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As we begin 2019, how is mainstream medicine doing in curing the chronic diseases responsible for the vast majority of mortality among the older portion of many populations? Some would point to drugs given the honor of being in the miracle category. However, the definition of miracle in this context is a bit flaky. So-called miracle cancer cures occur only in a few rare types, mostly blood cancers. Many cancer therapies do not "get it all" and metastasis is common. Except in rare cases, the life extensions for those with metastatic cancer are pathetic with a year considered a sensational achievement.

Type 2 diabetes is not cured, it is managed or controlled and generally progresses. The pharmaceutical prevention and treatment of coronary heart disease associated with atherosclerosis is characterized by absolute benefits that indicate 95-99% do not benefit over 5 or more years. Absolute benefits also seem to be a taboo subject. Relative risk reductions are much better for getting patients to take the medication, but lead to absurd expectations.

Dealing with Alzheimer's disease involves also almost entirely treating symptoms and controlling behavior. Visit a nursing home and see the results. Research in this disease is mainly stalled in a cul-de-sac at the end of a road called beta-amyloid. The guidelines issued by the American Cancer Society for cancer prevention are so general that they are really simply recommendations for staying healthy in general and contain no recent innovations. Chemoprevention of cancer offers poor absolute benefits, limited drugs, and focusses only on limited types of cancer.

In contrast, treatment of trauma is generally excellent, and for example, treatment of stroke if characterized and treated early enough can prevent permanent impairment. Even saving those with narcotic overdose has made exceptional progress. It is the vast majority out there with chronic diseases slowly killing them that are the problem.

Humans obviously depend on food; now it takes great effort and considerable faith to design a healthy diet, and nutritional research is tarnished by flip-flops and the difficulties associated with the confounding produced by food processing or ultra-processing, the nutrient deficiencies in today's food, soil depletion of nutrients due to modern farming practices, and the impact of factory-produced protein sources like chicken, beef, etc., and finally the toxic

content not only of some foods but practically all consumer goods (e.g. out gassing of flame retardants or leaching of hormone disruptors). Half the fish marketed or served in restaurants is not what it is called on the label or menu; it is fake, cheaper fish. Concentration on organic foods involves great faith which is challenged by readily observed human greed for profits, the tendency to deceive without guilt, and the low risk of detection of cheating.

Attempts to find cures for chronic diseases outside the officially approved areas (read—alternative medicine) are plagued by powerful status-quo forces, many with ample if not astounding financing from the big special interest groups which have infiltrated the media, academia, government, scientific editorial policies and professional societies naively believed to be sources of unbiased truth concern the various chronic diseases. When a highly attractive alternative or non-pharmaceutical protocol is actually supported by a number of studies published in excellent journals, the standard approach of the status-quo group is to ignore it. The Newcastle Diet to reverse type 2 diabetes is a fine example. Approaching cancer therapy from the point of view that it is a metabolic disorder is another. Treating Alzheimer's with a multiple almost 100% non-pharmaceutical approach as UCLA's Professor Bredesen does is another. Similar examples could be cited for multiple sclerosis and autism. Salvestrols for prevention and treatment of cancer, much discussed in IHN is another. Studies required to obtain regulatory approval cost multi-millions of dollars. Thus alternative medicine will continue be dismissed by the Supreme Court of evidence-based medicine. Status-quo, ego, vested interest in pet theories or even dogma, professional aspirations, especially academic and personal financial considerations all stand in the way of science being properly and effectively used for the benefit of medicine and patients.

The good news is that some appear to be finally realizing this sad state of affairs and are acting accordingly.

Wishing you and your family good health,

William R. Ware, PhD, Editor

Highlights

DIETARY FAT, THE OMEGA-3 AND OMEGA-6 FATTY ACID FAMILIES, HEART DISEASE AND RAMPANT CONFUSION

The American Heart Association in 2017 issued a *Presidential Advisory* concerning dietary fats and cardiovascular disease [1]. This advisory is remarkably consistent with the conventional wisdom which has not been modified for some time and dates back to the 1960s This statement, published in the journal *Circulation* prompted considerable counter arguments and the suggestion of cherry picking evidence, strongly biased selection of the evidence base (four studies from the 1960s) and avoiding anything that seriously contradicted the AHA point of view and recommendations. It was a lengthy defense of a decades-old position having the status of an almost sacred dogma which had been under increasing attack. It must be remembered that statements and guidelines must be suitable for a simplified summary for the general public, and the seemingly best way to prompt adherence and changes in diet is to use fear, in this case of the consequences of not complying, i.e. cardiovascular disease (CVD), heart attack and death. The official position and recommendations were as follows:

- High cholesterol and especially low-density lipoprotein cholesterol (LDL) *cause* atherosclerosis and thus heart disease.
- Consumption of saturated fat is a positive risk factor for CVD, acting by elevating LDL.
- To lower the risk and incidence of cardiovascular disease (CVD) with diet, reduce the intake of saturated fat. Replace saturated fat with polyunsaturated fat from vegetable oils, mainly omega-6 linoleic acid.
- Replacing saturated fat with polyunsaturated fat reduces incidence and induces regression of coronary atherosclerosis.

In short, the dietary daemon lurking in food supply and ready to disable or kill with CVD is saturated fat and the best choice of a substitute fat is omega-6 vegetable oils such as corn and soybean oil.

One of the principal pillars supporting the above position, actually only a hypothesis, involves the long-standing belief, having the status of a sacred dogma, that LDL causes cardiovascular disease. It is also a pillar supporting the hugely profitable pharmaceutical interventions for lowering both total cholesterol and LDL not only with statins but other more recent drugs, the latest being very expensive. There is also a corollary belief that for LDL, the lower the better. Readers are reminded that hypotheses are not proven but stand until falsified. Recall the famous black swan argument. The most systematic, detailed and completely documented attempt to falsify this hypothesis has recently appeared.[2] This paper also reviews the merits of statin therapy in primary and secondary prevention and uses absolute benefits to demonstrate the extreme exaggeration of benefits (their Table 1). The perspective is authored by a number of prominent and respected medical scientists. All aspects of the hypothesis are challenged and supported by 107 citations. Rather than providing a point-by-point

summary, the reader is referred to the very readable paper. Google *LDL does not cause cardiovascular disease.*

There is also the matter of those with lifelong familial hypercholesterolemia (FH) who have lived from an early age with their coronary arteries bathed with high levels of LDL and yet remarkably a population study (age 31-59) found that half of all those with FH had coronary calcium scores of zero, i.e. no coronary atherosclerosis![3] This score reflects the atherosclerosis plaque burden. A score of zero is also commonly found in about 50-60% of similar non-FH populations with vastly lower arterial LDL exposure. See the editorial in the December 2018-January 2019 IHN.

The AHA advisory takes a dim view of coconut oil simply because it raised LDL. However, coconut oil contains medium chain triglycerides MCT) which are composed of three saturated fatty acids attached to a glycerol molecule. They are either used immediately as an energy source or converted in the liver into ketones which are also energy sources, and in addition cross the blood brain barrier and provide an energy source for brain cells independent of insulin. This unique source of brain nutrition has important implications in mild cognitive impairment and dementia including Alzheimer's disease. In her recent book concerning the health benefits of coconut oil, Dr. Mary Newport includes Parkinson's disease, mild cognitive impairment and Alzheimer's dementia, amyotrophic lateral sclerosis and multiple sclerosis.[4] Condemning coconut oil or MCT oil ignores these benefits.

Central to the AHA position outlined above is that saturated fats (actually fatty acids) are bad and that omega- polyunsaturated fatty acids are innocuous or beneficial. A recent attempt to falsify this hypothesis and the notion that replacing saturated fat with polyunsaturated fat is beneficial was recently published in the *Mayo Clinic Proceedings*.[5] The case presented against the hypothesis is summarized as follows:

- Ten randomized controlled crossover trials found high intake of saturated fat, up to 50% caloric intake, had little effect or none at all on blood LDL.
- Two meta-analyses found no association between CVD mortality and saturated fat intake. Furthermore, in 10 studies of individuals with stroke, 3 found no difference in saturated fat intake between stroke patients and healthy individuals and in 7 studies where stroke patients had eaten significantly less saturated fat.
- Meta-analysis of 16 long-term cohort follow-up studies found a *reduction in risk* for all-cause mortality, atherosclerosis related heart disease, stroke and incident diabetes associated with consumption of saturated fat. The greatest reduction was found for individuals with the highest diary consumption of saturated fat vs. those with the lowest.
- Meta-analysis of 16 similar studies found high-fat dairy intake was *inversely* associated with fat accumulation (adiposity) and unassociated with either CVD or diabetes.
- Meta-analyses of dietary trials found for coronary heart disease (CHD) only trivial or no benefit at all from decreasing saturated fat intake and/or increasing intake

of polyunsaturated fatty acids. Saturated fat intake also lowered the levels of small dense LDL particles and raised the levels of large buoyant LDL particles, both changes in the direction of benefit rather than risk for initiation of CHD.

Thus there is substantial evidence falsifying one of the central hypotheses of the AHA position.

Finally, there is the very important issue with the AHA recommendations favoring commercial oils high in omega-6 fatty acids since this ignores the vast amount of evidence that what is critical in this context is the omega-6/omega-3 ratio (6/3 ratio). The primary food sources of these two fat families are alpha-linolenic acid (ALA), a precursor to the omega-3 fatty acids EPA and DHA, and linoleic acid (LA), precursor to arachidonic acid and other longer chain omega-6 fatty acids. Both biochemical chains use the same enzymes at each step. It has been estimated and widely discussed that we have evolved to favor a 6/3 ratio of 2 to 1. In the developed world consuming the modern diets, this ratio is always significantly elevated. For example, it is estimated currently that average values are 4 in Japan, 15 in the UK and Northern Europe, 17 in the US and 38-50 in urban India.[6] This large increase in the ratio accompanied the acceptance some time ago of the saturated fat is bad hypoesthesia and promotion of margarine and commercial (industrial) seed oils such as corn and soybean for a healthy diet. These commercial oils are also inexpensive and convenient. In their book *Super Fuel* Mercola and DiNicolantoino discuss and document the following fascinating intra-country population studies of this dietary fat ratio, mostly in the context of heart disease.[7]

- **GREENLAND INUITS**. Greenland Inuits have a diet that is high in fish and other marine foods. On average they get about 2% of their calories from omega-6 and 5% from omega 3. Thus the 6/3 ratio is 0.4. Between 1974 and 1976 mortality from ischemic HD in age group 45-65 was 5.3% vs 40.4% in US (8X). In addition, CVD was 7% vs. 45% in the US. Greenland Inuits are known for low rates of diabetes, autoimmune and inflammation related disorders as well as low incidence of chronic diseases. A study reporting in 2002 found a 6/3 tissue ratio of 1:1 in Greenland and 12:1 in Japan and 50:1 in US. Japan has an omega-3 intake between Greenland and US, but still has a low tissue ratio.

- **OKINAWA**. A remote island but part of Japan is among the Blue Zones with remarkable health and longevity.[8,9] Before WW II Okinawans had the highest longevity in the world and low rates of stroke, heart diseases, and cancer. They cooked mostly with pork fat. After WW II this changed as they bought into the saturated fat is bad dogma being aggressively promoted by the US nutritional experts and the food industry. By 1990 they were consuming 6 to7 times as much omega-6 as omega-3 whereas in the rest of Japan it was only about 4 times. They no longer held the longevity gold medal worldwide and in Japan, men younger than 50 (who had been exposed to enhanced omega-6 intake) had the highest all-cause mortality in Japan whereas the older generation were

apparently still benefiting from the pre-war diet. From about 1950 to the early 1990s, the 6/3 ratio was about 3:1. Then the intake of dietary omega-6 fatty acid increased from 4 g/day to 12 g/day in 1970. During this 20 year period there was an increase in a number of different types of cancer. The increase in lung cancer is especially interesting since only one of the two types is related to smoking. More than half the lung cancer deaths after 1950 now included an increase of the type not related to smoking. In fact, animal studies indicate that corn oil which is high in omega-6, promotes the non-smoking type of lung cancer whereas omega3- fats inhibit it.

- **INDIA**. The story from India is the same but it develops in a different fashion. A study of heart disease mortality involving more than a million railway workers between 18 and 55 years of age was conducted between 1958 and 1962. It was found that more than six times as many workers died from heart disease in southern India as compared to northern India and the average age at death in southern India were 10 years lower than in the north. Among those who did manual work, mortality was 15 times higher among those in the south compared to the north. However, fat consumption was 19 times higher in the north than the south. These mortality results were confirmed in another study conducted in 1963-4 and at this time saturated animal fats including diary made up the majority of the dietary fat in the north but in the south the major source of dietary fat came from peanut and sesame oils which are high in omega-6 fat, and saturated fat consumption was low. In the north where fat intake contributed about 23% of total calories, most came from ghee, milk fat and fermented milk products, i.e. mostly saturated fat. It is hard to find a better example of observations contradicting the conventional wisdom that was at that time rapidly developing in the US regarding the alleged dangers of saturated fat. The experience in India also highlights the problems with using seed oils high in omega-6.

Thus while there seems to be no question that both families of these fatty acids are important, the ratio appears to be what is critical. It is beyond the scope of this discussion to cover the quite considerable biological and physiological evidence justifying the concern about having a high 6/3 ratio. As will also be discussed in this issue are the inconsistent results in addressing the question of dietary and supplementary and prescription omega-3 fatty acids in the context of cardiovascular disease and mortality. Confounding by omega-6 intake is never considered. In addition, there is evidence that oxidized linoleic acid is a significant player in coronary heart disease.[10] Frying with many omega-6 rich oils can result in unhealthy oxidized linolenic acid. Using saturated fats such as coconut oil or butter avoids this problem.

An interesting aspect of the 6/3 ratio is the influence of insulin on the conversion of ALA to EPA and DHA. The conversions are controlled and facilitated by enzymes. Elevated insulin inhibits the third step on the way from dietary ALA to EPA and DHA. High levels

of insulin also increase the metabolism of the dietary omega-6 fatty acid. This means that individuals with insulin resistance, metabolic syndrome, or diabetes can be come deficient in these two vital omega-3 fatty acids and suggests the potential value of supplementation.

One implication of the above is that since the same enzyme converts the dietary parent omega-3 and omega-6 fats to the first metabolite, they compete and high omega-6 intake reduces the metabolism of omega-3 food derived fatty acids. In addition, diets high in salt increase the need for EPA and DHA since reduced salt diets reduce the activity of two critical enzymes.

One is left to wonder about the motivation of the AHA in their Presidential recommendations and question the scientific integrity of the project.

CARDIOVASCULAR RISK REDUCTION WITH OMEGA-3 FATTY ACIDS (FISH OIL)

In 2017 the American Heart Association published a Scientific Advisory which was mainly a systematic review of the evidence concerning the above subject.[11] The conclusion was that omega-3 polyunsaturated fats supplements were recommended for patients with recent heart attacks, and to prevalent heart failure in those without preserved left ventricular function. Specifically not recommended was this intervention for diabetics or prediabetics to prevent coronary heart disease (CHD), incident stroke in those with high cardiovascular disease (CVD) risk and recurrent atrial fibrillation and for primary prevention of CHD. These negative recommendations were primarily dictated by lack of satisfactory evidence even in the presence of several favorable studies. These recommendations are consistent with a recent Cochrane study[12] (see also news release July 18, 2018 available on internet). Most of the studies examined by Cochrane used supplements but a few estimated intakes from fish to enhance intake. No satisfactory evidence was found to justify use of omega-3 supplements to reduce the risk of heart disease.

A study just published (REDUCE-IT) has suggested that these negative views may need revision. This study used a drug (Vascepa) form of eicosapentaenoic acid (EPA) made by simply forming a derivative of the natural acid (the ethyl ester made by reacting the acid with ethyl alcohol, the beverage alcohol).[13] An advantage is a high degree of purity and acceptance by mainstream medicine because of status as a “real medicine.” However, creating the ethyl ester of EPA is a routine procedure in the process of preparing a purified product containing both EPA and DHA. The primary endpoint of the study was a composite of cardiovascular death, non-fatal heart attack, nonfatal stroke, coronary revascularization (i.e. artery bypass operation or angioplasty), or unstable angina. The secondary endpoint simply omitted the revascularization and angina, viewed by some as soft endpoints, the inclusion of which can provide deceptive

elevation of benefit. The trial was randomized, double blind, placebo controlled and focused on individuals receiving statin therapy and having elevated fasting triglycerides 135-499 mg/dL (1.52-5.63 mmol/L), a recognized risk factor. About 8000 patients were enrolled with about 70% qualifying to be considered secondary prevention (established cardiovascular disease). The dose was 4 g/d of ethyl EPA or a placebo. Compared to most previous studies, this was a high dose. When ingested, the drug is converted back to EPA form in fish oil and absorbed and thus there is no difference between this intervention and straight purified EPA from fish oil, but fish oil also contains as well the omega-3 fatty acid (DHA). Note all patients were on low, moderate or high statin therapy and a bit over half had diabetes.

The results were somewhat impressive. For the primary endpoint, there was a 5.8% absolute risk reduction and the number needed to treat to prevent one event over 5 years (NNT), was 17. For the secondary endpoint it was 3.6% with a NNT of 25. The prevalence of patients with endpoint events over 5 years was independent of achieved triglyceride levels at year 1. Over 1 year the median triglyceride levels decreased by 18% in the EPA group and increased by 2.2% in the placebo group. At baseline, the median blood EPA level was 26 µg/mL with a range of about a factor of 2. The EPA therapy increased this level to about 180 µg/mL. A Japanese study reported in 2007 found that 1.8 g/day of EPA ethyl ester produced a similar increase (170 µg/mL with a dose of 1.8 g/day of the ethyl EPA). However, in this trial absolute benefits of 0.25% for primary prevention and 2% for secondary prevention were observed,[14] but plasma EPA values at baseline were significantly higher in the Japanese study (approx. 100 µg/mL}, consistent with the much higher fish consumption in this population, an important point.

Thus there is an indication of the importance of dose as well as a dependence on baseline EPA levels. Incidentally, in the Japanese study, the ratio of EPA to a metabolite of the omega-6 dietary source was about 0.6 at baseline in both the intervention and control groups, a number in line with the modern Japanese omga-6/omega-3 ratio of about 1.7. The significance of this ratio is discussed in the first piece in this issue. However, is rare in this type of study to even consider confounding by the omega-6 intake.

The dose dependence of absolute benefit will require more studies. However, if one decides to take 4g/d, then the prescription drug Vascepa runs about $300 US per month, whereas a highly purified EPA sold over the counter costs about $200 US. Thus a very important question is whether or not the presence of DHA interferes with the beneficial action of EPA. Typical prices on Amazon for EPA/DHA at a ratio of 2:1 would run $30 US for about 4g/d of EPA for a month. Obviously, there is no incentive either for a pharmaceutical company or a supplement formulator to conduct a 5-year study of 5000 or more subjects to answer the dose dependence and interference by DHA questions. The baseline omega-6/omega-3 ratio in the REDUCE-IT cohort could have

been 15-50. Confounding by the unfavorable effect of omega-6 fatty acids discussed in this issue was not evaluated.

Thus it appears that only high doses of EPA have benefit and this applies only to populations with low baseline EPA. While by clinical trial standards, a large one, still found about 94% failed to benefit from prescription EPA, and yet if they have paid for the drug would have cost $3600 US per year. Before undertaking such a venture, knowledge of ones calcium score would be useful since there appears to be a 50-50 chance it would be zero (but this depends on age) and the risk of the events at issue would be negligible.

HEALTHY VS. UNHEALTHY AGING AND LONGEVITY. THE COMPLEX ROLE OF EVOLUTION AND NUTRITION

We frequently hear the conventional wisdom that we get all the vitamins and minerals we need from our modern diet, and supplements are dangerous because they are unregulated, can be taken in too high doses, and are with increasing frequency found to have contaminants judged dangerous. Interestingly, some common pharmaceuticals have recently also been found to contain carcinogen contamination. Population studies focused on modern countries seem always to find a significant if not major fraction deficient in essential micronutrients i.e. those that the body does not make but must come from external sources such as food, water or the sun. There is a good chance that these deficiencies are important. For example, selenium is necessary for the function of 25 enzymes, magnesium is necessary for 600 as enzyme cofactors and 200 as necessary for enzyme activators. Nor do we make any of the 600 carotenoids synthesized by plants, some of which are vital for health. Enzymes which are in fact specialized proteins, act like catalysts to assist in carrying out the synthesis of countless biochemicals needed by our multitude of processes and pathways starting in gestation and only ending at death and are essential to life and health. They are made from amino acids. Messenger RNA provides the blueprint.

If one wants an example of the complexity of what goes on inside of us and the role of the food we eat, these essential mineral numbers are a good start. In addition, consider just two essential chemicals humans do not make, vitamin C and vitamin D. The former comes mostly from fruit, the latter by a process initiated by ultraviolet light absorbed by cholesterol in the skin. Severe deficiencies produce scurvy and rickets. Scurvy was fatal for many early sailors. Some think modern populations may have subclinical scurvy.

The notion of the adequacy of diet in supplying all our needs for micronutrients was discussed in the February 2011 IHN wherein the following table was presented showing the extent of **deficiencies** found by a large US population survey. It provides the

percentage of the population that *did not* meet the estimated average requirement (EAR) for each nutrient. MVMS = multivitamin/mineral supplements.

Nutrient	Food Only, %	Food + MVMS, %
Potassium	100	100
Vitamin D	94.3	74.6
Choline	91.7	91.6
Vitamin E	88.5	67.1
Vitamin K	66.9	62.8
Magnesium	52.2	46.6
Calcium	44.1	39.5
Vitamin A	43	35
Vitamin C	38.9	31.2
Zinc	11.7	9.6

This table[15] contains only selected important vitamins and minerals and it is obvious that for a significant number, deficiency is large. Other vitamins and minerals with deficiencies between 10% and 4% include thiamin, riboflavin, niacin, vitamin B6, folate, iron, and copper. It is emphasized that the EAR probably seriously underestimates the threshold for deficiency and certainly does if optimum health is the issue. Furthermore, these numbers are based on 2007-2010 US data. In the subsequent 8 years, nutrient content of foods and intake have probably decreased due to ultra-processing and soil depletion and changes in dietary patterns. Surveys which find significant or even profound deficiencies in many populations are based on standards which may actually be much too conservative.[16] Determining optimum amounts for health in large populations present an almost unsurmountable challenge. The answer for vitamin D is still being debated.

Possibly the most important leader of the opposition to this flawed view of the adequacy of modern diets and the importance of supplements is Dr. Bruce Ames, Professor Emeritus of biochemistry and molecular biology at the University of California, Berkeley, and senior scientist at Children's Hospital Oakland Research Institute. He has published several articles directly related to the role of micronutrients in human biochemistry[17-19] and many more indirectly related. He has very recently published a definitive perspective titled *Prolonging healthy aging: longevity, vitamins and proteins* in the *Proceeding of the National Academy of Science* (US).[20] This paper provides the basis for the following discussion.

In 2006 Professor Ames proposed the *Triage Theory,* an intriguing hypothesis based on evolutionary considerations that view vitamins and minerals from an unconventional perspective.[18] The term triage is nicely illustrated by what happens when one goes to the hospital ED (aka ER) and is seen by a triage nurse who decides who needs urgent attention and who can sit for hours waiting, and then attempts to rank all those in-

between. This paper was reviewed in the June 2010 IHN. Vitamins and minerals are segregated into two categories. One involves those that are essential to survival and reproduction. The vitamin/mineral dependent proteins involved, including enzymes, are preferentially retained or conserved when there is a shortage, e.g. famine or multiple chronic deficiencies.

The other class includes vitamin and mineral dependent proteins needed for maintaining long-term health. These may reach dangerously low levels due to this triage driven conservation, thus leading to an increase in the so-called diseases of aging since the associated adverse results such as those due to DNA or mitochondrial damage may require a long time to develop clinical symptoms. Thus this damage is generally asymptomatic until later in life. This might also be termed evolution related triage of a significant number of vitamin and mineral dependent biochemical processes. Compensation driven by the importance of survival and reproduction favors younger individuals and as they get older they suffer from its insidious effects, no doubt including the chronic diseases of aging. Thus Ames introduces the concept of *survival* and *longevity* vitamins and minerals. The term vitamin in this context includes many biochemicals most readers would not recognize as vitamins. However, it is not that simple since some survival vitamins and minerals can also be identified as longevity ones. Ames also identifies what he calls *conditional vitamins* which are synthesized by the body but not necessarily at levels necessary for optimum health. Living organisms of course do not synthesize minerals or convert one mineral to another—all must come from external sources. This is of course the essential aspect of the definition of an element. A large percentage of all the existing elements are involved in human biochemistry, either as cofactors, activators, or associated with molecules in many cells (e.g. iron and iodine).

The details provided by Ames concerning the triage theory in both the main text and supplemental material of the recent paper and the 2006 paper[18] are too voluminous to include in this discussion. However, he proposes a relatively simple approach to achieving the goals at issue. Have sufficient take of the well-known vitamins and minerals from diet but it is not clear that this can be accomplished without supplementation. There are of course many vitamin/mineral formulations, even available online from physicians such as Dr. Julian Whitaker (forward), Dr. Joseph Mercola, and what appears to be a safe source, the Life Extension “One a Day’ or “Two a day” formulations. He also emphasizes selected longevity vitamins indicated by considerable evidence. Included below are those along with significant food sources.

- α-carotene. Carrots cooked or juiced, canned pumpkin.
- β-carotene. Aside from those also important for α-carotene, they are spinach, sweet potato, collards, kale and turnip greens.
- β-cryptoxanthin. Pumpkin cooked, papayas raw.

- Lutein and zeaxanthin. Spinach, kale, turnip greens, collards. Among more common vegetables, peas and broccoli.
- Lycopene. Tomatoes and derivatives of tomatoes such as paste, cooked or canned. Cooking releases lycopene.
- Ergothioneine. Kidney or liver, black and red beans and oat bran.
- Pyrroloquinoline quinone. Parsley, green pepper, spinach, kiwi fruit, fermented soybeans (natto), tofu (bean curd).

This list is of course entirely consistent with the common advice to eat a wide variety of fruits and vegetables. However, it is common to satisfy hunger with ultra-prepared, junk and convenience food, to dislike many vegetables and to find fruits in many locations very expensive. Adding ample fruits and vegetables to a common modern way of eating is thus problematic and probably inconvenient compared to opening prepared food packages. The old fashioned way of eating only home grown or locally acquired fruit and vegetables that were never sprayed with anything and eating mostly home-cooked meals is for many cultures now only a thing of the past.

The central problem for optimum health through diet is of course the amounts needed and if supplementation is required. The answer depends importantly on the individual status of these nutrients and this is obviously highly variable in and depends not only on eating habits but education, presence or absence of poverty and local availability and the nutritional quality of the food. There are no comprehensive blood and urine tests along with reference ranges that accompany many of the chemicals at issue and there is growing suspicion that commonly used reference levels when the chemicals can be measured are not really evidence based. Furthermore, tissue levels may differ importantly from blood levels, and it is highly unlikely that tissue level assays will ever become common. The patient sitting in the physician's examining room is truly a black box and modern medicine gets only to peek at the big picture. The necessary studies are difficult, require long follow-up, and are so easily confounded that this makes such research either professionally unattractive or the results potentially useless. In many cases there are no satisfactory studies addressing optimum amounts of most micronutrients and how they vary from one person to the next. A simple solution is first to eat a highly varied diet which includes at least one of the major sources of each the nutrients listed above, although not necessarily every day. To play it safe, it might be wise to also take a really well formulated multivitamin/mineral supplement, paying attention in particular to the amounts of vitamin D and magnesium since they may be too low. In addition, men and post-menopausal women should probably avoid iron supplements since building up high body stores of ferritin is undesirable, although blood donation neatly solves this problem. Supplementing with large amounts of calcium can disturb the healthy magnesium/calcium intake ratio. [21]

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