Reversal of Neurological Damage And Acute Metabolic Irregularities Using A Modified Medical Enteral Nutritional:

Implications for the Development of Medical Enteral Nutritionals to Enhance Recovery From Stroke, and Prevent HAI & C- Difficile, Thromboembolism, Arrhythmia, Hyperglycemia, and Generalized Inflammation

Sam Bock, Director of Research, Paragon Technologies
Cyrus Kuhzarani, R.Phm., B.Sc.Phm., Paragon Technologies

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Abstract

Purpose — To investigate whether nutritional imbalances in widely used medical enteral nutritional products are:

- increasing platelet aggregation and potential for thrombosis, embolism, cardiac infarct, and/or stroke,
- increasing inflammation and the potential for infection, and from that, the secondary development of anti-biotic induced C-difficile,
- inhibiting normal cellular metabolism, increasing potential for arrhythmia & other metabolic abnormalities,
- reducing cellular regeneration and healing,

and, whether improved enteral formulas might:

- prevent and reverse such problems, significantly enhancing patient recovery,
- be used to as agents to target specific disease states,
- reduce hospitalization times, subsequent procedures, and overall health care expenditures.

Background — Peer reviewed research published in November 2005 (see below) clearly shows that specific nutrients modulate specific aspects of genetic expression, which in turn regulate cellular regeneration, platelet aggregation and other critical bodily functions. (Paragon’s in-house research came to the same conclusion in 2004 using different methods.)

Millions of in-patients & out-patients, including infants, who are deemed unable to ingest whole foods are being fed similar types of medical enteral nutritionals, whether through tube-feeding, or other commercially available medical preparations. These formulas typically contain high levels of rapidly digestible refined carbohydrate, an excess of Omega 6 fatty acids relative to Omega 3, and incomplete blends of amino acids, minerals, vitamins and other co-factors. These formulas do not take into account more recent well-established peer-reviewed research regarding health complications associated with nutrient imbalances. Currently there are no widely available commercial substitutes for these formulas.

Methods — In this case study we clinically monitored one stroke patient and his metabolic reactions to various nutrient imbalances in a common medical enteral formula he ingested as treatment while at the McGill University Health Centre in Montreal.

We then used data from peer reviewed research (investigating metabolic reactions to various nutrient balances) to modify the medical enteral formula, thereby achieving nutritional balance according to the most current research. The modified enteral formula was then given to the patient and clinical observations were continued at both the McGill University Health Centre and at the Lindsay Centre for Rehabilitation in Montreal.

Results — The patient’s status remained unchanged for the first 26 days of treatment with the poorly balanced enteral formula, with little to no recovery of various cognitive and motor functions lost due to the stroke. As the patient’s attending neurologists had seen no recovery of any lost neurological function 5 days subsequent to the stroke, and since the situation was only slightly better on Day 16 when he was further assessed by the neurological team, the patient’s prognosis was for partial loss of the function in the right arm, complete loss of lower right side
limb function, inability to initiate thought, and altered personality. In summary – the patient’s condition was not expected to improve, as at least some minor recovery is expected in the first two weeks if there is to be further recovery later.

In addition, other specific metabolic functions in the patient rapidly deteriorated over the first 26 days, as research findings indicated they might. The serious reactions observed corresponded directly with the findings related to specific nutrient imbalances noted in prior research.

This indicated the poorly balanced enteral formula contributed significantly to the patient’s suffering hyperglycemia, atrial arrhythmia, pneumonia, 3 life-threatening pulmonary embolisms, and most serious, the contraction of colitis due to an intestinal overgrowth of Clostridium difficile (after the patient was given anti-biotics for treatment of the pneumonia.)

On Day 27, once proper nutritional balances were restored with modifications to the medical enteral formula, the patient’s metabolic abnormalities began to quickly re-normalize, further indicating the original formula contributed to many of the serious health problems the patient initially developed while at the hospital.

Moreover, after Day 27, the patient began an unexpected and significant recovery of the cognitive and motor function lost after the stroke. On Day 131 the patient walked his first steps with no assistance. (Update October 15, 2007: On day 278, unassisted the patient squat lifted 150 lbs of free weight on an Olympic bar across his back, and did 5 pull-ups. A few months later he did 11 pull-ups.)

In addition, the patient’s cholesterol levels completely normalized after being extremely elevated for more than 15 years.

Conclusions— This case study, and the clinical research cited, indicates:
- this, and other commonly used, enteral formulas in widespread use around the world, are contributing to health problems in thousands, if not millions, of patients using such formulas as a sole or partial source of nutrition,
- improved medical enteral formulas will save lives; dramatically enhance patient recoveries; and significantly reduce subsequent procedures, hospital durations, and overall health care costs.

Moreover, the patient’s subsequent and unexpected:
- recovery from serious brain injury
- normalization of highly abnormal cholesterol metabolism
indicates that enteral formulas can be developed as agents to counter specific disease states.

The evidence collected indicates significantly improved medical enteral nutritionals can be quickly developed and inexpensively tested, and that their use will:
- decrease potential for platelet aggregation and thrombosis leading to embolism, cardiac infarct, and stroke
- reduce inflammation, and possibly the development of primary infection, and the secondary development of anti-biotic induced C-difficile
- decrease potential for arrhythmia & other metabolic abnormalities
- enhance potential for overall cellular regeneration
- enhance potential for cerebral cellular regeneration and recovery in stroke patients
- target specific disease states.
Summary of Clinical Observations and Related Peer-Reviewed Research

Brief Patient History - Pre-op: Prior to admission to hospital for heart by-pass surgery for myocardial ischemia, the patient, 75, was a busy full time executive, used no medications (other than one baby aspirin/day), exercised regularly, weighed 150 lbs at 5’11”, was not diabetic, had low-normal blood pressure, had no prior history of arrhythmia or thrombosis, and showed no symptoms of cardiac related discomfort, other than shortness of breath in recent months when exercising.

Post Op History and Clinical Observations: About 36 hours subsequent to the heart bypass operation the patient suffered a left-side anterior cerebral artery infarction that was thought to be either caused by dislodged coronary plaque, or a clot that may have formed in the heart/lung machine.

While most of the right side was affected, the patient’s face and neck were not. While he appeared capable of swallowing, due to a lack of readily available hospital equipment, the patient could not be scheduled for a barium swallow for four days. As such, he was put on the Ross Nutritional OSMOLITE 1 CAL via NG tube. Within days problems began to occur as described below.

The Ross Nutritional OSMOLITE 1 CAL (“Osmolite”) is similar in make up to many other commercially available medical nutritional. Such formulas typically contain high levels of rapidly digestible refined carbohydrate, an excess of Omega 6 fatty acids relative to Omega 3, and unbalanced ratios of amino acids, minerals, vitamins and other co-factors. These formulas do not take into account more recent well-established peer-reviewed research regarding health complications associated with nutrient imbalance. Osmolite was the subject of this study because it is the formula most commonly used in the cardiac intensive care unit at the McGill University Health Centre in Montreal where this study was conducted.

The clinical observations and related peer-reviewed research discussed below indicate 3 primary manners in which Osmolite, or any other similar medical formula, may compromise the health of patients using such medical enteral formulas.

1) Potential for Osmolite, and similar formulations, to enhance inflammation, the development of primary infection, and the secondary development of C-difficile:

As discussed in detail below, we believe the overly high levels of rapidly digesting carbohydrate in combination with the Omega 6 / Omega 3 fatty acid imbalance in the Osmolite led to the:

- patient’s hyperglycemia and pro inflammatory state
- subsequent development of a primary bacterial infection,
- subsequent administration of antibiotics,
- subsequent development of Clostridium difficile.

It’s well established that the development of Clostridium difficile infection often follows the administration of antibiotics for an earlier primary infection, particularly in hospitals. 3 4 5

If the hypothesis outlined below proves correct, and inflammation & primary infections requiring antibiotic treatment can be prevented, the potential for developing secondary C difficile infections in hospitals would be dramatically reduced. As the potential causative factors (excess simple
sugar and fatty acid imbalances) can easily be eliminated from a hospital patient’s diet, this hypothesis can be quickly and inexpensively verified, or discarded.

The reasons why Osmolite, or a similar formula, might cause inflammation or infection follow below.

- 54% of the calories in the Osmolite formula are from maltodextrin, a source of sugar that digests as rapidly as glucose. The World Health Organization recommends that no more than 10 percent of daily total calories be derived from simple sugars.

The patient was not diabetic. However, when fed the Osmolite the patient immediately required regular injections of insulin to lower elevated blood sugar levels.

Excess glucose in the blood accelerates glycation, a well known contributor to degeneration and aging. Glycation reduces or destroys the function of many enzymes. Glycation occurs when glucose binds to and chemically alters proteins, lipids and other molecules. These damaged molecules are called advanced glycation end products (AGEs).

Many of the long-term complications of diabetes (e.g., blindness, kidney failure, and peripheral neuropathy) are probably due to the glycation of proteins or lipids.

Moreover, it’s well known that high levels of simple sugars in the GI-tract provide an ideal environment for the proliferation of bacteria that use simple sugars to fuel their anaerobic metabolism.

- The large imbalance of Omega 6 to Omega 3 fatty acids (5:1) in the Osmolite would lead to increased synthesis of arachidonic acid (a complex Omega 6 fatty acid) and of proinflammatory leukotrienes in the body. Leukotrienes are synthesized in the cell from arachidonic acid by 5-lipoxygenase. Leukotrienes are released by several types of cells and can cause bronchoconstriction and inflammation. Leukotrienes assist in the pathophysiology of asthma. Asthma is a chronic inflammatory disease that causes the following:

  - airflow obstruction
  - increased secretion of mucus
  - mucosal accumulation
  - bronchoconstriction
  - infiltration of inflammatory cells in the airway wall.

The patient experienced all of the above symptoms shortly after being administered a diet consisting of 100% of calories from Osmolite. (Observation: Many of the patients in this hospital ward on the same nutrition showed the same symptoms.)

As such, when considering the above:

a) We believe simple & inexpensive experiments can be done to show that an excess of simple carbohydrate & Omega 6 fatty acids in a fatigued patient’s diet are making that patient more susceptible to inflammation & infection requiring subsequent antibiotic treatment.

b) Should this hypothesis be correct, then the following more problematic scenario is likely:
Upon administration of antibiotics, the patient’s previously normal colon & bacterial balance becomes compromised, the patient continues to receive high levels of simple carbohydrate, some of which passes unabsorbed into the compromised colon, this simple sugar is available to support the anaerobic metabolism of problematic bacteria upon termination of the antibiotic, this enhances the potential of resistant spores of bacteria like C-difficile to quickly proliferate upon termination of the antibiotic, as has been firmly established.  

If such a sequence of events is established to frequently occur in hospital-based clinical trials, then nutrient induced hyperglycemia and inflammation could be a primary factor behind the rapidly increasing number of cases of HAI involving C difficile and other resistant organisms.

2) The use of Osmolite, or other similar formulas, may diminish the potential for cellular regeneration and enhance potential for arrhythmia & other metabolic abnormalities:

Based on a review of:
- the patient’s hospital blood work,
- the log of the patient’s nutrition intake and corresponding physiological responses
- well established peer reviewed research cited below,

we feel the lack, and/or significant imbalance, of important nutrients in the Osmolite was also adversely affecting the patient’s:
- cardiac rhythm
- genetic expression and derivative cellular regeneration
- intracellular acid/alkaline balance.

- The amino acid taurine is vital for the proper utilization of sodium, potassium, calcium and magnesium, and has been shown to play a particular role in sparing the loss of potassium from the heart muscle. This helps to prevent the development of potentially dangerous cardiac arrhythmias. The Osmolite enteral formula contains negligible levels of taurine relative to the other amino acids therein.

As well there are insufficient levels of the amino acids cystine/cysteine; Vitamin’s B3, B6, B12 & folic acid; and the proper forms of zinc, magnesium, and other minerals in the formula. These are necessary for the normal synthesis of taurine from cysteine, the synthesis of cysteine & taurine from methionine, and to support SAMe cycle detoxification pathways.

Paragon research also shows that high intakes of refined sugars quickly deplete the body’s stores of intracellular potassium and magnesium, which can lead to arrhythmias. Paragon case studies, and other’s clinical research, show that such arrhythmias can often be quickly controlled with supplementation of the properly chelated forms of those nutrients.

The patient’s intracellular balances of potassium and magnesium may have been affected by the taurine deficiency and by the high levels of maltodextrin (54% of caloric intake), as he developed atrial arrhythmia after only 3 days on the formula. (This was immediately stabilized with medication. The patient was then provided with bio-available sources of potassium and magnesium from fresh concentrated vegetable juice. When the patient’s medication was discontinued, he never required subsequent medication to stabilize his heart rhythm.)
The digestion and metabolism of Osmolite also appeared detrimental to the pH of his tissues (causing it to be significantly lowered, as was measured by taking readings of sublingual fluids).

As concentrated green vegetables juices are rich in the most bioavailable forms of both alkaline minerals, they are often ideal for the treatment of arrhythmia. After 5 days of no other nutrition other than Osmolite, we were given permission by the doctors to provide the patient with vegetable juice through his NG feeding tube. When the patient’s diet was supplemented, his tissue pH rose dramatically, he became more alert, and the arrhythmia did not return.

- The data indicates the patient suffered serious complications due to other nutrient imbalances in the Osmolite. After 21 days on the Osmolite formula, the patient developed pulmonary embolisms (discussed in the next section below). Peer reviewed research discussed below shows that a lack of certain nutrients, that are severely deficient in this formula, was probably involved.

To remedy those nutrient deficiencies and imbalances, on Day 26, a tube was surgically inserted into the patient’s stomach to allow the introduction of those nutrients deficient or missing in the Osmolite formula.

Beginning on Day 27, once he began receiving nutritional supplementation containing extra taurine and ample Omega 3 fatty acids pumped into his stomach, the patient’s PT, INR and potential for thrombosis was immediately & dramatically affected by the supplemented nutrients as can be seen in tables found in the discussion below. More importantly, the patient rapidly and unexpectedly began to recover lost motor function in his paralyzed limbs, after showing very little progress while on the Osmolite and missing these critical nutrients.

Since the attending neurologists had seen no recovery of any lost neurological function 5 days subsequent to the stroke, and since the situation was only slightly better on Day 16 when he was further assessed by the neurological team, the patient’s prognosis was for partial loss of the function in the right arm, loss of lower right side limb function, inability to initiate thought, and altered personality. In summary – the patient’s condition was not expected to improve, as at least some minor recovery is expected in the first two weeks if there is to be further recovery later.

The patient’s status remained unchanged for the next 11 days. However, once the patient began receiving the necessary fatty acids, amino acids, vitamins, and minerals neurological recovery began and was rapid. Remarkably, on Day 133 the patient took his first unassisted steps walking.

- The research found below showed the lack of specific nutrients in Osmolite to be detrimental to the overall rate of cellular regeneration in the patient’s body, particularly that of his brain, thereby affecting his overall potential to recover from the stroke while on the formula.

We believe the patient’s lack of initial neurological recovery to prior to Day 27 was due to the following factors:

- Insufficient levels in the Osmolite formula of taurine, and/or the taurine precursors cysteine, or the necessary nutrient cofactor precursors for cysteine synthesis from methionine.
• Insufficient base level requirements of certain nutrients in the Osmolite formula. Sufficient base level requirements of less complex Omega 3 fatty acids, various amino acids, and other minerals & vitamins are critical for healthy brain metabolism.30

Specifically:

  o the acute imbalance of less complex Omega 6 and 9 fatty acids to Omega 3 in the Osmolite formula would inhibit the internal synthesis of the complex Omega 3 fatty acids31 – including DHA, EPA and phospholipids – those fatty acids required in the largest quantities of any by the brain, and necessary for normal brain metabolism and repair. The Omega 6 / 3 ratio in the brain is about 1.0 - 1.0. 32 33 The balance in the Osmolite formula is 5.0 - 1.0.

  o insufficient levels of the amino acids methionine and/or cysteine; Vitamin’s B6 & B3; and the proper forms of zinc, magnesium, and other minerals in the Osmolite formula. These are necessary for the normal synthesis of taurine from cysteine34 and for the synthesis of DHA & EPA.

• As well, there is no preformed DHA, EPA, or phospholipids critical to cellular regeneration and/or normal brain metabolism in the Osmolite enteral preparation. As these nutrients are rapidly used by the body they must be replaced just as quickly.35 From the time of the stroke until Day 27 afterwards, those critical nutrients necessary to brain function were missing in the patient’s diet.

Research attached below supports the use of DHA/EPA and phospholipid supplementation as soon as possible in cases where a stroke has been caused by blockage.

• The low quality oils used in the manufacture of Osmolite contain toxic pesticide residues, as well as damaged molecules caused by oxidation and free radical activity, due to methods of cultivation, pressing, and packaging.36

• The formula is 54% maltodextrin. This very high level of nutrient-depleting refined sugar made the patient hyperglycemic, requiring regular injections of insulin. As well, high levels of sugar in combination with low taurine, make an individual susceptible to Candida and yeast proliferation that can interfere with brain metabolism and cloud thinking.37

Further, on Day 34 a respected New York neurologist following the case indicated that as applies to stroke, “the only rule that we follow is to keep blood sugar concentration low, since high levels are known to extend infarcts and lead to worse outcomes.” 38

In part, the reason for these worse outcomes is that excess glucose in the blood:

  • damages the blood vessels, in part by increasing free radical damage39
  • makes the blood thicker, more concentrated, and less able to deliver oxygen and other nutrients40
  • impairs circulation, restricting blood flow to organs.41

As well, as discussed above, excess glucose in the blood accelerates glycation, a well known contributor to degeneration and aging.42 Glycation occurs when glucose binds to and chemically alters proteins, lipids and other molecules. These damaged molecules are called
advanced glycation end products (AGEs). They accumulate in cells and hamper normal metabolism.\(^3\)

3) The use of Osmolite, and other similar formulas, may increase platelet aggregation & potential for thrombosis, and with that, the potential for embolism, cardiac infarct, and/or stroke.

Based upon:

- well established peer reviewed research discussed below,
- the balance of nutrient ingredients in the Osmolite formula,
- this patient’s INR (international normalized ratio) records & clinically monitored metabolic responses, both prior and subsequent to nutritional intervention & supplementation,

it is fair to conclude that, after ingesting Osmolite for a few weeks, the patient had increased his potential for thrombosis, cardiac infarct, and/or stroke. In our opinion, it likely contributed in part to the pulmonary embolisms suffered on Day 21.

The formula is devoid of several key nutrients required to prevent excessive platelet aggregation, and contains others which increase excessive platelet aggregation. This is due primarily to:

- the severe imbalance/deficit of specific fatty acids in the formula which would:
  - promote platelet aggregation\(^4\) and the potential for thrombosis
  - inhibit synthesis of the complex fatty acids (including DHA & EPA)\(^45\)\(^46\). The molecular structure and electromagnetic properties of such complex Omega 3 fatty acids cause fats to disperse\(^47\), and are known to affect anti-coagulation\(^48\).

- the omission of a significant level of taurine or its precursors in the formula. Taurine is necessary to prevent blood clotting\(^49\)\(^50\). (The situation is made worse by the omission of cysteine, a precursor to taurine synthesis, and by the inclusion of significant quantities of other amino acids in the formula (tyrosine, lysine, arginine) that increase the uptake and metabolism of the body’s available stores of taurine\(^51\).

- the high levels of maltodextrin in the formula create the potential for excess glucose and a hyperglycemic condition in the patient’s inactive body, resulting in the generation of high levels of sticky saturated lipids in his blood, as insulin converts the excess sugar in the blood into triglycerides\(^52\).

As discussed above, excess glucose also accelerates glycation – and the production of AGEs. Accumulations of AGEs also attract platelets encouraging the formation of blood clots\(^53\).

More specifically as applies to lipid imbalance:

1) the high concentrations of both: a) saturated fats to Omega 3 fatty acids (8.6 : 1), and b) of Omega 6 fatty acids relative to Omega 3 fatty acids (5.0 : 1.0) would accelerate Series-2 prostaglandin production, and dramatically reduce Series 1 & 3 prostaglandin synthesis, significantly promoting platelet aggregation.\(^54\) Ideal omega 6/omega 3 intake is considered by many to be 1.5 : 1.0. Harvard’s Dr. Mark Puder, and others doing parenteral lipid research, think its closer to 1.0 : 1.0.\(^55\) The omega 6 - 3 ratio in the Osmolite formula is 5.0 : 1.0.
Peer reviewed research, referenced briefly above and discussed in greater detail below, shows that blood clotting and other factors are affected by vitamin K and prostaglandin & leukotriene synthesis, which are in turn are affected by the balance of green vegetables, various lipids, amino acids and other nutrients being ingested by the patient.

On Day 22, one day after the patient’s pulmonary embolisms, we reviewed the amino acid make-up of the Osmolite nutritional formula and discovered that it was devoid of cysteine & had only negligible levels of taurine. That same day we sourced peer-reviewed evidence showing that significant levels and a balanced ratio of Omega 3 fatty acids are necessary to prevent blood platelet aggregation. This new evidence was presented to the patient’s doctors.

Subsequent to the pulmonary embolism, and upon reviewing this evidence, the doctors allowed a nutritional intervention and supplementation of the patient’s Osmolite with an additional enteral supplement rich in taurine and Omega 3 fatty acids to provide balanced levels of amino acids and lipids (ratios and ingredients below). As discussed in detail below, the resulting effects on the patient’s potential for platelet aggregation and thrombosis were significant and almost immediate.

A review of the patient’s coumadin protocol and INR data after Day 25 indicate the low level of vitamin K in the small amount of vegetable juice being provided did not have a material effect on the patient’s PT (prothrombin time) and INR. As coumadin inhibits the action of vitamin K, should excess vitamin K have contributed significantly to the patient’s prior hypercoagulable state, the coumadin should have had a greater effect on the patient’s INR immediately thereafter. Instead, the patient’s INR rose very slowly. However, eight days later, just after taurine and Omega 3 fatty acids were added to his diet, the patient’s INR rose quickly. This indicates a lack of taurine/cysteine and Omega 3 fatty acids increases the potential for a hypercoagulable state, as seen in previous studies. As seen below, a proper balance of these nutrients appears critical to preventing thrombosis.

**Result of Taurine and Omega 3 Fatty Acid Supplementation on Patient’s INR**

To best manage the INR/Coumadin dosages, we and the doctors agreed that the patient would receive a constant level of green vegetable juice, taurine and Omega 3 fatty acids each day. These were to be included in the patient’s nutritional supplement, which was to be prepared and delivered to the hospital daily by the researchers, and which was to be administered through a tube that was inserted surgically in the patient’s stomach until his swallowing of food was restarted. As such:

- INR was taken the night before and reported in the AM
- PM coumadin dosage was based on the AM INR report, and would affect INR the next day and possibly as long as 96 hours after administration. Target INR was 2.0 - 3.0
- Taurine/Omega 3 rich nutritional supplement received on given day would affect patient INR the following day and in days beyond.

As can be seen in the chart below, as the patient’s Omega 3 lipid and taurine intake increased, his INR rose both quickly and proportionately to the dose of nutritional supplement received, requiring that his coumadin dosage be held and then reduced.
We anticipated we might see a rise in the patient’s INR after the administration of this nutritional supplement and suggested to the doctors that a gradual reduction of anti-coagulant drugs might be considered in that eventuality.

Beginning on Day 28, one day after starting the nutritional supplement, the patient’s INR went up quickly and steadily, despite later subsequent reductions in coumadin dosages. (Even when considering the potential for coumadin to take 72-96 hours to affect change, as can be seen in the chart below, 8 days or 192 hours passed before the INR rose significantly.)

The rapid upward movement in the patient’s INR corresponded with the ingestion of the nutritional supplement. It appears as though the taurine & lipid imbalances in the Osmolite significantly affected blood coagulation factors in the patient.

Note: The DHA and EPA rich wild salmon in the nutritional supplement was discontinued after 4 days, as we were concerned that the complex fatty acids in the fish might spoil once exposed to air and left in the fridge overnight for the early AM feeding. Organic chicken was substituted, lowering the omega 3 lipid levels slightly thereafter, and affecting the INR accordingly.

### Nutritional Supplement Dosage

<table>
<thead>
<tr>
<th>Date</th>
<th>AM INR</th>
<th>PM Coumadin</th>
<th>Taurine/Omega 3 Nutritional supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 25</td>
<td>1.16</td>
<td>5mg</td>
<td>None</td>
</tr>
<tr>
<td>Day 26</td>
<td>1.20</td>
<td>5mg</td>
<td>None</td>
</tr>
<tr>
<td>Day 27</td>
<td>1.49</td>
<td>5mg</td>
<td>250cc diluted PM</td>
</tr>
<tr>
<td>Day 28</td>
<td>1.8</td>
<td>6mg</td>
<td>500cc diluted AM/PM</td>
</tr>
<tr>
<td>Day 29</td>
<td>2.8</td>
<td>4mg</td>
<td>500cc diluted AM/PM</td>
</tr>
<tr>
<td>Day 30</td>
<td>3.3</td>
<td>1mg</td>
<td>500cc diluted AM/PM</td>
</tr>
<tr>
<td>Day 31</td>
<td>3.8</td>
<td>held</td>
<td>500cc diluted AM/PM</td>
</tr>
<tr>
<td>Day 32</td>
<td>3.98</td>
<td>held</td>
<td>500cc diluted AM/PM</td>
</tr>
<tr>
<td>Day 33</td>
<td>3.34</td>
<td>held</td>
<td>500cc diluted AM/PM</td>
</tr>
</tbody>
</table>

Note: Due to errors by hospital staff when measuring out dosages, the administration of the nutritional supplement was inconsistent on Day 34 & 35. On Day 34 the patient only received 300ccs, instead of 500cc in two equal doses of 250cc. The next day the nutritional supplement was delivered in unequal dosages of 400cc and 100cc.

With the discovery of the patient’s infection with C-difficile on Day 36, all other nutrients other than the Osmolite were temporarily held by the doctors. Then, when the nutritional supplement was re-started on Day 39 & 40 the Omega 3’s in the supplement were temporarily discontinued per the orders of an attending resident. The lead doctor, later overruled this decision, as it would affect our ability to determine the appropriate coumadin dosages, so the Omega 3 lipids began again with the Day 41 PM feeding, but at lower levels, as the Osmolite dosage was reduced from a 125 flow rate (2 liters/day) to 60 (just under 1 liter).

<table>
<thead>
<tr>
<th>Date</th>
<th>AM INR</th>
<th>PM Coumadin</th>
<th>Taurine/Omega 3 Nutritional supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 34</td>
<td>2.92</td>
<td>2mg</td>
<td><strong>300cc</strong> diluted AM/PM</td>
</tr>
<tr>
<td>Day 35</td>
<td>2.81</td>
<td>2mg</td>
<td>500cc diluted AM/PM</td>
</tr>
<tr>
<td>Day 36</td>
<td>3.24</td>
<td>2mg</td>
<td>discontinued – C-difficile</td>
</tr>
<tr>
<td>Day 37</td>
<td>3.54</td>
<td>2mg</td>
<td>discontinued – C-difficile</td>
</tr>
<tr>
<td>Day 38</td>
<td>3.97</td>
<td>held</td>
<td>discontinued – C-difficile</td>
</tr>
<tr>
<td>Day 39</td>
<td>3.24</td>
<td>2mg</td>
<td>500cc diluted AM/PM taurine only, Omega 3 oils held</td>
</tr>
<tr>
<td>Day 40</td>
<td>2.56</td>
<td>3mg</td>
<td>500cc diluted AM/PM taurine only, Omega 3 oils held</td>
</tr>
<tr>
<td>Day 41</td>
<td>2.57</td>
<td>3mg</td>
<td>500cc diluted <strong>oils restarted @ lower level to reflect reduction in Osmolite from 125 flow rate, to 60 flow rate</strong></td>
</tr>
</tbody>
</table>
It was suggested that in the event that the patient’s INR rose too high while still on the Osmolite, the administration of a large serving of green vegetable juice might be beneficial, as it is had shown itself to be beneficial to his brain’s recovery, and was a source of Vitamin K. Green vegetable juice concentrate was resumed at an increased double dose of 250 cc on Day 44 to help regulate the INR down. However, despite this doubled dose, it appeared not to have a significant impact on the patient’s INR.

Additionally, since resuming normal food by mouth, the oil balance in the patient’s nutrient intake swung towards a higher balance of Omega 6 to Omega 3, due to increased meat consumption. Due to the patient’s C-difficile, extra meat was temporarily allowed in a effort to help firm his stools, and reduce sugar intake to prevent any excess from reaching the colon.

On Day 46, in addition to the coumadin being reduced to just 0.5mg, the patient did not receive any taurine. As can be seen the INR dropped more substantially that day.

The data above indicates that the Omega 3 fatty acids and taurine had immediate effects on this patient’s PT and INR. The doctor’s had to reduce the dosage of coumadin to keep the INR from rising too high when that patient’s diet was supplemented with taurine and Omega 3 fatty acids.

The patient’s coumadin was discontinued early on Day 131. To help prevent any potential thrombotic recurrence thereafter, the patient’s diet continued to be supplemented with Omega 3 fatty acids, phospholipids, and taurine. Despite daily consumption of green vegetable juice (Vitamin K), and meat & eggs rich in Omega 6 fatty acids (all nutrients which would contribute to a lowering of INR), the patient’s INR remained at 1.2, slightly above normal (0.9 – 1.1) as desired.

**Patient’s Blood Sugar Levels Normalize Upon Terminating Osmolite**

On Day 46 the administration of Osmolite to the patient was terminated. The patient’s blood sugar levels dropped dramatically once he began receiving balanced meals prepared by the research team. From that point on the patient no longer required injections of insulin.

The patient continued to receive balanced nutrition once the supplemented Osmolite formula was discontinued on Day 46.

**Conclusions**

The patient’s seriously deteriorating health began to improve once the Osmolite formula was supplemented with the necessary nutrients to achieve a proper nutritional balance.
Moreover, once that balance was achieved, the patient made an unexpected and remarkable recovery from neurological injuries suffered during the stroke.

This recovery was unexpected as a second neurological examination done 16 days after the stroke indicated the patient was not responding as hoped, and that there was most likely significant and permanent neurological damage. The prognosis was for partial loss of function to the right arm, probable loss of lower right limb function, inability to initiate thought, and altered personality.

However, upon receiving the nutritional supplementation after Day 27, the patient began to gradually recover all neurological function. He walked unassisted for the first time on Day 133. (Update October 15, 2007: On day 278, unassisted the patient squat lifted 150 lbs of free weight on an Olympic bar across his back, and did 5 pull-ups. A few months later he did 11 pull-ups.)

The patient’s chronic and highly elevated cholesterol levels also completely normalized. For 15 years previously, his LDL levels had been between 4.0 - 5.2 mmol/L, with HDL between 2.30 - 2.65 mmol/L. On Day 135, the patient’s LDL was 1.73 and HDL was 1.71, without any other medication to control cholesterol levels.

The evidence strongly indicates the nutritional formula for Osmolite, and similar products, are poorly balanced, are potentially detrimental to patient health when used a sole source of nutrition, and need to be improved.

As millions of in-patients and out-patients have, and will continue to, use these products, there is an immediate need to improve and test new medical enteral nutritionals that will:

- optimize ongoing genetic expression to:
  - enhance and achieve balanced prostaglandin synthesis
  - prevent excessive platelet aggregation, and potential for thrombosis & infarcts
- prevent arrhythmia
- prevent deterioration of brain function
- be used as agents to target specific disease states
- prevent hyperglycemia, inflammation, and potentially:
  - primary infection requiring antibiotic treatment
  - secondary development of C-difficile
- potentially allow the regeneration of damaged tissue in the brain and other organs.

Peer reviewed research can be used to rapidly develop improved products for testing. Clinical trials could then promptly confirm or dismiss various hypotheses by tracking patient:

- INRs, and rates of thrombosis, embolism, stroke, and heart attack
- rates of primary infection, and secondary antibiotic induced C-difficile
- intracellular mineral levels, and rates of arrhythmia
- blood levels of glucose, cholesterol, homocysteine and other important biomarkers
- rates of recovery, hospital durations, and cost savings to the healthcare system.
The Effects of Excess Omega 6 Fatty Acids on Platelet Aggregation

Since dietary sources of Linoleic Acid (LA) Omega 6 fatty acids are abundant (as is the case with Osmolite), LA may be found to be above normal in some adults.

Because of the need for balanced prostanoid and leukotriene synthesis, excessive linoleic acid can contribute to an overproduction of the PGE2-series local hormones.\(^{60}\)

PGE2 hormones promotes platelet aggregation, the first step in clot formation.\(^{61}\)

The Effects of Taurine Deficiency on Platelet Aggregation

Taurine stabilizes platelets against aggregation. Platelets from taurine depleted animals are twice as sensitive to aggregation as platelets from those receiving taurine.\(^{62}\) In addition, human subjects with normal taurine status show increased resistance to platelet aggregation by 30 or 70% when supplemented with taurine at 400 or 1600mg/d respectively.\(^{63}\) Plasma taurine is easily raised by dietary supplementation.\(^{64}\) Concurrent low cysteine is also relevant in taurine depletion.\(^{65}\) (Cysteine addition to formulas used for home parenteral nutrition normalizes plasma taurine concentrations in children with short gut syndrome.)\(^{66}\)

Taurine is produced in the body from L-cysteine. The first reaction in the pathway is the formation of cysteine sulfinic acid. Cysteine sulfinic acid (CSA) is converted to hypotaurine via the enzyme CSA-decarboxylase, and taurine is formed from hypotaurine.

Cysteine should not be confused with cystine. Cystine is an oxidized dimeric form of cysteine. It can not be used as a substrate to produce taurine derivatives.

There are negligible amounts of taurine and no cysteine in the Osmolite formulation. The only way for the body to produce taurine is through cysteine synthesis from the essential amino acid methionine. However the formula is relatively low in methionine as well, and more importantly lacks the nutrient cofactors necessary for its conversion and synthesis to taurine. (See below)

The Effects of Taurine Deficiency on Other Important Functions

High concentrations of taurine are found in the heart muscle, white blood cells, skeletal muscle, and central nervous system. It is a building block of other amino acids as well as key component of bile, which is needed for the digestion of fats, the absorption of fat soluble vitamins, and the control of serum cholesterol levels. Taurine can be useful for people with atherosclerosis, edema, heart disorders, hypertension, or hyperglycemia.\(^{67}\)

It is vital for the proper utilization of sodium, potassium, calcium and magnesium, and has been shown to play a particular role in sparing the loss of potassium from the heart muscle. This helps to prevent the development of potentially dangerous cardiac arrhythmias.\(^{68}\)

Taurine has a protective affect on the brain, particularly if the brain is dehydrated. It is used to treat anxiety, epilepsy, hyperactivity, poor brain function, and seizures.\(^{69}\)
The Effects of Excess Omega 6 Fatty Acids on Inflammation

PUFAs (polyunsaturated fatty acids) have great impact on health due to their conversion to the compounds collectively called "eicosanoids". Eicosanoids possess extremely potent biological activities, and their homeostatic functions in regulating blood vessel leaking, lipid accumulation, and immune cell behaviour are relevant to the initiation and progress of heart and blood vessel disease.  

Because of the need for balanced prostanoid and leukotriene synthesis, excessive linoleic acid can contribute to an overproduction of the proinflammatory 2-series local hormones.  

The Need for DHA, EPA and Phospholipids for Healthy Brain Function

The following research on the brain’s fatty acid requirements, nutrition, and metabolism was sourced from the Educational Technology Department at The Franklin Institute, Philadelphia, PA.  http://www.fi.edu/brain/fats.htm. For a full list of all the research reference please see http://www.fi.edu/brain/references.htm. Endnotes found in this specific section are in addition to the Franklin Institute references.

- A balanced ratio of the two fatty acid families (omega-3 and omega-6) is necessary for a healthy brain, which is structurally composed of a 1.0 : 1.0 ratio of omega-6 to omega-3.  (Osmolite formula is 5.0 : 1.0)

- DHA (docosahexaenoic acid) is the most abundant fat in the brain. Loss in DHA concentrations in brain cell membranes correlates to a decline in structural and functional integrity of this tissue. (No DHA in the Osmolite formula)

- These more complex fatty acids are also available, preformed, directly from food. This is important, because the brain's ability to assemble these fatty acids can be compromised by stress, infections, alcohol, excess sugar, and vitamin or mineral deficiencies – factors common today. (The Osmolite formula is vitamin deficient, and heavy on sugar in the form of maltodextrin - a nutrient depleting polysaccharide.)

- DHA (docosahexaenoic acid) is the most abundant fat in the brain. Loss in DHA concentrations in brain cell membranes correlates to a decline in structural and functional integrity of this tissue.

- Also, the oxidative damage that comes with age causes a decline in membrane DHA concentrations, and with it, cognitive impairment.

- Scientists at the National Institutes of Health associated the increase in depression in North America during the last century with the decline in consumption of DHA (docosahexaenoic acid) during the same period. Although many stresses of modern life contribute to the prevalence of depression, Joseph R. Hibbeln, M.D., and Norman Salem, Jr., Ph.D., concluded in 1995 that the "relative deficiencies in essential fatty acids may also intensify vulnerability to depression." They also pointed to lower rates of major depression in societies that consume large amounts of fish, a key dietary source of DHA. North American and European populations showed cumulative rates
of depression 10 times greater than a Taiwanese population that consumed a lot of fish. The Japanese, whose diet is rich in fish, have a significantly lower prevalence of depression compared to North America and Europe.

- DHA (docosahexaenoic acid) was the subject of an April 1997 conference on nutrition and the brain. Leading experts discussed the link between low levels of DHA and certain neurological conditions. At the conference, "Keeping Your Brain in Shape: New Insights Into DHA," researchers also noted studies showing a link between deficient DHA levels and hostility and aggression.

Ernst Schaefer, M.D., of the Human Nutrition Research Center on Aging at Tufts University, has found that a low level of DHA is a significant risk factor for dementia, including Alzheimer's disease. He has discovered that the body may experience a decreased ability to make DHA as it ages. "The data I have seen suggest that DHA may be an important therapeutic modality in some age-related conditions, including Alzheimer's and heart disease," Schaefer commented.

Adam Drewnowski, Ph.D., director of the Program in Human Nutrition at the University of Michigan, added that cognitive deficits and dementia in the elderly may be associated with inadequate diets. "Current studies on nutrition in the elderly suggest that many conditions associated with aging, such as loss of appetite and forgetfulness, may be avoided if optimal nutrition is maintained through a diet including nutrients like DHA."

Research indicates that "DHA may be a critical component of the diet of people of all ages," said Barbara Levine, R.D., Ph.D., director of the Nutrition Information Center at the New York Hospital-Cornell Medical Center.

- Studies show that the trans fatty acids we eat do get incorporated into brain cell membranes, including the myelin sheath that insulates neurons. They replace the natural DHA in the membrane, which affects the electrical activity of the neuron. Trans fatty acid molecules disrupt communication, setting the stage for cellular degeneration and diminished mental performance. (Lipids, 1994;29/4:251-58)

Most Medical Nutritionals Contain More Than Five Times the WHO Recommendation for Rapidly Digested Sugars

The human body is designed to derive glucose from a wide range of both fast and long burning carbohydrates, thereby providing our body with fuel that can be digested in minutes or hours. Carbohydrates vary widely in their structure, sweetness, and effects on our health.

Simple carbohydrates, often called "sugars," consist of one or two molecules, and provide energy very quickly. Complex carbohydrates are composed of several to thousands of molecules, and depending on the carbohydrate chain length will slowly provide fuel for the body over several hours.

Monosaccharides are one molecule carbohydrates and include glucose, fructose (found in fruit), & galactose and are the easiest to digest. Glucose is the carbohydrate utilized by the body’s cells. The other monosaccharides can be converted to glucose.
Most monosaccharides in modern western diets come from the breakdown of disaccharides, which are two carbohydrate molecules. An exception would be fructose which is found in fresh fruits, and also in a variety of processed foods as high-fructose corn syrup.

*Disaccharides* include table sugar or sucrose (glucose + fructose), lactose the sugar found in milk (glucose + galactose), and maltose (glucose + glucose). These "simple" carbohydrates are also relatively easy to digest.

The World Health Organization recommends that no more than 10-percent of daily total calories comes from simple sugars, considerably less than the National Academy of Science recommendation of 25-percent of total caloric intake. This is because most people are not active enough to consume high levels of simple sugars without becoming hyperglycemic.

Hospital patients are some of the least active citizens in society, yet many hospital nutritionals contain more than 50% of calories as rapidly digesting sugars, or 5 times as much as the WHO recommends. (As discussed below, this would cause many patients to become hyperglycemic.)

For example, Abbott’s Osmolite and Jevity nutritionals contain 54% of calories from maltodextrin, a processed saccharide that digests as quickly as glucose (see below). Novartis’ and Nestlé’s products provide less ingredient nutritional data, but have very similar lists of ingredients.

Most hospital food products, and the majority of tube feeding systems, have similar very high levels of these refined sugars, often from a single source, such as maltodextrin or corn syrup.

Technically, *complex* carbohydrates that contain three to ten carbohydrate molecules are considered oligosaccharides. These include many manufactured carbohydrates found in hospital nutritionals, such as maltodextrin (also found in some sports drinks) and corn syrup (found in processed foods). However, this is misleading as discussed below.

Dextrins, such as maltodextrin, are a group of low-molecular-weight carbohydrates produced by the hydrolysis of starch. Dextrins find widespread use in industry, due to their non-toxicity and their low price.

Maltodextrin is a sweet, easily digested carbohydrate made from cornstarch. The starch is cooked, and then acid and/or enzymes (a process similar to that used by the body to digest carbohydrates) are used to break the starch into smaller chains (3-20 chains long in maltodextrin). These chains are composed of several dextrose molecules held together by very weak hydrogen bonds.

Dextrose, commonly called glucose, d-glucose, or blood sugar, occurs naturally in food, and is moderately sweet. It is a monosaccharide (basic unit of carbohydrates, C6H12O6) and has a high glycemic index (or GI, the index showing a digested carbohydrates ability to raise blood glucose levels) ranking of 100.

Dextrose is classified as a simple carbohydrate and maltodextrin is classified as complex, but it does not behave like a natural complex carbohydrate. The hydrogen bonds holding maltodextrin together are very weak, and are readily broken apart by the enzymes in the mouth and duodenum; moreover, the chains are short in composition. The weak bonds, and fragile composition of maltodextrin cause it to be digested a fraction slower than dextrose, and as rapidly as glucose. As such, maltodextrin has the potential to rapidly raise blood sugar levels, causing
hyperglycemia. This was the case with the patient. He was regularly given insulin injections while on the Osmolite formula.

Oligosaccharides also include carbohydrates like rafinnose and stachyose that are found in nutrient rich foods such as legumes. Other complex carbohydrates or polysaccharides are composed of over ten and often hundreds of glucose molecules joined together, and include amylose and amylopectin. Most carbohydrates found in the plant world are unprocessed complex carbohydrates from whole food sources, and are known as polysaccharides.

Indigestible carbohydrates are commonly referred to as fiber and include cellulose, hemicellulose, gums, and pectins, and are very important for gastrointestinal tract health and disease prevention.

A Theory As To Why Hospital Patients Often Require Antibiotics

It’s well established that many bacteria thrive, feed, and multiply
- in moist, warm, anaerobic environments
- with ample supplies of simple sugars to provide fuel for their anaerobic metabolisms.

As such, a sick individual with reduced aerobic function has the potential to provide bacteria with an optimum breeding ground. All that is missing to achieve an ideal environment for bacterial proliferation is a ready source of simple sugars for anaerobic consumption.

Our case studies indicate that high sugar dietary intake that results in temporary or longer term hyperglycemia can lead to rapid proliferation of hostile virus in the body. Exactly why this occurs, we don’t know. However since viruses are obligatory intracellular parasites, and they require a growth medium composed of living cells, it’s possible that the increase in bacterial proliferation brought on by sugar excess may create well nourished bacterial hosts in the patients’s body in which the parasite virus can thrive.

If a patient with reduced aerobic function is allowed to become hyperglycemic, and/or insulin resistant, that patient’s blood would readily provide the simple sugar required to feed hostile bacteria, as well as host bacteria supporting viral replication and development.

Clostridium Difficile Is Most Often Caused By Antibiotic Use

Antibiotic-associated colitis caused by the bacterium Clostridium difficile is one of the most common nosocomial infections. If the primary infection requiring antibiotic treatment can be prevented, the potential for developing C–difficile would be dramatically reduced.

We believe certain easily eliminated factors and conditions in most hospitals are leading to an excess of preventable primary infections, as outlined below. This hypothesis can be quickly and inexpensively verified, or discarded.
Clostridium Difficile is Spreading Quickly Through the World’s Hospitals

There were 44,488 cases of Clostridium difficile detected among over-65s in England's hospitals in 2004. This represents a two-fold increase from 2001. It is the first time the England’s Department of Health has published the results of its mandatory surveillance of the infection.

In 2003 and 2004, C-difficile spread through hospitals in Quebec and Alberta and, in one institution alone, contributed to the deaths of 100 patients, mainly older patients. The rate of patients contracting C-difficile increased from 2.1 cases per 1,000 admissions in 2002 to 10 per 1,000 in 2003 and the upward trend continued in 2004.

(It should be remembered that these figures would be higher if calculated using only the number of patients admitted who were prescribed antibiotics at the time of their stay in the hospital. Additionally, we hypothesize that that number would be even higher for those on antibiotics receiving diets high in sugar and Omega 6 rich fatty acids.)

The following background information on recurrent C difficile sections was excerpted from:

Natural history of C Difficile

*C difficile* is a spore-forming, gram-positive bacillus discovered in 1935 as part of the normal colonic flora of newborn infants. Pseudomembranous colitis became more prevalent in the 1970s with the proliferation of broad-spectrum antibiotics and the increased use of empirical antibiotic therapy (3).

Initially, *Staphylococcus aureus* was thought to cause pseudomembranous colitis, because vancomycin hydrochloride (Vancocin, Vancoled) cured the infection. However, toxins released by *C difficile* later were identified as the cause (4). The epidemiologic and pathophysiologic factors of *C difficile* infection have been well elucidated, but it continues to be endemic in hospitalized patients.

Pathophysiologic factors

Antibiotics are known to disrupt the colonic microflora, facilitating *C difficile* colonization and growth--primarily in hospitalized patients. The combination of nosocomial exposure to *C difficile* and loss of normal protective colonic bacteria leads to colonization. As the organism proliferates, toxins A and B are elaborated and released.

Toxin A is an enterotoxin that has been shown to elicit an acute inflammatory response in animals. Toxin B is a cytotoxin that has no enterotoxic effect in animals but recently has been shown to be pathogenic in humans (5). These toxins cause release of proinflammatory mucosal cytokines, which results in an exuberant inflammatory exudate on the colonic mucosal surface with intervening areas of normal mucosa. These plaques of inflammatory cells, disrupted crypts, and cellular debris appear macroscopically as yellow to grey pseudomembranes (figure 1: not shown). The classic appearance of the exudate on microscopic examination is volcanos of inflammatory infiltrate that erupt from the mucosal surface (figure 2: not shown).
Etiologic factors

_C difficile_ infection has been reported with use of virtually all antibiotics and some antiviral and antifungal agents. It most commonly occurs with use of the penicillins ampicillin and amoxicillin (Amoxil, Trimox, Wymox), the cephalosporins, and clindamycin (Cleocin). The prevalence of complicating pseudomembranous colitis is variable but can be as great as 10% in patients taking clindamycin or lincomycin (6).

About 80% of cases of _C difficile_ diarrhea occur in people who are still taking antibiotics, but increased risk can persist for months after antibiotic exposure. Populations predisposed to _C difficile_ infection include the elderly and patients with colonic disease (e.g., inflammatory bowel disease, colorectal cancer) or another severe underlying disease (7).

Clinical presentation

Infection with _C difficile_ results in a wide spectrum of clinical manifestations. Antibiotic-associated diarrhea that is not caused by _C difficile_ is characterized by three or four loose bowel movements a day, usually without any other systemic complaints. It can be treated conservatively by stopping the inciting antibiotic. _C difficile_ colitis is complicated by more frequent bowel movements, abdominal pain, and fever. Systemic manifestations may include dehydration, prerenal azotemia, sepsis syndrome, toxic colitis, and even death in seriously ill patients. Laboratory tests may demonstrate a marked elevation in the white blood cell count with a left shift to immature forms. Extreme presentation of fulminant colitis may require a colectomy and could even result in death (8).

Diagnosis

The standard test to detect _C difficile_ toxins in the stool is the enzyme-linked immunosorbent assay (ELISA). This is the most commonly used test because it is easy to perform and has a sensitivity of 70% to 90% and a specificity of 90%. ELISA usually detects only toxin A.

Treatment

Standard therapy consists of (1) discontinuation of the inciting antibiotic, (2) avoidance of such antimitility agents as loperamide hydrochloride and diphenoxylate hydrochloride with atropine sulfate, and (3) oral administration of metronidazole (Flagyl) or vancomycin for 10 to 14 days (table 1). Metronidazole is first-line therapy for reasons of cost as well as concern about antibiotic resistance. The cost differential between similar courses of metronidazole and oral vancomycin can be several hundred dollars. Both metronidazole and oral vancomycin have high in vivo activity against _C difficile_. However, development of vancomycin-resistant _Enterococcus faecium_ infection is a concern (10). For patients with severe _C difficile_ colitis, oral vancomycin or intravenous metronidazole is used.

Table 1. Standard therapy for _Clostridium difficile_ infection

<table>
<thead>
<tr>
<th>Agent</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole (Flagyl)</td>
<td>250-500 mg PO tid or qid X 10-14 days</td>
</tr>
<tr>
<td>Vancomycin HCl (Vancocin, Vancoled)</td>
<td>125 mg PO qid X 10-14 days</td>
</tr>
</tbody>
</table>

Resistance to metronidazole and vancomycin has been reported but has not been a significant clinical problem (8). It is suggested that patients with _C difficile_ infection who require long-term antibiotic therapy...
(e.g., those with bacterial endocarditis or osteomyelitis) should continue metronidazole or vancomycin therapy for 1 week after completion of long-term antibiotic therapy.

**Recurrent *C difficile* infection**

Relapses of *C difficile* diarrhea occur in about 20% of patients treated with standard courses of vancomycin or metronidazole. Relapses can occur 1 week to 2 months after the cessation of treatment. When a patient experiences diarrhea after completion of treatment, recurrence should be highly suspected. A stool sample should be retested for infection before initiating therapy.

**Pathophysiologic factors**

The exact mechanism of recurrent *C difficile* colitis is unclear. It usually is not related to bacterial resistance to standard antimicrobial therapies but rather to breakdown of the normal flora barrier of the colon after antibiotic treatment. This problem usually does not occur in patients who receive conservative treatment, because the colonic flora is not exposed to further antibiotics.

Vancomycin and metronidazole kill the vegetative form of *C difficile* but do not kill the spores (8), which can germinate and eventually produce toxins. Other sources of recurrent *C difficile* infection are viable bacterial spore forms, which can exist in the local environment for up to 6 months (11). Finally, repeated use of antibiotics that disrupt normal colonic bacteria predisposes to recurrent *C difficile* infection; restoration of this barrier may have a role in treatment.

**Clinical presentation**

After completion of a course of antibiotics, symptoms usually resolve, only to recur. The signs and symptoms of primary *C difficile* infection include diarrhea, abdominal pain, low-grade fever, and marked leukocytosis. Patients with recurrent *C difficile* infection have been shown to have more severe illness, abdominal pain, and fever than with initial infection, and they usually are female (2). Patients who have one recurrence are 65% more likely to have further recurrences. Failure of a standard course of oral vancomycin also predisposes to recurrence (12).

Fekety and colleagues (2) studied the characteristics of patients with recurrent *C difficile* infection. Such patients have five predisposing factors: previous *C difficile* diarrhea, onset of disease in spring, exposure to additional antibiotics for treatment of other infections, infection with immunoblot type 1 or type 2 strains of *C difficile*, and female sex.

**Treatment**

Recurrent *C difficile* infection can be treated with multiple methods (table 2). The first course of treatment is continuation of the initial antibiotic (i.e., vancomycin or metronidazole) for an additional 10 to 14 days.
**Table 2. Therapy for recurrent Clostridium difficile infection**

**Tapering oral antibiotic dose**
Vancomycin, 125 mg qid X 7 days, 125 mg bid X 7 days, 125 mg qd X 7 days, 125 mg qod X 7 days, 125 mg q3d X 14 days

**Anion-binding resin**
Cholestyramine (LoCHOLEST, Prevalite, Questran), 4 g PO tid or qid X 14 days

\[\text{plus}\]
Vancomycin, 125-250 mg PO qid X 14 days

**Antibiotics**
Vancomycin, 125-250 mg PO qid X 14 days

\[\text{plus}\]
Rifampin, 150-300 mg PO bid X 14 days

\[\text{or}\]
Bacitracin, 25,000 U PO qid X 14 days

The goal of initial treatment is to eliminate the bacteria and vegetative spores. Tapering the dose of vancomycin or metronidazole over 4 to 6 weeks has been shown to be effective. Tapering the dose works to kill viable *C. difficile* bacteria while allowing restoration of normal colonic flora (13). An alternative is cholestyramine (LoCHOLEST, Prevalite, Questran), an anion-binding resin that binds clostridial toxin, used in conjunction with vancomycin (14). Patients must take the medications at separate times because the resin of cholestyramine can bind vancomycin, rendering the treatment ineffective. Vancomycin in combination with rifampin (Rifadin, Rimactane) or oral bacitracin also has been found to be effective against recurrent *C. difficile* infection (15).

**Oral probiotic therapy for recurrent Clostridium difficile infection**

Altered bowel flora increases susceptibility to recurrent *C. difficile* infection. Thus, another approach to therapy is to use probiotics to repopulate or restore colonic bacteria as an adjunct to antibiotic therapy (16) (table 3). *Saccharomyces boulardii* is a nonpathogenic yeast that releases a protein that interferes with the binding of toxin A to its receptor (17). The administration of *S. boulardii* has been shown to be effective both on its own and in combination with metronidazole or vancomycin in patients with recurrent *C. difficile* infection. In a randomized placebo-controlled trial (18), *S. boulardii* in combination with vancomycin or metronidazole reduced the relapse rate by 50% and was well tolerated.

**Table 3. Oral probiotic therapy for recurrent Clostridium difficile infection**

*Saccharomyces boulardii*, 500 mg bid X 4 wk

\[\text{plus}\]
Vancomycin HCl (Vancocin, Vancoled), 125 mg qid X 10-14 days

Lactobacillus GG (Lactinex), 1-g packet (10^10 organisms) qid X 7-14 days, \(\text{after}\) vancomycin, 125 mg qid X 10-14 days

(Paragon Researcher’ Note: Lactinex is not the trade name for Lactobacillus GG. This is an error. Lactinex refers to other more general strains of Lactobacillus, as a search of the OTC product will show. Culturre TM, however, does make a Lactobacillus GG.)

A small study by Gorbach and associates (19) showed that the probiotic lactobacillus GG is effective against relapsing *C. difficile* infection because it inhibits proliferation of the bacteria. Other lactobacillus preparations also have activity when used with antibiotics directed against *C. difficile*.

This background on recurrent *C. difficile* sections was excerpted from:
Nutrient Content Of Wild Salmon and High Protein Organic Vegetable Nutritional Supplement

The following tables provide the nutrient and energy figures for the wild salmon & organic vegetable based nutritional supplement given by the researchers to the patient starting on June 13th. (See table below)

Fresh wild pacific salmon contains DHA and EPA necessary for optimum cerebral metabolism. Studies show that conversion of less complex Omega 3s (like those found in flax oil) into DHA/EPA, or the 5 & 6 times polyunsaturated fatty acid (PUFA) forms, is often compromised by a lack of synergistic vitamins, minerals, & other nutrients necessary for completion of the synthesis pathway.

(Lightly boiled organic chicken was substituted for fish after the first 4 days, as we were concerned the fish might spoil when left in the refrigerator overnight for the patient's early AM feeding.)

In addition to being free of pesticides and antibiotics, the organic vegetables used contain between 65-99% more of different minerals as compared to conventionally grown produce raised on synthetic fertilizers.

1500mg of free-form taurine was added to this blend to supplement that found in the fish and chicken.

Additional antarctic krill oil (2g), borage oil (.5g), organic flax oil (18g), and organic olive oil were added to the nutritional supplement to achieve optimum lipid balances for the patient’s recovery.

continued below
<table>
<thead>
<tr>
<th>Food Group</th>
<th>Protein : Fats : Carbs</th>
<th>Calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 cups High Protein</td>
<td>30% : 10% : 60%</td>
<td>approx 200/cup</td>
</tr>
<tr>
<td>Organic Vegetable Soup</td>
<td>30g : 4.4g : 60g</td>
<td>___</td>
</tr>
<tr>
<td>Total Grams</td>
<td>94.4g</td>
<td>___</td>
</tr>
<tr>
<td>Total calories</td>
<td>400</td>
<td>___</td>
</tr>
</tbody>
</table>

per 6.5g soup solids:
2.3g P x 4 cal = 9.2 cal or 34.2 % of cal
0.2g F x 9 cal = 1.8 cal or 6.6 % of cal
4.0g C x 4 cal = 16.0 cal or 59.2 % of cal

31.7% Protein by weight
4.6% Fat by weight
63.5% Carbs by weight

Flax oil (ALA, LA 2:1) 3 Tablespoons: 42g 124 cal/T 372
Borage oil (GLA 10 %) 1 g 1g 9 cal 9
Krill oil (DHA EPA phospholipids) 2g 18 cal 18
Olive oil (oleic) 1 Tablespoon 14g 120 cal/T 124
59 g total fat 523

Total Protein, Vegetable and Oil Nutritional Supplement Base Calories 923

Wild Salmon 4 ounces: 31g protein, 8.5g total fat
(1.5g saturated, 2.5g unsaturated)

78.5% Protein by weight
21.5% Fat by weight

31.0g P x 4 cal = 124.0 cal or 61.8 % of cal
8.5g F x 9 cal = 76.5 cal or 38.2 % of cal
total salmon calories 200.5

Total calories in Nutritional Supplement 1123.5

Percentage of Protein/Fat/Carb by weight 31.7% P, 37.1% Fat, 31.2% C
Percentage of Protein/Fat/Carb by calories 21.6% P, 57.0% Fat, 21.3% C
Breakdown of Fatty Acids in Osmolite, Omega 3 Nutritional Supplement, and the Two Combined

Caloric Distribution

<table>
<thead>
<tr>
<th></th>
<th>Per 8 fl oz</th>
<th>Per Liter</th>
<th>Per 1500 mL</th>
<th>% Calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>250</td>
<td>1060</td>
<td>1590</td>
<td></td>
</tr>
<tr>
<td>Protein, g</td>
<td>10.5</td>
<td>44.3</td>
<td>66.4</td>
<td>16.7</td>
</tr>
<tr>
<td>Total Fat, g</td>
<td>8.2</td>
<td>34.7</td>
<td>52.1</td>
<td>29</td>
</tr>
<tr>
<td>Total Carbohydrate, g</td>
<td>33.9</td>
<td>143.9</td>
<td>215.7</td>
<td>54.3</td>
</tr>
<tr>
<td>Water, g*</td>
<td>199</td>
<td>842</td>
<td>1260</td>
<td></td>
</tr>
</tbody>
</table>

*1 g water = 1 mL water = 1 cc water.

Percent of total calories from fat

<table>
<thead>
<tr>
<th>Serving size in litres</th>
<th>1</th>
<th>1.75</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Fat</td>
<td>34.7 g/L</td>
<td>34.7</td>
<td>60.7</td>
</tr>
<tr>
<td>Polyunsaturated fatty acids</td>
<td>5.9 g/L</td>
<td>5.9</td>
<td>10.3</td>
</tr>
<tr>
<td>Monounsaturated fatty acids</td>
<td>17.9 g/L</td>
<td>17.9</td>
<td>31.3</td>
</tr>
<tr>
<td>Saturated fatty acids</td>
<td>8.6 g/L</td>
<td>8.6</td>
<td>15.1</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;20 mg/L</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Omega 3 per each gram of total polyunsaturates (OSMOLITE)

<table>
<thead>
<tr>
<th>Serving size in litres</th>
<th>1</th>
<th>1.75</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omega 3 per each gram of total polyunsaturates (OSMOLITE)</td>
<td>0.2</td>
<td>1.0</td>
<td>1.7</td>
</tr>
<tr>
<td>Saturated fatty acids</td>
<td>8.6 g/L</td>
<td>8.6</td>
<td>15.1</td>
</tr>
</tbody>
</table>

Total Sat Fat+ omega 6 (promotes Series 2 prostaglandin synthesis and clotting)

<table>
<thead>
<tr>
<th>Serving size in litres</th>
<th>1</th>
<th>1.75</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Sat Fat + Omega 6</td>
<td>13.5</td>
<td>23.7</td>
<td>27.0</td>
</tr>
</tbody>
</table>

Omega-6 / omega-3 ratio (desirable is 2.5 : 1)

<table>
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<tr>
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<th>1</th>
<th>1.75</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omega-6 / omega-3 ratio</td>
<td>5:0:1</td>
<td>5:0</td>
<td>5:0</td>
</tr>
</tbody>
</table>

Flax Oil in Soup:

<table>
<thead>
<tr>
<th>(For 2, 3 &amp; 4 Tablespoons)</th>
<th>15 ml (1 Tablespoon)</th>
<th>2T / 30ml</th>
<th>3T / 45ml</th>
<th>4T / 60ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omega 3</td>
<td>7.5</td>
<td>15.0</td>
<td>22.5</td>
<td>30.0</td>
</tr>
<tr>
<td>Omega 6</td>
<td>2.2</td>
<td>4.4</td>
<td>6.6</td>
<td>8.8</td>
</tr>
<tr>
<td>Monounsaturated fatty acids</td>
<td>3</td>
<td>6.0</td>
<td>9.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Saturated fatty acids</td>
<td>1.3</td>
<td>2.6</td>
<td>3.9</td>
<td>5.2</td>
</tr>
</tbody>
</table>

SOUP & OSMOLITE COMBINED

| (Sat Fat + omega 6) / omega 3 ratio w/ 2T (30ml) Flax oil in 250 ml of soup | 1.8 |
| (Sat Fat + omega 6) / omega 3 ratio w/ 3T (45ml) Flax oil in 250 ml of soup | 1.4 |
| (Sat Fat + omega 6) / omega 3 ratio w/ 4T (60ml) Flax oil in 250 ml of soup | 1.2 |
Nutritional Imbalances Within OSMOLITE 1 CAL and Similar Formulations

<table>
<thead>
<tr>
<th>Caloric Distribution</th>
<th>Per 8 fl oz</th>
<th>Per Liter</th>
<th>Per 1500 mL</th>
<th>% Calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>250</td>
<td>1060</td>
<td>1590</td>
<td>—</td>
</tr>
<tr>
<td>Protein, g</td>
<td>10.5</td>
<td>44.3</td>
<td>66.4</td>
<td>16.7</td>
</tr>
<tr>
<td>Total Fat, g</td>
<td>8.2</td>
<td>34.7</td>
<td>52.1</td>
<td>29.0</td>
</tr>
<tr>
<td>Total Carbohydrate, g</td>
<td>33.9</td>
<td>143.9</td>
<td>215.7</td>
<td>54.3</td>
</tr>
<tr>
<td>Water, g*</td>
<td>199</td>
<td>842</td>
<td>1260</td>
<td>—</td>
</tr>
</tbody>
</table>

*1 g water = 1 mL water = 1 cc water.

The formula is only 16.7% protein, 54.3% refined sugar, and 29% poor quality fat. The sole source of carbohydrate in OSMOLITE 1 CAL is corn maltodextrin. The metabolism of maltodextrin often causes nutrient depletion, as it is highly refined and lacking most other nutrients required for its proper metabolism. Maltodextrin is easily digestible, being absorbed as rapidly as glucose. Dextrins find widespread use in industry, due to their non-toxicity and their low price.

As a high intake of maltodextrin has the potential to release too much sugar at once, it can easily cause hyperglycemia in less active individuals.

Amino Acid Profile

There are negligible levels of the amino acid taurine (175mg per 1500mL) required for normal blood clotting and other important functions as discussed above (It’s not included in the table below – it is listed separately under Nutrient Facts.) There is no cysteine and negligible cystine from which to synthesize taurine. There is methionine from which to synthesize cysteine, but inadequate levels of vitamin B6, magnesium, and betaine for synthesis.

Methionine is one of the amino acids most frequently found to be deficient in human serum testing because the methionine content of low quality protein sources is very low.
### Fatty Acid Profile

The saturated fat to Omega 3 ratio is 8.6 : 1. The Omega 6 to Omega 3 ratio is 5 : 1. This stimulates platelet aggregation and clotting as discussed above. There is no complex omega 3 (DHA/EPA) for improving brain regeneration, and overall oxygenation of tissues.

The Omega 3 and 6 oils it does contain are not pressed and packaged properly and are rancid or inactive, and contaminated with pesticides and other oil soluble toxins.

<table>
<thead>
<tr>
<th>Percent of total calories from fat</th>
<th>29.0</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Fat</strong></td>
<td>34.7 g/L</td>
</tr>
<tr>
<td>Polyunsaturated fatty acids</td>
<td>5.9 g/L</td>
</tr>
<tr>
<td>Monounsaturated fatty acids</td>
<td>17.9 g/L</td>
</tr>
<tr>
<td>Saturated fatty acids</td>
<td>8.6 g/L</td>
</tr>
<tr>
<td>Omega-6/omega-3 ratio</td>
<td>5.0:1</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;20 mg/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Fatty Acids</strong></th>
<th>8 fl oz</th>
<th>1000 mL</th>
<th>1500 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linoleic (18:2), mg</td>
<td>1130</td>
<td>4780</td>
<td>7177</td>
</tr>
<tr>
<td>α-Linolenic (18:3), mg</td>
<td>268</td>
<td>1134</td>
<td>1703</td>
</tr>
<tr>
<td>Caprylic (8:0), mg</td>
<td>880</td>
<td>3725</td>
<td>5594</td>
</tr>
<tr>
<td>Capric (10:0), mg</td>
<td>623</td>
<td>2637</td>
<td>3960</td>
</tr>
<tr>
<td>Lauric (12:0), mg</td>
<td>13</td>
<td>56</td>
<td>84</td>
</tr>
<tr>
<td>Myristic (14:0), mg</td>
<td>15</td>
<td>63</td>
<td>94</td>
</tr>
<tr>
<td>Palmitic (16:0), mg</td>
<td>342</td>
<td>1447</td>
<td>2173</td>
</tr>
<tr>
<td>Stearic (18:0), mg</td>
<td>146</td>
<td>620</td>
<td>931</td>
</tr>
<tr>
<td>Oleic (18:1), mg</td>
<td>4222</td>
<td>17867</td>
<td>26829</td>
</tr>
<tr>
<td>Arachidic (20:0), mg</td>
<td>21</td>
<td>89</td>
<td>134</td>
</tr>
</tbody>
</table>
Fatty acids equal approximately 95% of total fat.  
Key for values in parentheses (carbon atoms: double bonds).  
**Vitamin & Mineral Profile and Other Nutrient Facts**

The levels of vitamins C, B6, B5, B12, folic acid, beta-carotene and other important vitamins are too low for cysteine synthesis, SAMe cycle detoxification pathway function, and other biochemical function.

<table>
<thead>
<tr>
<th><strong>Vitamins</strong></th>
<th>8 fl oz</th>
<th>1000 mL</th>
<th>1500 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A, IU</td>
<td>895</td>
<td>3790</td>
<td>5690</td>
</tr>
<tr>
<td>Vitamin D, IU</td>
<td>72</td>
<td>305</td>
<td>455</td>
</tr>
<tr>
<td>Vitamin E, IU</td>
<td>8.1</td>
<td>35</td>
<td>52</td>
</tr>
<tr>
<td>Vitamin K, mcg</td>
<td>15</td>
<td>61</td>
<td>91</td>
</tr>
<tr>
<td>Vitamin C, mg</td>
<td>54</td>
<td>230</td>
<td>345</td>
</tr>
<tr>
<td>Folic Acid, mcg</td>
<td>110</td>
<td>455</td>
<td>685</td>
</tr>
<tr>
<td>Thiamin (Vitamin B1), mg</td>
<td>0.41</td>
<td>1.8</td>
<td>2.6</td>
</tr>
<tr>
<td>Riboflavin (Vitamin B2), mg</td>
<td>0.46</td>
<td>2</td>
<td>2.9</td>
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<tr>
<td>Vitamin B6, mg</td>
<td>0.54</td>
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<td>3.5</td>
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<tr>
<td>Vitamin B12, mcg</td>
<td>1.7</td>
<td>6.9</td>
<td>11</td>
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<tr>
<td>Niacin, mg</td>
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<td>23</td>
<td>35</td>
</tr>
<tr>
<td>Choline, mg</td>
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<td>455</td>
<td>685</td>
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<tr>
<td>Biotin, mcg</td>
<td>81</td>
<td>345</td>
<td>515</td>
</tr>
<tr>
<td>Pantothenic Acid, mg</td>
<td>2.7</td>
<td>12</td>
<td>18</td>
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<table>
<thead>
<tr>
<th><strong>Minerals</strong></th>
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<th>1000 mL</th>
<th>1500 mL</th>
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</thead>
<tbody>
<tr>
<td>Sodium, mg (mEq)</td>
<td>220 (9.6)</td>
<td>930 (40.4)</td>
<td>1395 (60.6)</td>
</tr>
<tr>
<td>Potassium, mg (mEq)</td>
<td>370 (9.5)</td>
<td>1570 (40.2)</td>
<td>2355 (60.4)</td>
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<tr>
<td>Chloride, mg (mEq)</td>
<td>340 (9.6)</td>
<td>1440 (40.7)</td>
<td>2160 (61.0)</td>
</tr>
<tr>
<td>Calcium, mg</td>
<td>180</td>
<td>760</td>
<td>1140</td>
</tr>
<tr>
<td>Phosphorus, mg</td>
<td>180</td>
<td>760</td>
<td>1140</td>
</tr>
<tr>
<td>Magnesium, mg</td>
<td>72</td>
<td>305</td>
<td>455</td>
</tr>
<tr>
<td>Iodine, mcg</td>
<td>27</td>
<td>115</td>
<td>175</td>
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<tr>
<td>Manganese, mcg</td>
<td>0.9</td>
<td>3.8</td>
<td>5.7</td>
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<tr>
<td>Copper, mg</td>
<td>0.36</td>
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<tr>
<td>Zinc, mg</td>
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<td>Iron, mg</td>
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<td>Chromium, mcg</td>
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<td>140</td>
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<td>Molybdenum, mcg</td>
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<td>175</td>
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<tr>
<td>Nutrient Facts</td>
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<td>1500 mL</td>
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<tr>
<td>----------------</td>
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<td>FAN (label number)</td>
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<td>7683-08</td>
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<tr>
<td>Cal/mL</td>
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<td>1.06</td>
<td>1.06</td>
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<tr>
<td>Energy, Cal</td>
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</tr>
<tr>
<td>Protein, g</td>
<td>10.5</td>
<td>44.3</td>
<td>66.4</td>
</tr>
<tr>
<td>% of total Calories</td>
<td>16.7</td>
<td>16.7</td>
<td>16.7</td>
</tr>
<tr>
<td>Fat, g</td>
<td>8.2</td>
<td>34.7</td>
<td>52.1</td>
</tr>
<tr>
<td>% of total Calories</td>
<td>29.0</td>
<td>29.0</td>
<td>29.0</td>
</tr>
<tr>
<td>Cholesterol, mg</td>
<td>&lt;5</td>
<td>&lt;20</td>
<td>&lt;30</td>
</tr>
<tr>
<td>Carbohydrate, g</td>
<td>33.9</td>
<td>143.9</td>
<td>215.7</td>
</tr>
<tr>
<td>% of total Calories</td>
<td>54.3</td>
<td>54.3</td>
<td>54.3</td>
</tr>
<tr>
<td>Water, g*</td>
<td>199</td>
<td>842</td>
<td>1260</td>
</tr>
<tr>
<td>Dietary Fiber, g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L-carnitine, mg</td>
<td>27</td>
<td>115</td>
<td>175</td>
</tr>
<tr>
<td>Taurine, mg</td>
<td>27</td>
<td>115</td>
<td>175</td>
</tr>
<tr>
<td>m-Inositol, mg</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Editorial: Human Genome Remains Full of Surprises

19 November 2005

BACK in June 2000, when Bill Clinton triumphantly announced the working draft of the human genome, it was tempting to believe that we would soon be masters of our own genetic make-up. Tempting but entirely wrong. Five years on, most of the profound possibilities stemming from the human genome project appear as far away as ever.

Take pharmacogenomics, the idea of tailoring medicines to an individual's genetic make-up. It was always going to take time to develop: identifying which genes act to alter a drug's impact on metabolism is a painstaking process, made still more complex and time-consuming by the fact that often several genes are implicated. As we head towards these horizons, much of what we discover threatens to push back still further the time when we can expect to understand what we are really dealing with. For the same reasons, and despite recent hype, diets tailored to genomes - or nutrigenomics - will not arrive any time soon.

But there are some fascinating hints of what may be in store. Last week, researchers reported finding a gene that codes for two hormones which act against each other: one suppresses appetite, the other stimulates it (see "The gene that can make you feast or starve"). Control over which of the two proteins is produced rests not in the genome, nor in the ribosome where they are made, but with enzymes that subsequently tweak the proteins according to some as yet undiscovered regulatory process. The driving force in this case appears to be the proteome, the massed ranks of interacting proteins within the body. The proteome was always known to be larger than the genome, and as estimates of the number of human genes has fallen - it now stands at about 25,000 - so the proteome has grown in importance.

However, the proteome is not the end of the story either. A Canadian group announced this week that a gene can be silenced in rats simply by giving them an amino acid, methionine (see "How the food you eat could change your genes for life"). Genes can be deactivated by adding methyl groups to their DNA, and in this case it seems likely that the methionine is donating methyl groups that makes this happen.

While this is not the first food found to exert such "epigenetic" control, it is especially interesting because it radically alters the behaviour of the rats. The hopeful implication of this work is that, with the right food supplements, we will be able to switch genes on and off at will to treat both physical and mental illness.

These studies show up the exquisite complexity of the human body and hint at the control we may eventually exert. But most of all, they highlight how far we still have to travel before we really understand what makes us what we are.
IT SOUNDS like science fiction: simply swallowing a pill, or eating a specific food supplement, could permanently change your behaviour for the better, or reverse diseases such as schizophrenia, Huntington's or cancer.

Yet such treatments are looking increasingly plausible. In the latest development, normal rats have been made to behave differently just by injecting them with a specific amino acid. The change to their behaviour was permanent. The amino acid altered the way the rat's genes were expressed, raising the idea that drugs or dietary supplements might permanently halt the genetic effects that predispose people to mental or physical illness.

It is not yet clear whether such interventions could work in humans. But there is good reason to believe they could, as evidence mounts that a range of simple nutrients might have such effects. Two years ago, researchers led by Randy Jirtle of Duke University Medical Center in Durham, North Carolina, showed that the activity of a mouse's genes can be influenced by food supplements eaten by its mother just prior to, or during, very early pregnancy (New Scientist, 9 August 2003, p 14). Then last year, Moshe Szyf, Michael Meaney and colleagues at McGill University in Montreal, Canada, showed that mothers could influence the way a rat's genes are expressed after it has been born. If a rat is not licked, groomed and nursed enough by its mother, chemical tags known as methyl groups are added to the DNA of a particular gene.

Now the team has shown that a food supplement can have the same effect on well-reared rats at 90 days old - well into adulthood. The researchers injected L-methionine, a common amino acid and food supplement, into the brains of well-reared rats. The amino acid methylated the glucocorticoid gene, and the animals' behaviour changed. "They were almost exactly like the poorly raised group," says Szyf, who announced his findings at a small meeting on environmental epigenomics earlier this month in Durham, North Carolina.

Though the experiment impaired well-adjusted animals, the opposite should be possible, and Szyf has already shown that a chemical called TSA that is designed to strip away methyl groups can turn a badly raised rat into a more normal one.

Rob Waterland from Baylor College of Medicine in Houston, Texas, who attended the meeting, says Szyf's ideas are creating a buzz, as they suggest that methylation can influence our DNA well into adulthood. A huge number of diseases are caused by changes to how our DNA is expressed, and this opens up new ways of thinking about how to prevent and treat them, he says.

But Waterland points out there is still much work to be done. Substances like methionine and TSA are, he says, a "sledgehammer approach", in that they are likely to demethylate lots of genes, and we don't even know which they will affect. But he speculates that techniques such as "RNA-directed DNA methylation", so far tested only in plants but theoretically possible in mammals, may allow us to target such methylation much more precisely.
Evaluation Of The Effects Of Neptune Krill Oil On The Clinical Course Of Hyperlipidemia

http://www.findarticles.com/p/articles/mi_m0FDN/is_4_9/ai_n9485702

Alternative Medicine Review, Dec, 2004 by Ruxandra Bunea, Khassan El Farrah, Luisa Deutsch

Abstract

OBJECTIVE: To assess the effects of krill oil on blood lipids, specifically total cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL). METHODS: A multi-center, three-month, prospective, randomized study followed by a three-month, controlled follow-up of patients treated with 1 g and 1.5 g krill oil daily. Patients with hyperlipidemia able to maintain a healthy diet and with blood cholesterol levels between 194 and 348 mg/dL were eligible for enrollment in the trial. A sample size of 120 patients (30 patients/group) was randomly assigned to one of four groups. Group A received krill oil at a body mass index (BMI)-dependent daily dosage of 2-3 g daily. Patients in Group B were given 1-1.5 g krill oil daily, and Group C was given fish oil containing 180 mg eicosapentaenoic acid (EPA) and 120 mg docosahexaenoic acid (DHA) per gram of oil at a dose of 3 g daily. Group D was given a placebo containing microcrystalline cellulose. The krill oil used in this study was Neptune Krill Oil (NKO), provided by Neptune Technologies & Bioresources, Laval, Quebec, Canada. OUTCOME MEASURES: Primary parameters tested (baseline and 90-day visit) were total blood cholesterol, triglycerides, LDL, HDL, and glucose. RESULTS: Krill oil 1-3 g/day (BMI-dependent) was found to be effective for the reduction of glucose, total cholesterol, triglycerides, LDL, and HDL, compared to both fish oil and placebo. CONCLUSIONS: The results of the present study demonstrate within high levels of confidence that krill oil is effective for the management of hyperlipidemia by significantly reducing total cholesterol, LDL, and triglycerides, and increasing HDL levels. At lower and equal doses, krill oil was significantly more effective than fish oil for the reduction of glucose, triglycerides, and LDL levels. (Altern Med Rev 2004;9(4):420-428)

Introduction

The balance of polyunsaturated essential fatty acids (PUFAs) in the body is critical for the maintenance of healthy cell membranes and hormone regulation. During the last few decades the fatty acid content of the U.S. diet has shifted so it now contains much higher levels of omega-6 and less omega-3 fatty acids. When long-chain omega-6 fatty acids predominate in the phospholipids of cell membranes, the
production of pro-inflammatory type-2 prostaglandins (PGs) and type-4 leukotrienes (LTs) are encouraged: whereas, the presence of omega-3 fatty acids promotes the production of anti-inflammatory PGs and LTs. (1,2)

Omega-6 fatty acids, mainly arachidonic acid, have been shown to initiate an inflammatory process by triggering a flux of inflammatory PGs and LTs. (34) Omega-3 fatty acids, mainly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), compete with the omega-6 species for the enzyme prostaglandin synthetase. Omega-3 fatty acids trigger secretion of less potent 5-series LTs and anti-inflammatory PGs of the 3 series (P[E.sub.3], P[I.sub.3] and thromboxanes-[A.sub.3]). (4-9) Consequently, supplementation with EPA and DHA promotes the production of less potent PGs and LTs, resulting in a decrease in the formation of inflammatory mediators. (10-13)

The exact mechanism of action by which omega-3 fatty acids favorably modify cardiovascular disease and associated disorders is not yet fully confirmed. Evidence suggests an increased intake of EPA and DHA results in an increase of EPA and DHA in tissue, cellular lipids, and circulatory lipids. (14) In parallel, they result in a simultaneous reduction of omega-6 fatty acids in the body. (14) This fatty acid shift is predominantly marked in cell membrane-bound phospholipids and results in alteration of the physicochemical properties of cell membranes. This favorably modifies cellular functions, including cell signaling, gene expression, biosynthetic processes, and eicosanoid formation. (15)

Human studies have revealed the ability of EPA and DHA to significantly reduce circulating levels of blood triglyceride and very low-density lipoprotein (VLDL), which have been associated with increased risk of cardiovascular disease. (16,17)

Krill oil is extracted from Antarctic krill, Euphausia superba, a zooplankton crustacean rich in phospholipids carrying long-chain omega-3 PUFAs, mainly EPA and DHA. Krill oil also contains various potent antioxidants, including vitamins A and E, astaxanthin, and a novel flavonoid similar to 6,8-di-c-glucosylluteolin, but with two or more glucose molecules and one aglycone.

Krill oil has a unique biomolecular profile of phospholipids naturally rich in omega-3 fatty acids and diverse antioxidants significantly different from the usual profile of fish oils. The association between phospholipids and long-chain omega-3 fatty acids highly facilitates the passage of fatty acid molecules
through the intestinal wall, increasing bioavailability and ultimately improving the omega-3:omega-6 fatty acid ratio. (18,19)

Materials and Methods

A 12-week, double-blind, randomized trial was conducted comparing krill oil to high EPA and DHA (3:2 ratio) fish oil and placebo. Eligible patients were 18-85 years and had at least a six-month diagnosis of mildly high to very high blood cholesterol (193.9-347.9 mg/dL) and triglyceride levels (203.8-354.4 mg/dL). Patients with familial hypercholesterolemia, severely high cholesterol (>349 mg/dL), pregnancy, known or suspected allergy to fish or seafood, known alcohol or drug abuse within the previous year, known coagulopathy or receiving anticoagulant therapy, or co-morbidity that would interfere with study results were excluded from the study.

Enrolled patients were randomly assigned to one of four groups:
* Group A: Krill oil (2-3 g once daily) Body Mass Index (BMI) < 30-2 g/day BMI > 30-3 g/day
* Group B: Krill oil (1-1.5 g once daily) BMI < 30-1 g/day BMI > 30-1.5 g/day Follow-up 500 mg/day for 90 days
* Group C: Fish oil (3:2) containing 180 mg EPA and 120 mg DHA per gram (3 g once daily)
* Group D: placebo (3 g once daily)

Patients were allowed to continue lipid-lowering medications at the usual daily dose and asked to report any change in dosage. Natural health products were discontinued for a two-week washout period prior to study initiation and thereafter for the study duration. Patients were asked to record concomitant medications taken daily.

The primary parameters tested were blood glucose, cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Fasting blood lipids and glucose were analyzed at baseline as well as 30 and 90 days after study initiation for all groups, and at 180 days for the 30 patients in Group B.
Statistical Rationale and Analysis

A sample size of 120 patients (30 patients/group) provided 90-percent power to detect a 15-percent change in total cholesterol from baseline to three months.

Within-group differences reflecting changes over time for the same patient were assessed for statistical significance with the Paired Student's t-test. Between-group differences were assessed with planned comparisons of one-way analysis of variance.

Results

One-hundred-twenty patients with a mean age of 51 years (standard deviation 9.46) and ranging between 25 and 75 years were enrolled in the trial. BMI, a tool indicating weight status in adults, was calculated according to the metric formula (\(\text{[weight in kilograms/(height in centimeters) \times (height in centimeters) \times 10,000]}\). Of the 120 patients enrolled, 30 (25%) had moderate-to-severe obesity, with a BMI higher than 30. Sixty-four (53%) subjects were overweight, and 26 (22%) were normal weight, with a BMI between 25 and 30 and lower than 25, respectively. Women had a higher mean BMI (28.2+ or -5.1) compared to men (25.4+ or -3.9) (p<0.001).

Among the 60 patients in the two groups receiving krill oil, 42 (70%) had a BMI of 30 or less. In Group A, 19 patients received 2 g krill oil daily and the remaining 11 received 3 g daily. In Group B, 23 patients were treated with a daily dose of 1 g krill oil and 7 with 1.5 g. All patients in Group B continued for an additional 90 days with a maintenance dose of 500 mg krill oil daily.

Baseline analysis of demographic criteria, laboratory data including total cholesterol and triglyceride levels, comorbidity, and concomitant medication at baseline showed no significant differences among the four groups (p=0.102-0.850).

After 12 weeks of treatment, patients receiving 1 or 1.5 g krill oil daily had a 13.4-percent and 13.7-percent decrease in mean total cholesterol, from 236 mg/dL and 231 mg/dL to 204 mg/dL (p=0.000) and 199 mg/dL (p=0.000), respectively (Tables 1 and 2). The group of patients treated with 2 or 3 g
Krill oil showed a significant respective reduction in mean total cholesterol of 18.1 and 18 percent. Levels were reduced from a baseline of 247 mg/dL and 251 mg/dL to 203 mg/dL (p=0.000) and 206 mg/dL (p=0.000), correspondingly (Tables 3 and 4). In comparison, people receiving 3 g fish oil had a mean reduction in total cholesterol of 5.9 percent, from a baseline 231 mg/dL to 218 mg/dL (p=0.000) (Table 5). Those enrolled in the placebo group showed a 9.1-percent increase in mean total cholesterol, from 222 mg/dL to 242 mg/dL (p=0.000) (Table 6).

An analogous effect on LDL levels was observed in all groups. Krill oil at a daily dose of 1 g, 1.5 g, 2 g, or 3 g achieved significant reductions of LDL of 32, 36, 37, and 39 percent, respectively (p=0.000). Baseline levels were decreased in the krill oil 1-g/day group from 168 mg/dL to 114 mg/dL, in the 1.5-g/day group from 165 mg/dL to 106 mg/dL, and in the 2- and 3-g/day groups from 183 mg/dL and 173 mg/dL to 114 mg/dL and 105 mg/dL, respectively. The laboratory results of patients treated daily with 3 g fish oil did not achieve a significant reduction in LDL (4.6%), with blood levels decreased from 122 mg/dL at baseline to 118 mg/dL (p=0.141) after 12 weeks. Patients receiving placebo showed a negative effect, with a 13-percent increase in LDL levels, from 137 mg/dL to 154 mg/dL (p=0.000).

HDL was significantly increased in all patients receiving krill oil (p=0.000) or fish oil (p=0.002). HDL levels increased from 57.2 mg/dL to 82.4 mg/dL (44% change) at krill oil 1 g/day; 58.8 mg/dL to 83.9 mg/dL (43% increase) for krill oil 1.5 g/day; 51 mg/dL to 79.3 mg/dL (55% increase) at krill oil 2 g/day; and from 64.2 mg/dL to 102.5 mg/dL (59% increase) at a daily krill oil dose of 3 g. Fish oil taken at 3 g/day increased HDL from 56.6 mg/dL to 59.03 mg/dL (4.2% increase). No significant decrease of HDL (p=0.850) was observed within the placebo group, with levels of HDL remaining almost stable, 56.8 mg/dL to 56.7 mg/dL.

Krill oil taken 1 g/day reduced blood triglycerides by a non-significant 11 percent, from 120.5 mg/dL to 107.2 mg/dL (p=0.114). A daily dose of 1.5 g krill oil resulted in a non-significant 11.9-percent reduction of triglycerides, from 122.7 mg/dL to 112 mg/dL (p=0.113). Subjects achieved a significant reduction of triglycerides at daily doses of 2 g and 3 g daily krill oil - 28 percent (p=0.025) and 27 percent (p=0.0228) -- decreasing from baseline levels of 160.4 mg/dL and 152.8 mg/dL to 116.1 mg/dL and 112.3 mg/dL, respectively. Fish oil at 3 g/day did not achieve a significant reduction of triglycerides.
(3.2%), decreasing from 140.9 mg/dL to 136.4 mg/dL (p=0.239). Interestingly patients in the placebo group experienced a 9.8-percent decrease in triglycerides (p=0.215).

Blood glucose levels were reduced by 6.3 percent, from 105 mg/dL to 98 mg/dL (p=0.025), in patients receiving 1 g and 1.5 g krill oil daily, and 5.6 percent, from 92 mg/dL to 88 mg/dL (p=0.011), in those receiving 2 g and 3 g krill oil daily. A daily dose of 3 g fish oil reduced blood glucose by 3.3 percent, from 90 mg/dL to 87 mg/dL (p=0.275). Placebo treatment resulted in a non-significant blood glucose increase of 0.1 percent, from 92 mg/dL to 93 mg/dL (p=0.750).

The between-group comparison showed 1 g and 1.5 g krill oil daily was significantly more effective than 3 g fish oil in reducing glucose and LDL, whereas 2 g and 3 g krill oil demonstrated a significantly greater reduction of glucose, triglycerides, and LDL compared to 3 g fish oil. Both fish oil and krill oil performed significantly better than placebo for the regulation of glucose, triglycerides, total cholesterol, and HDL.

As mentioned previously, patients receiving 1 g and 1.5 g daily krill oil continued for another 12 weeks with a lower maintenance dose of 0.5 g krill oil daily (Table 7). These patients maintained a mean total cholesterol level of 192.5 mg/dL, a reduction of 19 percent (p=0.000) from baseline. LDL was further reduced from baseline by 44 percent, a reduction from 233 mg/dL to 107.5 mg/dL (p=0.000). A moderate decrease in HDL was seen, from 36 percent increase at 90 days to 33 percent after 180 days of treatment, which was still a significant increase from baseline (p=0.000). Triglycerides were slightly decreased further to a reduction of 25 percent from baseline (p=0.000), compared to the 12-percent reduction observed after 90 days of treatment. Blood glucose decreased by 6.6 percent from baseline (p=0.20), versus the 6.3-percent decrease at 90 days.

Discussion

Arteriosclerosis is the generic term for a number of diseases in which arterial walls become thickened and lose elasticity, with atherosclerosis being considered the most important. With its effects on the brain, heart, kidneys, and other vital organs and extremities, and despite medical advancements,
atherosclerotic heart disease and stroke combined remain the number one cause of morbidity and mortality in the United States, Canada, and most Western countries. (22)

In the United States, cardiovascular disease has a mortality rate of 39.9 percent for males and 43.7 percent for females, a 15-21 percent difference from malignant disease, which ranks second. (22) It is estimated that 59.7 million Americans have one or more forms of cardiovascular disease. (22) Of the population with self-reported heart disease, 56-64 percent report restricted activity. 23-37 percent require one or more disability days per week, and 28-34 percent are unemployed because of disability or illness. (22) The primary lesion of atherosclerosis is the fatty streak, which eventually evolves into a fibrous plaque. Numerous randomized trials have proven that lowering serum cholesterol slows or reverses progression of coronary artery disease (CAD) and reduces coronary events. (22-29)

A daily intake of 1-3 g EPA and DHA or 3-9 g fish oil is currently recommended to reduce the risk of cardiovascular diseases. (22, 23) Nevertheless, epidemiological studies evaluating the effects of fish oil on coronary heart disease are contradictory, ranging from reverse associations to virtually no effect to a beneficial effect. (30-33) One issue in the efficacy of EPA/DHA may be the bioavailability of these fatty acids.

A recent study demonstrated in vivo PUFA bioavailability depends on several factors, such as the type of lipids in which they are esterified, their physical state; i.e., lipid solution or colloidal particle systems, and the presence of co-ingested lipids. (18) In vivo PUFA absorption was evaluated by fatty acid analysis of thoracic lymph of ductcannulated rats after intragastric feeding of dietary fats. (19) Evidence demonstrates oral essential fatty acid supplementation in the form of phospholipids is more effective than triglycerides in increasing concentrations of long-chain PUFAs in liver and brain. (18-19) DHA is better absorbed when delivered by liposomes than by fish oil (relative lymphatic absorption equal to 91 percent and 65 percent after liposome and fish oil administration, respectively). The best bioavailability of DHA delivered by liposomes is revealed by an increase in DHA proportions in both lymphatic triacylglycerols and phospholipids, compared to a fish oil diet. (18, 19)

Krill oil is a complex combination of multiple active ingredients with synergistic bioactivity. The exact mechanism of action for krill oil’s lipid-lowering effects is not yet entirely clear. However, krill oil’s unique biomolecular profile of omega-3 (EPA/DHA) fatty acids already incorporated into phospholipids has exhibited a lipid-lowering effect on the level of the small intestine, which distinguishes krill oil from other known lipid-lowering principals. (18, 19) Werner et al demonstrated essential fatty acids in the
form of phospholipids were superior to essential fatty acids as triglycerides in significantly decreasing
the saturated fatty acid ratios of liver triglycerides and phospholipids (each \( p < 0.05 \)), while significantly
increasing the phospholipid concentrations of the long-chain PUFAs (\( p < 0.05 \)). (19)

LDL oxidation is believed to increase atherosclerosis through high serum LDL levels inducing LDL
particles to migrate into subendothelial space. The process by which LDL particles are oxidized begins
with lipid peroxidation, followed by fragmentation to short-chain aldehydes. At the same time, lecithin is
converted to lysolecithin, a selective chemotactic agent for monocytes, which become macrophages that
ingest oxidized LDL. The new macrophage becomes engorged with oxidized LDL cholesteryl esters and
becomes a foam cell. Groups of foam cells form a fatty streak, the earliest indication of atherosclerosis.
(34, 35)

The unique molecular composition of krill oil, with its abundance of phospholipids and antioxidants, may
explain the significant effect of krill oil for blood lipid regulation. In comparison to fish oil, krill oil
significantly lowered blood lipids at lower doses.

The effect of fish oil on cardiovascular disease is tempered by the presence of methyl-mercury in many
fish. (33) In fact, the U.S. Food and Drug Administration has advised pregnant women and women who
may become pregnant not to eat swordfish, king mackerel, tilefish, shark, or fish from locally
contaminated areas. (36) Therefore, it may be prudent to obtain these essential fatty acids via
supplementation. Krill oil, and most fish oil concentrates, are molecularly distilled to remove heavy
metals.

Conclusion
Atherosclerotic cardiovascular disease is a major health problem in the Western world, with CAD being
the leading cause of mortality in the United States. Extensive observational epidemiologic data strongly
associate high CAD risk to elevated total and LDL cholesterol and low levels of HDL cholesterol.

Extensive clinical trial evidence has established that favorably altering dyslipidemias produces clear
improvements in CAD end points. (15-17)

The results of this clinical trial demonstrate that daily doses of 1-3 g krill oil are significantly more
effective than 3 g EPA/DHA fish oil in the management of hyperlipidemia. Furthermore, a maintenance
dose of 500 mg krill oil is significantly effective for long-term regulation of blood lipids. The unique
molecular composition of krill oil, which is rich in phospholipids, omega3 fatty acids, and diverse antioxidants, surpasses the profile of fish oils and offers a superior approach toward the reduction of risk for cardiovascular disease.

Table 1. Results of Krill Oil (1.0 g/day) on Lipids

<table>
<thead>
<tr>
<th>1.0 g Krill Oil</th>
<th>Time (d)/mg/dL</th>
<th>% Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>90.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>235.83</td>
<td>204.12</td>
<td>-13.44%</td>
</tr>
<tr>
<td>LDL</td>
<td>167.78</td>
<td>114.05</td>
<td>-32.03%</td>
</tr>
<tr>
<td>HDL</td>
<td>57.22</td>
<td>82.35</td>
<td>43.92%</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>120.50</td>
<td>107.21</td>
<td>-11.03%</td>
</tr>
</tbody>
</table>

Table 2. Results of Krill Oil (1.5 g/day) on Lipids

<table>
<thead>
<tr>
<th>1.5 g Krill Oil</th>
<th>Time (d)/mg/LM</th>
<th>% Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>90.00</td>
<td></td>
<td></td>
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<tr>
<td>Total Cholesterol</td>
<td>231.19</td>
<td>199.49</td>
<td>-13.71%</td>
</tr>
<tr>
<td>LDL</td>
<td>164.74</td>
<td>105.93</td>
<td>-57.01%</td>
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<tr>
<td>HDL</td>
<td>58.76</td>
<td>83.89</td>
<td>42.76%</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>126.70</td>
<td>111.64</td>
<td>-11.89%</td>
</tr>
</tbody>
</table>

Table 3. Results of Krill Oil (2.0 g/day) on Lipids

<table>
<thead>
<tr>
<th>2 g Krill Oil</th>
<th>Time (d)/mg/dL</th>
<th>Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>90.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>247.42</td>
<td>202.58</td>
<td>-18.13%</td>
</tr>
<tr>
<td>LDL</td>
<td>182.86</td>
<td>114.43</td>
<td>-37.42%</td>
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<tr>
<td>HDL</td>
<td>51.03</td>
<td>79.25</td>
<td>55.30%</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>160.37</td>
<td>112.07</td>
<td>-27.62%</td>
</tr>
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Table 4. Results of Krill Oil (3.0 g/day) on Lipids

<table>
<thead>
<tr>
<th>3 g Krill Oil</th>
<th>Time (d)/mg/dL</th>
<th>Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>90.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>250.52</td>
<td>205.67</td>
<td>-17.90%</td>
</tr>
<tr>
<td>LDL</td>
<td>172.81</td>
<td>105.16</td>
<td>-39.15%</td>
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<tr>
<td>HDL</td>
<td>64.18</td>
<td>102.45</td>
<td>59.64%</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>152.77</td>
<td>112.27</td>
<td>-26.51%</td>
</tr>
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</table>

Table 5. Results of Fish Oil (3.0 g/day) on Lipids

<table>
<thead>
<tr>
<th>3 g Fish Oil</th>
<th>Time (d)/mg/dL</th>
<th>% Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>90.00</td>
<td></td>
<td></td>
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</tbody>
</table>
Total Cholesterol 231.15 217.55 -5.88% 0.000
LDL 121.67 117.83 -4.56% 0.141
HDL 56.64 59.03 4.22% 0.002
Triglycerides 140.87 136.44 -3.15% 0.239

Table 6. Results of Placebo on Lipids

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Time (d)/mg/dL</th>
<th>% Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>90.00</td>
<td></td>
<td></td>
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<tr>
<td>Total Cholesterol 221.91 242.01 9.06% 0.000</td>
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<td></td>
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<tr>
<td>LDL 136.47 154.25 13.03% 0.000</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HDL 56.83 56.70 4.00% 0.850</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides 143.53 129.36 -9.88% 0.215</td>
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Table 7. Effect of a Lower Maintenance Dose of Krill Oil on Lipids

<table>
<thead>
<tr>
<th>0.5 g Krill Oil</th>
<th>Time (d)/mg/dL</th>
<th>% Change</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>0.00</td>
<td>180.00</td>
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<tr>
<td>Total Cholesterol 235.83 192.53 18.90% 0.000</td>
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<td></td>
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<tr>
<td>LDL 167.78 107.47 -44.40% 0.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL 57.22 77.71 33.40% 0.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides 120.50 89.89 25.40% 0.025</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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(36.) Center for Food Safety and Applied Nutrition. Consumer advisory: an important message for pregnant women and women of childbearing age who may become pregnant about the risks of mercury in fish. College Park, MD: Food and Drug Administration, March 2001. (Accessed November 1, 2002). Ruxandra Bunea, MD--Assistant Professor, Department of Internal Medicine, McGill University; Riverview Medical Center, Montreal, Quebec, Canada. Correspondence address: 1586 Ave des Pins O. #302, Montreal, Quebec, Canada H3G 1B4. Khassan El Farrah, MD, MSc--JSS Medical Research, Montreal, Quebec, Canada. Luisa Deutsch, MD--JSS Medical Research, Montreal, Quebec, Canada.

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The Patient’s Saliva pH Readings

The Patient’s Saliva pH:

Day 8 pH of 5.2

Then after receiving 60 cc/day of juice:

Day 13 pH of 6.0,

Then after increasing juice to 120cc/day

Day 16 pH of 7.0
Background On Paragon Technologies Ltd.

Paragon Technologies Ltd., is a private environmental, medical, & health sciences R&D and consulting company. Paragon has helped successfully design, develop, and manufacture leading technologies and/or provide advanced technical analysis in a wide range of fields, spanning industry, sport, and medicine.

Paragon conducts ortho-molecular medical research on cardio-vascular, neurological, gastrointestinal, and other forms of degenerative disease.

Paragon has realized a 90+% success/recovery rate in more than 130 medical case studies it has conducted over the past 10 years. Paragon’s research team normally works together with the doctor/patient team. We provide metabolic analysis and make recommendations for nutritional intervention based on this analysis.

Paragon and it’s Director of Research Sam Bock also work with leading laboratory and university research partners to develop advanced metabolic diagnostics & medical systems for the treatment of disease, for use in toxin screening & detoxification, and for use in Olympic & professional sport. With our partners we have developed advanced metabolic diagnostics, pharma-nutraceuticals, & comprehensive nutritional interventions to enhance cellular regeneration – as applies to disease recovery and human performance.

Paragon's advanced diagnostics & treatments for degenerative disease have reversed paralysis, multiple sclerosis, rheumatoid arthritis, various cancers, and many other serious diseases and conditions. This research initially began with advanced research into developing enhanced human athletic performance for Canada’s Olympic sport development programs.

Athletes using Bock’s athletic coaching and Paragon’s metabolic diagnostics & sport equipment technologies have won numerous Olympic Gold medals, world championships, and have set more than 45 world bests and records in professional and Olympic sport.

Paragon’s clients in sport have included Nike, adidas/Reebok, and other major sports companies for commercial development of various products.

Paragon nutrition and metabolic research has affected Canadian federal environmental policy. In 1999 Bock addressed the Canadian Government’s Senate Committee on Energy, Environment and Natural Resources regarding the problematic effects of randomly produced industrial chemical by-products on the food chain and plant and animal enzyme chemistries. As indicated in the Committee’s final report, he helped persuade the Senators to recommend that the Canadian Environmental Protection Act be put into a perpetual state of review.

Bock received a degree in Economics and Environmental Science from Middlebury College in Vermont in 1982. His study of particle physics and chemistry led to his thesis, which was a an economic / scientific analysis and forecast of North America’s future energy needs and technology use, focusing on fossil fuels, nuclear power and alternative sources. While considered controversial by many at the time, it accurately forecast the decline of the American nuclear power industry due to excessive ionizing radiation and associated metal fatigue in reactor cores and heat exchangers.
Some Internet Links To The Latest Important Research As Relates To The Patient’s Recovery From Stroke

http://www.fi.edu/brain/fats.htm
http://www.fi.edu/brain/proteins.htm

Dietary supplementation with blueberries, spinach, or spirulina reduces ischemic brain damage: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WFG-4FG4B7D-5&_user=10&_handle=V-WA-A-W-WC-MsSayza-Uuw-U-aacYdyBuv-AabVceAuv-WveuAeW-Wc-U8_fmt=summary&coverDate=05%2F31%2F2005&rdoc=&orig=browse&srch=%23toc%236794%232005%2399869998%23679163218794&view=c&acct=C000000221&version=1&_urlVersion=0&userid=10&mrd=84bf4d32abbcd1869c760822d201c85f

Red yeast: http://drguberman.com/cardio.cfm

Krill oil
http://www.raysahelian.com/krilloil.html
http://www.google.ca/search?hl=en&q=%22Evaluation+of+the+effects+of+Neptune+krill+oil+on+the+clinical+course+of+hyperlipidemia%22&btnG=Google+Search&meta=  Google search

Clotting
End Notes

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