to January 2009 (median, 6.0 years; range, 5.0-8.1 years).

Main Outcome Measures We measured leukocyte telomere length at baseline and again after 5 years of follow-up. Multivariable linear and logistic regression models were used to investigate the association of baseline levels of omega-3 fatty acids (docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) with subsequent change in telomere length.

CONCLUSION: Among this cohort of patients with coronary artery disease, there was an inverse relationship between baseline blood levels of marine omega-3 fatty acids and the rate of telomere shortening over 5 years.

loss of telomere length emerging as a novel marker of biological age, which integrates the cumulative lifetime burden of genetic factors and environmental stressors independent of chronological age.⁹ Moreover, a robust association between short telo-

psychiatry (Dr Epel), and Epidemiology and Biostatistics (Dr Whooley), University of California, San Francisco, and Veterans Affairs Medical Center (Dr Whooley), San Francisco; and Sanford Research/USD and Sanford School of Medicine, University of South Dakota, Sioux Falls (Dr Harris).

Corresponding Author: Ramin Farzaneh-Far, MD, Division of Cardiology, Room 5G1, San Francisco General Hospital, 1001 Potrero Ave, San Francisco, CA 94110 (rfarzanehfar@medicine.ucsf.edu).

Ramin Farzaneh-Far, MD

Jue Lin, PhD

Elissa S. Epel, PhD

William S. Harris, PhD

Elizabeth H. Blackburn, PhD

Mary A. Whooley, MD

Fish Oil May Help You Live Longer

Life span is prolonged in food-restricted autoimmune-prone (NZB x NZW)F(1) mice fed a diet enriched with (n-3) fatty acids.

Abstract

Vitamin K₂, an essential nutrient, is associated with the clotting cascade. The focus of this research has been on demonstrating an anticancer effect of this research has focused on although vitamins K₂ and K₁ shown to have anticancer effects of vitamin K₂ employed and explain the anticancer effect *in vitro* and *in vivo* studies; however, does not adequately address vitamins K₁ and K₂. Research demonstrated the anticancer effect of K₂ may act at the level of tyrosine phosphatases, modulating transcription factors such as Myc and kinases associated with cell cycle shown to be affected by vitamin K₂ lead to cell cycle arrest and (Altern Med Rev 2003;8(2):20)

Introduction

After earlier research, vitamin K₂, phyloquinone, was isolated from plants in 1939 and used to treat a nutritional deficiency characterized by decreased prothrombin levels. Henrik Dam received the Nobel Prize in 1943 for his discovery of vitamin K (the "coagulation" vitamin). The role of vitamin K as a cofactor in normal blood coagulation stems from the post-translational modification of a number of plasma proteins such as factors II (prothrombin), VII, IX, X, as well as proteins C, S, and Z. Vita-

CONCLUSION: The profound additive effects of food restriction and (n-3) fatty acids in prolonging life span in B/W mice. These observations may have additional implications in the management of obesity, diabetes, cancer and/or the aging process.

Davis W. Lamson, MS, ND - Coordinator of Oncology, Bastyr University, Kenmore, WA; Private practice, Tahoma Clinic, Renton, WA. Product consultant, Thorne Research. Correspondence address: 9803 17th Ave NE, Seattle, WA 98115
E-mail: davis@seanet.com

Steve Plaza, ND, LAc - Faculty member of Oncology department, Bastyr University, Kenmore, WA; Private practice, Northwest Center for Natural Medicine, Olympia, WA.

Muthukumar A, Avula CP, Nutr., 2001;131(10):2753-2760.

Fish Oil Freshness – A Critical Issue

- ◆ Fish oil exposed to any light, heat, or oxygen is subject to oxidative rancidity.
- ◆ EPA and DHA are long chain fatty acids, which have many double bonds in the chain.
- ◆ Everywhere there is a double bond, there is good opportunity for oxidation and rancidity.



Montine KS, *Chem Phys Lipids* 2004

Milatovic D J, *Chromatogr B Analyt Technol Biomed Life Sci* 2005

THE ART OF FISH OIL PROCESSING

OIL EXTRACTION

Boiling and Pressing



Raw
Fish Oil

PURIFICATION

Stripping

Removal of over 210 potential impurities to meet strict European Pharmacopoeia guidelines



Purified
Fish Oil

IMPURITIES

Note:
EVERY fish oil manufacturer needs to go through a stripping process to extract impurities and meet guidelines for purity. As this process requires heat from 200–300° C, technical expertise and the complete absence of oxygen are crucial.

KEY TO QUALITY

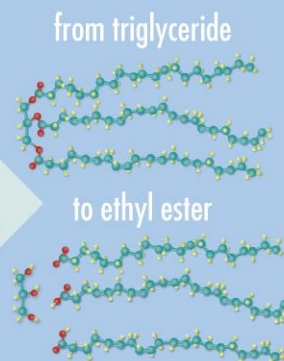
- Fresh Raw material
- Small fish—high in omega-3s with sustainable, short reproductive cycles
- Minimize heat
- Oxygen-free environment to eliminate oxidation

KEY TO QUALITY

- Technological proficiency
- Minimize heat
- Maximize vacuum
- Oxygen-free environment to eliminate oxidation
- Removal of minerals and trace elements (iron, copper, etc.)

MEDIUM CONCENTRATION

Cleaving off fatty acids—binding them to alcohol to allow for EPA+DHA concentration to ~50%



TECHNOLOGIES

- Molecular distillation—molecularly selecting EPA+DHA fatty acids
- Cool-down fractionation—freezing to remove short-chain crystallized molecules. Limitation: concentration level and waste
- Enzymatic processing—segregation of longer carbon chains (EPA+DHA)

KEY TO QUALITY

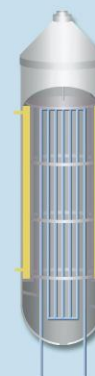
- Minimize heat
- Oxygen-free environment
- Technological expertise

HIGH CONCENTRATION

Further concentration of fish oil to yield EPA+DHA concentration over 90%

TECHNOLOGIES

- Molecular concentration
- Enzymatic processing
- CO2 processing



WHICH TECHNOLOGY IS PREFERRED?

As each technology can produce both low and high quality oil, third-party product analysis focusing on freshness and purity is the ultimate documentation when choosing a superior product.

Ask your supplier for lab analysis.

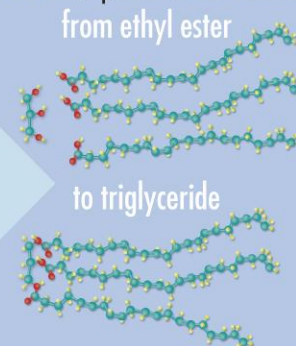
KEY TO QUALITY

- Overall processing control
- Technological expertise

MEDIUM/HIGH CONCENTRATION TRIGLYCERIDES

Added Step

Fatty acids are reattached to glycerol backbone forming a natural triglyceride dominated by EPA+DHA in the center position of the molecule.



98% of fats found in nature and consumed by humans are in natural triglyceride form.

HIGH QUALITY FISH OIL

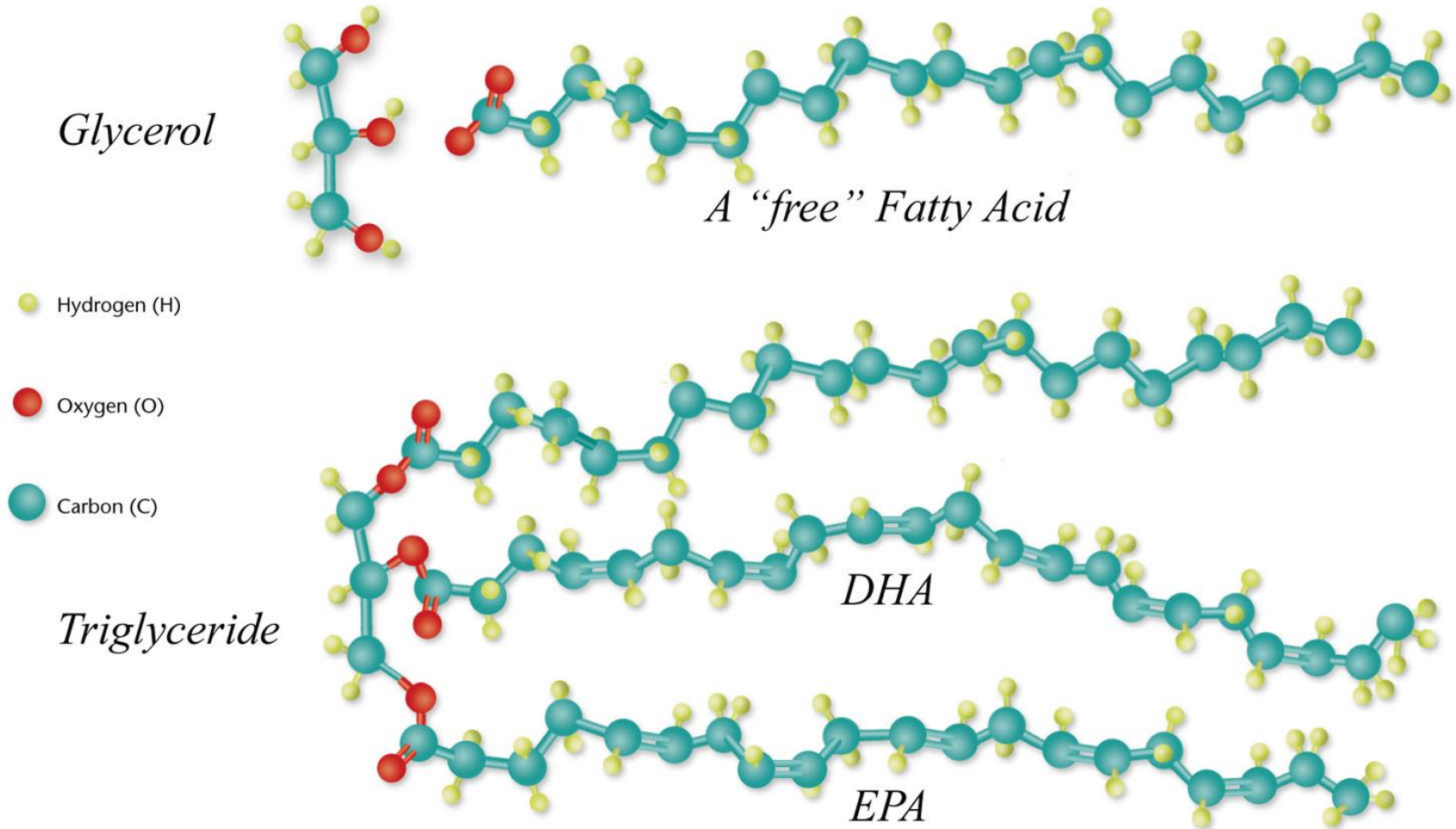
- Uses high quality raw materials
- Has exceptional purity values documented by third party
- Has NO fishy taste or odor

KEY TO QUALITY

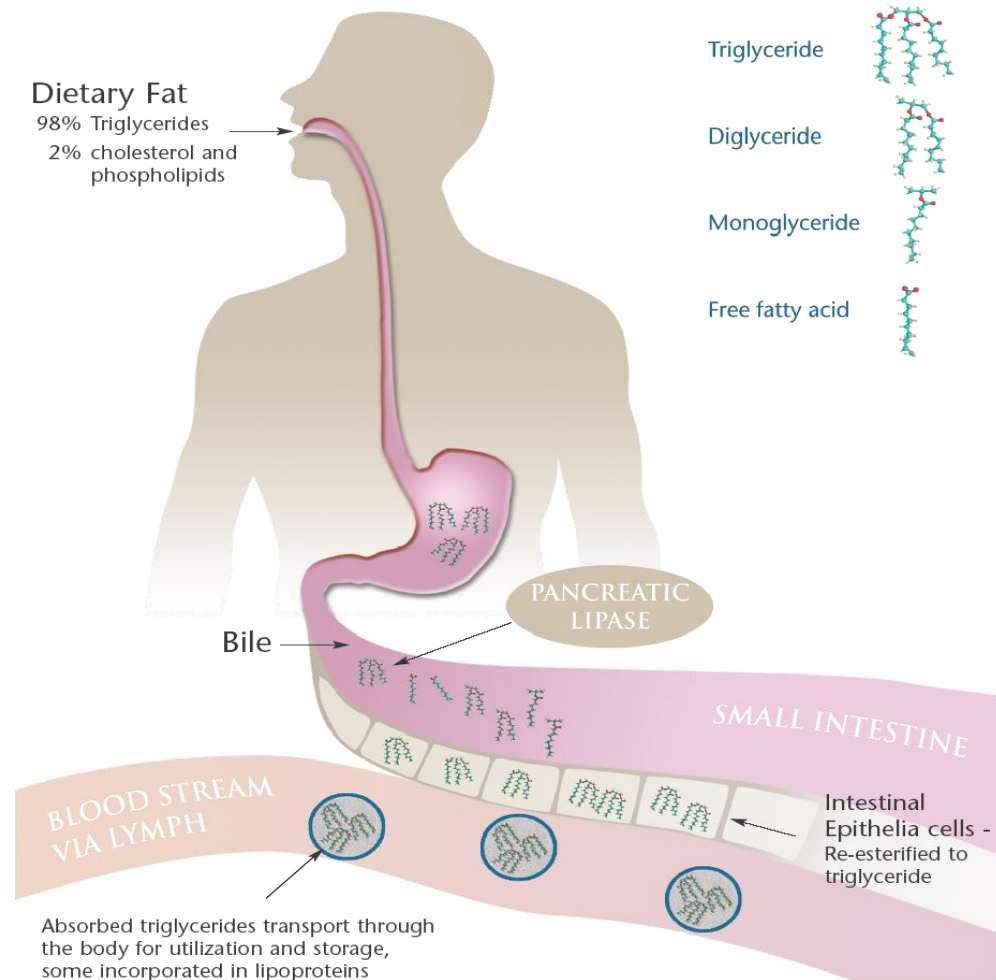
- Technological expertise
- Dedication to quality
- 98% conversion to true triglycerides



Omega-3s - Triglycerides are the preferred form



Absorption – designed to digest triglycerides



Not All Fish Oils are Created Equal

Choose a fish oil based on:

- ◆ **Purity = Safety**

Purity of a fish oil protects you from potentially harmful toxins such as mercury, lead, dioxins, PCB's and other environmental contaminants

- ◆ **Freshness = Efficacy**

Oxidative rancidity occurs when the double bonds of a fatty acid react with oxygen. A nitrogen processing environment ensures that exposure to oxygen is avoided. In fact, consumption of oxidised fatty acids may cause free radical damage

- ◆ **Taste = Compliance**

High quality fish oils have a clean, fresh taste. On a comparative tasting with a lower quality fish oil, one can taste the difference

- ◆ **Triglyceride form = Better Absorption**

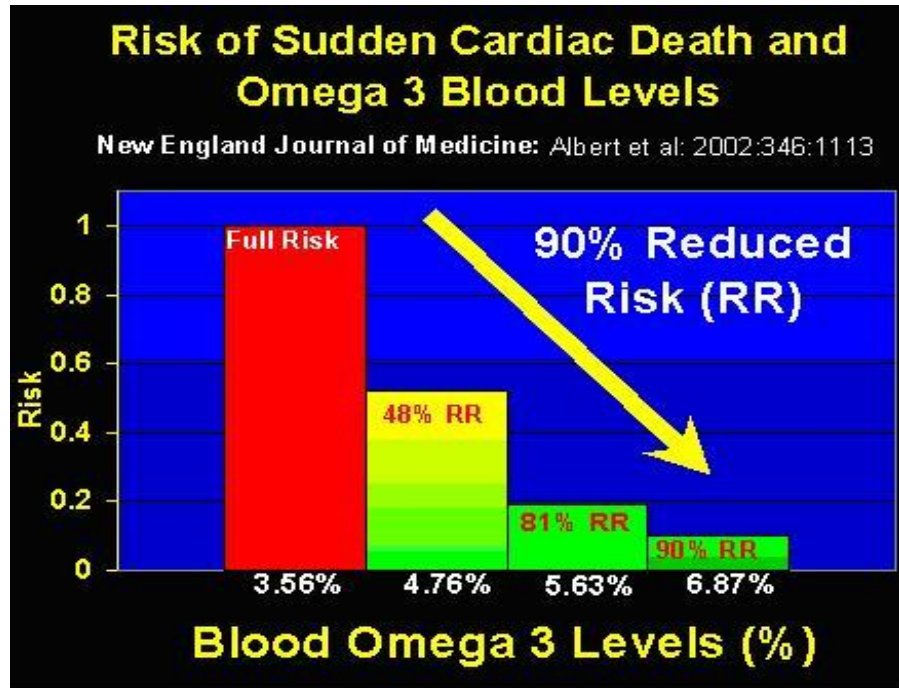
Bioavailability of triglyceride form has proven to be 70% higher than the ethyl ester form

- ◆ **Third Party Analysis = Proof**

This is the only objective proof. Check third party results on Purity, Freshness and Concentration levels.

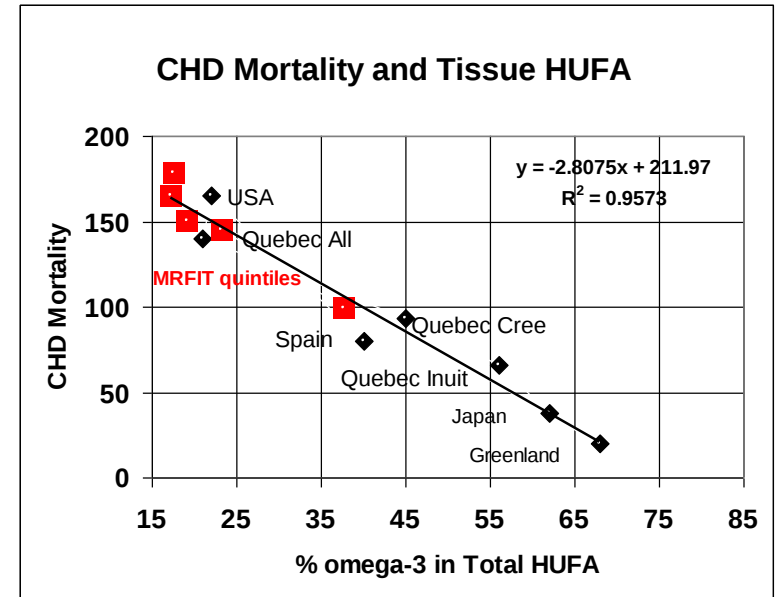
Omega 3 Index

- ◆ The combined value of two omega 3 fatty acids (EPA and DHA) The work of Siscovick and Albert summarised that increasing omega 3 blood values from 3.58% to 6.76% is correlated with a 90% reduction in risk of sudden death.



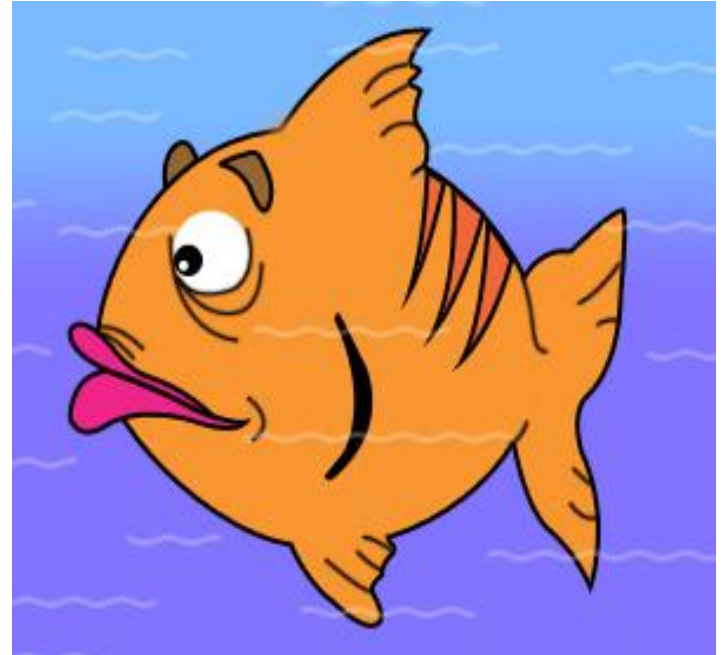
The Holman Omega 3 Test

- ◆ Based on a blood spot sample, you can get for your patient:
- ◆ **Total Omega 3 Score** – in certain populations such as the Japanese who consume large amount of marine based foods, the total omega 3 score is typically over 15%
- ◆ **% Omega 3 in HUFA** – a higher score has a direct correlation to reduction of mortality from heart disease



**“I SWEAR TO GOD,
WHEN I EVOLVE I’M
GOING TO KILL YOU
ALL.”**

- MAGIKARP



Website Dedicated to Fish Oil Research

www.omega-research.com

- ◆ Research abstracts
- ◆ Published reviews
- ◆ News
- ◆ Easy to navigate
- ◆ Free
- ◆ Great resource for professionals and consumers

