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Clerk of Science and Technology Sub-Committee I
House of Lords
London SW1A 0PW

3rd March 2009

Dear Professor the Lord Krebs,

RE: the House of Lords Science and Technology Select Committee: Call for Evidence: Nanotechnologies and Food.

I submit the information below on the recommendation of Professor David Tolfree, Vice President - Africa/Europe of the Micro and Nanotechnology Commercialization Education Foundation (MANCEF) http://www.mancef.org/

My general interest is how better nutrition can help prevent the modern diet induced "diseases of civilization" and includes the potential of nanotechnology food products. I am currently a post-doc researcher at the Institute of Environmental Sustainability, Biological Sciences, Swansea University, UK and likely to move soon to do post-doc research elsewhere.

On behalf of Swansea University, UK, I spoke about preventing diet induced disease on BBC Radio 4 on 29th May 2008. I was paid as a consultant to talk to Kellogg's® (cereal company) nutritionists about preventing diet induced disease in December 2007 (cereals are truly humanity's double-edged sword).

The information I provide is based on my latest (2009) review of peer reviewed scientific research publications, including my own. For example:

Robson A (2006) Shellfish view of omega-3 and sustainable fisheries. Nature 444 (7122), 1002 http://www.nature.com/

Robson A (2008) Preventing Diet Induced Disease. Proceedings from the 13th International Conference of the Commercialization of Micro and Nano Systems, held August 27-31, 2008 in Puerto Vallarta, Mexico http://mancef-coms2008.org/

Robson AA (in review) Preventing Diet Induced Disease. Nutrition Research Reviews http://journals.cambridge.org/action/displayJournal?jid=NRR

Please do not hesitate to contact myself if the committee requires any further information. I would be honoured to give oral evidence at Westminster that has the potential to help prevent the modern diet induced disease epidemic. To help prevent the diet induced diseases of civilization policy makers, nanotechnologists, food producers and consumers need to be made aware of the causal mechanisms of disease by understanding how people die. The fact that modern diet induced inflammatory eicosanoids are major mediators of mortality is not widely known in the public domain, even though the extensively used drug Aspirin is a cox-enzyme blocker that prevents the formation of inflammatory eicosanoids.

Yours sincerely,

Dr Anthony Robson

## Questions answered

## State of the science and its current use in the food sector

The answer to the question below is referenced using superscript Arabic numerals in parentheses. Please refer to the Appendix on page 12 for further information. Acting on the information in the appendix would be a great service to public health.

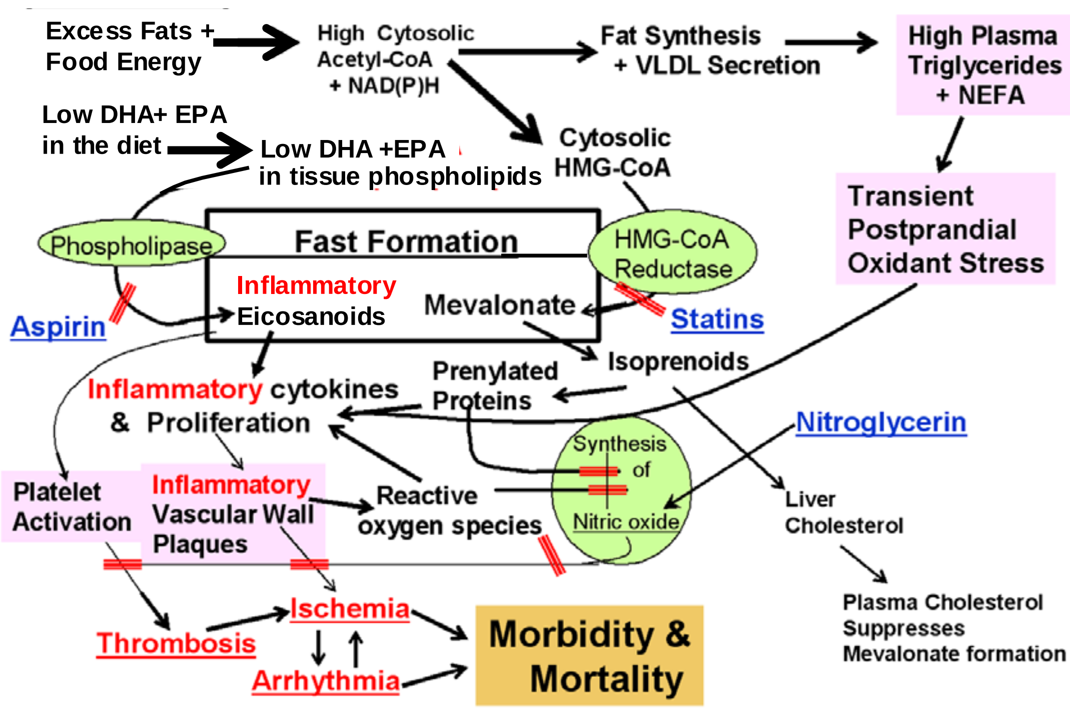
- What are the main potential applications and benefits of nanotechnologies and nanomaterials in the food sector, either in products or in the food production process?

1. What the World needs is a joined up and sustainable food policy that makes the best, and most appropriate use of the technologies at our disposal. You might be surprised, or not, of how few experts there are in this area - a lot of hype, misinformation and biased views, often based on the distortion of scientific facts and of course deliberate intentions to mislead for political and commercial reasons.

2. Nanotechnology food products have great potential to help prevent unnecessary human suffering and premature death, especially in future generations. Fundamental changes in the human diet, beginning with the introduction of agriculture and animal husbandry ~10 000 years ago, account for the largest burden of chronic illnesses and health problems Worldwide. In modern societies diet induced diseases typically afflict 50–65% of the adult population. Cardiovascular diseases are the number one cause of death globally (30% of all deaths) and cardiovascular diseases are predicted to continue increasing(1). In the Europe Union, brain disorders have now overtaken all other burdens of ill health at an estimated cost of €386 billion (€829 a year for each European citizen) in 2004(2) and mental ill health is predicted by the Global Forum of Health (www.globalforumhealth.org) to be in the top three burdens of ill health Worldwide by 2020. Heart disease and mental ill health can start in the foetus in the womb.

3. Primary prevention of cardiovascular disease and mental ill health starts, crucially, with maternal nutrition before the inception of pregnancy and continues throughout life of the new born and includes consuming more DHA, EPA and ALA (alpha-linolenic acid) omega-3 fats and bio-available brain minerals and less LA (linoleic acid) omega-6 fat (e.g. seed and nut oils) to enhance DHA and EPA synthesis from ALA, so tissues have less intense inflammatory eicosanoid action (e.g. ~0.35-3.5 g DHA + EPA $day^{-1}$ based on a 2000-kcal diet dependant on LA intake). The fats and oils from aquatic based-foods contain high contents of these beneficial omega-3 fatty acids but increased consumer demand has also increased strain on the ability of the World's fisheries to meet demand from wild capture. Molecular biology now allows the engineering of oilseeds for the production of DHA + EPA omega-3 HUFAs in a seed oil with an omega-3:6 ratio 1.5:1 (a ratio close to that of many fish oils). Food nanotechnology may also be able engineer currently pro-inflammatory food products to reduce the formation of inflammatory

mediators - eicosanoids, cytokines, and reactive oxygen species and increase the formation of anti-inflammatory mediators termed resolvins (Figure 1). Uncontrolled excessive production of inflammatory eicosanoids over prolonged periods of time is associated with heart attacks, thrombotic stroke, arrhythmia, arthritis, asthma, headaches, dysmenorrhea (menstrual cramps), inflammation, cancer (such as colon, breast, kidney and prostate) and osteoporosis[3, 4]. It is important to note that if DHA and EPA oils undergo oxidation it may attenuate their beneficial effects and food nanotechnology may be able to help prevent oxidation. Further, the excessive consumption of anything may cause disease or premature death, even omega-3[e.g. 5, 6, 7].




**Example of Diet Induced Disease**

Figure 1. Low DHA and EPA dietary intake and excess food energy link diet to disease and premature death[modified from 8]. Three types of medication, Aspirin, Nitroglycerin, and Statins used widely to diminish the processes set in motion by the two nutritional factors shown in the upper left of Figure 1 are noted, to show the step in the process at which these familiar drugs intervene. It should be noted that the hydrophilic statin Pravastatin may promote the development of cancer (inflammation) by causing an increase in mevalonate synthesis in extrahepatic tissues[9-11].

4. Globally in 2005, at least 20 million children under the age of 5 years were overweight, approximately 1.6 billion adults (age 15+) were overweight and at least 400 million adults were obese[12]. The World Health Organization further projects that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese. Within the past twenty years, substantial evidence has accumulated showing that long term consumption of high glycemic load carbohydrates can adversely affect metabolism and health[13-15]. A healthy diet-plus-exercise is most effective for preventing diabetes mellitus[16]. Nanotechnology may be able to engineer the novel Neolithic and Industrial Era foods that dominate the typical modern diet (generally energy dense, nutrient poor, processed foods such as breakfast cereals, bread, cake, cookies, crackers, cheese, fried food, pizza, pasta, kebabs, sandwiches, soft drinks, alcoholic drinks, sweets, chocolate bars, ice cream, condiments and salad dressings) to maintain low glycemic loads (diet low in refined sugars with moderate levels of carbohydrates and not as low in fat and protein as a low fat diets[see 17]) and reduce any insulinotropic properties with potential positive effects on metabolism and health.

5. Protein has more than three times the thermic effect of either fat or carbohydrate[18] and because it has a greater satiety (feeling of fullness) value than fat or carbohydrate[18, 19], increased dietary protein may represent an effective weight-loss strategy for the overweight or obese. Studies have indicated that fish protein may have a greater effect on satiety compared to other protein sources of animal origin [see 20]. Clinical trials have shown that calorie-restricted, high-protein diets are more effective than are calorie-restricted, high-carbohydrate diets in promoting[21-23] and maintaining[24] weight loss in overweight subjects while producing less hunger and more satisfaction[25]. Furthermore, high protein diets have been shown to improve metabolic control in patients with type two diabetes[26-28]. In obese women, hypocaloric, high-protein diets improved insulin sensitivity and prevented muscle loss, whereas hypocaloric, high-carbohydrate diets worsened insulin sensitivity and caused reductions in fat free mass[29]. In numerous population studies, summarized by Obarzanek et al[30], higher blood pressure has been associated with lower intakes of protein. An increasing body of evidence indicates that high-protein diets (approximately one third of total food energy intake at the expense of lowered carbohydrate) may improve blood lipid profiles[27, 28, 31-33] and thereby lessen the risk of diet induced disease. Improvements in the nutritional value of crop plants, in particular the protein composition has been a major long-term goal of plant breeding programs. The future of bio-nanotechnology/molecular biology looks promising to increase protein consumption at the expense of carbohydrate in the human diet, with potential health benefits.

6. Endemic clinical and sub-clinical iodine deficiency is present in about 20% of humans Worldwide. Two billion people, over 30% of the World's population are anaemic, many due to lack of iron[34]. Iron and other key minerals needed for brain development and function (zinc, copper, selenium) are more bio-available from shellfish and fish than from plant-based diets where their absorption is impaired by phytates and other anti-nutrients. Plant based diets rich in staples like cassava or soy (the basis of many vegan and vegetarian food products) are not only a very poor source of iodine but they also contain goiterogens which inhibit iodine absorption[35]. Bio-fortification of novel foods through modern methods of nanotechnology and biotechnology has the potential to help offset

essential nutrient deficiencies and improve human health through elevated levels of essential nutrients, reduced levels of toxic factors and anti-nutrients that impact bioavailability and utilization of nutrients, and increased levels of factors that enhance bioavailability of nutrients[36, 37].

7. Diets low in dietary fibre may underlie or exacerbate constipation, appendicitis, hemorrhoids, deep vein thrombosis, varicose veins, diverticulitis, hiatal hernia, and gastroesophageal reflux[38]. Fibre type and quantity are undoubtedly under genetic control, although this topic has received little attention. The technology to modify fibre content and type by nano-engineering would be a great benefit in persuading the many individuals who, for taste or other reasons, do not include adequate amounts of fibre in their daily diet. For example, fibre content could be added to more preferred foods (e.g. milk, cheese, ice cream, refined cereals and white bread – but these are all novel foods that can promote the diet induced diseases of civilization) or the more common sources of dietary fibre could be altered for greater health benefits.

8. In conclusion, to promote health and help prevent disease the future direction of food production should be towards greater production of anti-inflammatory (DHA, EPA, ALA, LA and ARA profile similar to aquatic foods e.g. mussels *Mytilus spp.*), higher protein (~ one third of total food energy intake at the expense of lowered carbohydrate), low glycemic load, high fibre (25–30 g $day^{-1}$), bio-available nutrient rich, high potassium – low sodium, brain foods (foods rich in preformed DHA, EPA, Iodine, Iron, Copper, Zinc and Selenium). Advances in food bio-nanotechnology that focus on these diet issues will in the long-term help prevent unnecessary suffering and premature death.

## References


1. World Health Organization (2007) Cardiovascular diseases. Fact sheet N°317.
2. Andlin-Sobocki P, Jonsson J, Wittchen H-U *et al.* (2005) Cost of disorders of the brain in Europe. *Eur J Neurol* **12**, 1-27
3. Samuelsson B (1979) Prostaglandins, thromboxanes, and leukotrienes: formation and biological roles. *Harvey Lect* **75**, 1-40
4. Lands WEM (1986) Fish and human health. Orlando, Fla: Academic Press
5. Church MW, Jen K-LC, Jackson DA *et al.* (2009) Abnormal neurological responses in young adult offspring caused by excess omega-3 fatty acid (fish oil) consumption by the mother during pregnancy and lactation. *Neurotoxicol Teratol* **31**, 26-33
6. Lichtenstein AH (2005) Remarks on clinical data concerning dietary supplements that affect antithrombotic therapy. *Thromb Res* **117**, 71-73
7. Iso H, Sato S, Folsom AR *et al.* (1989) Serum Fatty Acids and Fish Intake in Rural Japanese, Urban Japanese, Japanese American and Caucasian American Men. *Int J Epidemiol* **18**, 374-381

8. Lands WEM (2005) Dietary fat and health: the evidence and the politics of prevention - careful use of dietary fats can improve life and prevent disease. *Ann N Y Acad Sci* **1055**, 179-192
9. Duncan RE, El-Sohemy A, Archer MC (2005) Statins and cancer development. *Cancer Epidemiol Biomarkers Prev* **14**, 1897-1898
10. Duncan RE, El-Sohemy A, Archer MC (2007) Statins and cancer. *Epidemiology* **18**, 520
11. Duncan RE, El-Sohemy A, Archer MC (2006) Statins and the risk of cancer. *JAMA* **295**, 2720
12. World Health Organization (2006) Obesity and overweight. Fact sheet N°311.
13. Liu S, Willett WC (2002) Dietary glycemic load and atherothrombotic risk. *Curr Atheroscler Rep* **4**, 454-461
14. Ludwig DS (2002) The glycemic index physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. JAMA: Am Med Assoc; 2414-2423.
15. Cordain L, Eades MR, Eades MD (2003) Hyperinsulinemic diseases of civilization: more than just Syndrome X. *Comp Biochem Physiol A Mol Integr Physiol* **136**, 95-112
16. Madden SG, Loeb SJ, Smith CA An integrative literature review of lifestyle interventions for the prevention of type II diabetes mellitus. *J Clin Nurs* **17**, 2243-2256
17. Pereira MA, Swain J, Goldfine AB *et al.* (2004) Effects of a low-glycemic load diet on resting energy expenditure and heart disease risk factors during weight loss. *JAMA-J Am Med Assoc* **292**, 2482-2490
18. Crovetti R, Porrini M, Santangelo A *et al.* (1998) The influence of thermic effect of food on satiety. *Eur J Clin Nutr* **52**, 482-488
19. Stubbs RJ (1998) Appetite, feeding behaviour and energy balance in human subjects. *Proc Nutr Soc* **57**, 341-356
20. Borzoei S, Neovius M, Barkeling B *et al.* (2006) A comparison of effects of fish and beef protein on satiety in normal weight men. *Eur J Clin Nutr* **60**, 897-902
21. Baba NH, Sawaya S, Torbay N *et al.* (1999) High protein vs high carbohydrate hypoenergetic diet for the treatment of obese hyperinsulinemic subjects. *Int J Obes* **23**, 1202-1206
22. Skov AR, Toubro S, Ronn B *et al.* (1999) Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *Int J Obes* **23**, 528-536
23. Layman DK (2003) The role of leucine in weight loss diets and glucose homeostasis. *J Nutr* **133**, 261S-267S
24. Westerterp-Plantenga MS, Lejeune M, Nijs I *et al.* (2004) High protein intake sustains weight maintenance after body weight loss in humans. *Int J Obes* **28**, 57-64
25. Johnston CS, Tjonn SL, Swan PD (2004) High-protein, low-fat diets are effective for weight loss and favorably alter biomarkers in healthy adults. *J Nutr* **134**, 586-591
26. Seino Y, Seino S, Ikeda M *et al.* (1983) Beneficial-effects of high protein-diet in treatment of mild diabetes. *Human Nutrition-Applied Nutrition* **37**, 226-230
27. Odea K (1984) Marked improvement in carbohydrate and lipid-metabolism in diabetic australian aborigines after temporary reversion to traditional lifestyle. *Diabetes* **33**, 596-603

28. Odea K, Traianedes K, Ireland P *et al.* (1989) The effects of diet differing in fat, carbohydrate, and fiber on carbohydrate and lipid-metabolism in type-II diabetes. *J Am Diet Assoc* **89**, 1076-1086
29. Piatti PM, Monti LD, Magni F *et al.* (1994) Hypocaloric high-protein diet improves glucose-oxidation and spares lean body-mass - comparison to hypocaloric high-carbohydrate diet. *Metab Clin Exp* **43**, 1481-1487
30. Obarzanek E, Velletri PA, Cutler JA (1996) Dietary protein and blood pressure. *J Amer Med Assoc* **275**, 1598-1603
31. Wolfe BM, Giovannetti PM (1991) Short-term effects of substituting protein for carbohydrate in the diets of moderately hypercholesterolemic human-subjects. *Metab Clin Exp* **40**, 338-343
32. Wolfe BM, Giovannetti PM (1992) High protein-diet complements resin therapy of familial hypercholesterolemia. *Clin Investig Med* **15**, 349-359
33. Wolfe BMJ, Piche LA (1999) Replacement of carbohydrate by protein in a conventional-fat diet reduces cholesterol and triglyceride concentrations in healthy normolipidemic subjects. *Clinical And Investigative Medicine-Medecine Clinique Et Experimentale* **22**, 140-148
34. World Health Organization (2009) Micronutrient deficiencies: Iron deficiency anaemia http://www.who.int/nutrition/topics/ida/en/print.html.
35. Cunnane SC, Plourde M, Stewart K *et al.* (2007) Docosahexaenoic acid and shore-based diets in hominin encephalization: a rebuttal. *Am J Hum Biol* **19**, 578-581
36. Chassy BM, Hlywka JJ, Kleter GA *et al.* (2004) Nutritional and safety assessments of foods and feeds nutritionally improved through biotechnology. *Comp Rev Food Sci Food Safety* **3**, 35-104
37. Gilani GS, Nasim A (2007) Impact of foods nutritionally enhanced through biotechnology in alleviating malnutrition in developing countries. *J AOAC Int* **90**, 1440-1444
38. Trowell H (1985) Dietary fibre: a paradigm. *Dietary Fibre, Fibre-Depleted Foods and Disease*, 1-20

- What is the current level of public awareness of the issues surrounding the use of nanotechnologies in the food sector?

1. Almost non-existent. When informing the public on any matter, great care must be taken because most of the population is scientifically illiterate. I often read, see and hear the over-simplification and miscommunication of rigorously peer reviewed and well established health science by health agencies and health charities in the press, on the radio and TV (e.g. the Food Standards Agency advert about eating excess saturated fat is misleading. It is eating too much food energy per meal that is the problem – see Figure 1). It is very easy to make a convincing argument to the majority of consumers by adding two bits of (im)plausible science together and then coming to an implausible conclusion. See **Science communication** on page 24 in the appendix for further information.

2. In my experience, even when aware of the diet induced diseases of civilization, most people still want to have their cake (modern diet) and eat it. We can make the consumer aware of several options:

1. eat wild ancestral (e.g. shore-based) foods, which is almost impossible for the vast majority of the population in countries surrounded by novel and domesticated human foods and polluted coastal waters. Further, there are more humans on Earth, than can be sustained by the natural World.

2. continue eating the modern diet and thus, continue the diet induced disease epidemic (unnecessary suffering and premature death).

3. modify the novel foods in the modern diet (while still looking and tasting the same as before modification), so they cannot induce the diseases of civilization.

- What are the risks posed to consumers by the use of nanotechnologies and nanomaterials in the food sector?

1. The risks of well regulated and rigorously tested food nanotechnology products that help prevent disease are likely to be insignificant when compared with the magnitude of the current problem of the diet induced disease epidemic. Using bio-nanotechnology (or molecular biology) to engineer novel foods so they cannot promote the diet induced diseases of civilization is likely to be of great benefit to mankind. In reality there are already more humans on Earth, than can be sustained by the natural World.

2. The World spent US$4.4 trillion on health in 2005[30]. Chronic illnesses and health problems either wholly or partially attributable to diet account for the largest burden of chronic illnesses and health problems Worldwide. The modern diet (the replacement of ancestral foods (e.g. aquatic-based foods) by the excessive consumption of refined seed and nut oils, cereals, dairy products, refined sugars, fatty meats, salt, and combinations of these foods) adversely affects the following dietary indicators *1*) fatty acid composition, *2)* glycemic load , *3*) macronutrient composition, *4*) micronutrient density, *5*) acid-base balance, *6*) sodium-potassium ratio and *7*) fibre content[39].

# APPENDIX

## Preventing diet induced disease

## bio-available nutrient rich, low-energy-dense diets

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Key Words: nanotechnology, diet, disease, cardiovascular disease, diabetes, cancer, prevention, DHA, EPA, brain, mental, ill, health, obesity, food, pregnancy, salt, energy, nutrition

## Abstract

What the World needs is an integrated and sustainable food policy that makes the best, and most appropriate use of the technologies at our disposal to promote health and help prevent disease. Diet induced diseases account for the largest burden of chronic illnesses and health problems Worldwide. Historically a lack of knowledge about the human nutritional requirements (including for the brain) helped promote diet induced disease. The scientific knowledge exists to help prevent many of the current deficiencies and imbalances in human diet. Primary prevention of cardiovascular disease and mental ill health starts, crucially, with maternal nutrition before the inception of pregnancy and continues throughout life of the new born and includes consuming more DHA, EPA and ALA (alpha-linolenic acid) omega-3 fats (and their co-factors) and bio-available brain minerals and less high-energy-dense foods (e.g. refined sugars and land-based fats and oils), so tissues synthesize less inflammatory mediators and lower transient short-lived meal-induced oxidative stress, inflammation, proliferation and impaired nitric oxide (e.g. ~0.35-3.5 g DHA + EPA $day^{-1}$ dependant on energy intake and availability of co-factors). Micro- and nanotechnologies are already engineering foods for human (and livestock) consumption that may eventually (without excessive consumption) prevent the current diet induced disease epidemic, especially in future generations, by preventing the causal mechanisms of disease. Greater knowledge about the causal mechanisms of disease awaits to be discovered, which could further enhance the human desire to increase longevity in optimum health (creating more problems and challenges for society).

# Introduction

Diet (oral ingestion) has always been a major mediator of disease and mortality in humans e.g. malnutrition, typhoid fever and polio. Currently many of the chronic diseases epidemic in human populations are diet induced diseases. This paper attempts to provide an understanding of the magnitude of the problem of diet induced disease. The primary objective is to provide information on how to help prevent diet induced disease, including the use of food nanotechnology. Nanotechnology promises to transform medicine from being therapeutic to being preventative. It is estimated that within the next two decades human life expectancy for healthy people will approach 100 years[(1)]. This means that many people reading this paper could see the twenty-second century. Meeting people's aspirations to increase life expectancy, with all the problems it will bring to society, should be coupled with living as long as possible in good health (disease free). To achieve that future potential, it is necessary to look beyond the *status quo* e.g. medical efforts focusing more on treatments for older people than on preventing primary causes of diet induced disease before they occur - starting with appropriate maternal nutrition before the inception of pregnancy and continuing throughout the life of future generations. To understand our dietary needs it is necessary to look at human diets in relation to the causal mechanisms of disease. The review begins with the importance of diet as a fuel supply for the brain.

# Nutrition for the brain

The brain evolved containing DHA (omega-3) in the sea 500-600 million years ago[2]. DHA has been used in neural signalling systems over a 500-600 million year stretch of evolution. DHA is involved in neural receptor domains, gene expression with derivatives providing protection from oxidative stress in the brain and resolution of injury [3]. Shellfish, fish and shore-based animals and plants are the richest dietary sources of the key nutrients needed by the brain; the preformed dietary omega-3 fatty acids - DHA, EPA, iodine (I), iron (Fe), copper (Cu), zinc (Zn) and selenium (Se)[4, 5]. The omega-6 fatty acid arachidonic acid (AA) is also important for brain development and present in shellfish and other aquatic-based foods (Table 1). DHA and AA are transferred across the placenta and accumulated in the brain and other organs during fetal development and maternal diet impacts fetal DHA and AA accretion[6, 7]. Postnatal nutrition is also a priority to ensure good maternal health and nutrition for the mother and her breast milk[8]. Increasing dietary alpha-linolenic acid (ALA) intake has little effect on increasing maternal transfer of DHA to the foetus, or on increasing DHA secretion in breast milk[9, 10]. Similarly, increasing the intake of ALA in infants, as in adults, has little effect on increasing circulating levels of DHA[e.g. 11, 12].

Historically a lack of knowledge about the human nutritional requirements (including for the brain) helped promote diet induced disease. There is growing awareness that the profound environmental changes (e.g. in diet and other lifestyle conditions) that began with the introduction of agriculture and animal husbandry ~10 000 years ago occurred too recently on an evolutionary time scale for the human genome to adapt[13-16]. In conjunction with this discordance between our ancient, genetically determined biology and the nutritional, cultural and activity patterns in modern societies, many of the so-called diseases of civilization have emerged[13-23].

## Chronic disease epidemic

The World spent US$4.4 trillion on health in 2005[24]. Chronic illnesses and health problems either wholly or partially attributable to diet account for the largest burden of chronic illnesses and health problems Worldwide. Cardiovascular diseases are the number one cause of death globally (30% of all deaths) and cardiovascular diseases are predicted to continue increasing[25]. An estimated 17.5 million people died from cardiovascular diseases in 2005[25]. Cancer is a leading cause of death Worldwide and accounted for 7.9 million deaths (around 13% of all deaths) in 2007 and deaths attributable to cancer are projected to continue rising[26]. An estimated one-third of all cancer deaths are due to nutritional and life style factors[27, 28]. Taking into account deaths in which diabetes was a contributory condition (heart disease or kidney failure) approximately 2.9 million deaths in 2005 were attributable to diabetes[29]. Type 2 diabetes is rapidly becoming a disease of children and adolescents. In 2000, it was estimated that 30% of boys and 40% of girls born in the USA are at risk for being diagnosed with type 2 diabetes at some point in their lives[30]. Globally in 2005, at least 20 million children under the age of 5 years were overweight, approximately 1.6 billion adults (age 15+) were overweight and at least 400 million adults were obese[31]. The World Health Organization further projects that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese. In the Europe Union, brain disorders have now overtaken all other burdens of ill health at an estimated cost of €386 billion (€829 a year for each European citizen) in 2004[32] and mental ill health is predicted by the Global Forum of Health (www.globalforumhealth.org) to be in the top three burdens of ill health Worldwide by 2020.

# Human diet

There are universal characteristics of pre-agricultural hominin diets that are useful in understanding how the modern diet may predispose humans to chronic disease. Increasingly, clinical trials and interventions that use dietary treatments with nutritional characteristics similar to those found in pre-industrial and pre-agricultural diets have confirmed the beneficial health consequences predicted by the template of evolutionary discordance theory[15, 16, 33].

Before the development of agriculture and animal husbandry hominin dietary choices would have been necessarily limited to minimally processed, wild foods. Agriculture, introduced novel foods as staples for which the hominin genome had little evolutionary experience. More importantly, food-processing procedures were developed, particularly following the Industrial Revolution, which allowed for quantitative and qualitative food and nutrient combinations that had not previously been encountered over the course of hominin evolution. Although refined seed (vegetable oils) and nut oils, dairy products, cereals, refined sugars, and alcohol make up 72.1% of the total daily energy consumed by all people in the USA, these types of foods would have contributed little or none of the energy in the typical pre-agricultural hominin diet[34]. Additionally, mixtures of these foods make up the ubiquitous, generally energy-dense, nutrient poor, processed foods (e.g. breakfast cereals, bread, cake, cookies, crackers, cheese, fried food, pizza, pasta, kebabs, sandwiches, soft drinks, alcoholic drinks, sweets, chocolate bars, ice cream, condiments and salad dressings) that dominate the typical modern diet.

The novel foods (refined seed and nut oils, cereals, dairy products, refined sugars, fatty meats, salt, and combinations of these foods) introduced as staples during the Neolithic and Industrial Eras fundamentally altered several key nutritional characteristics of ancestral hominin diets and ultimately had far-reaching effects on health and well-being. As these foods gradually displaced the minimally processed wild foods in human diets, they adversely affected the following dietary indicators *1*) fatty acid composition, *2)* glycemic load , *3*) macronutrient composition, *4*) micronutrient density, *5*) acid-base balance, *6*) sodium-potassium ratio and *7*) fibre content[(33)].

Using cereals (e.g. wheat, rice and maize) as an example, cereal grain consumption may appear to be historically remote but it is biologically recent; consequently the human immune, digestive and endocrine systems have not yet fully adapted to a food group which provides 56% of humanity's food energy and 50% of its protein[(21)]. Cereal grains are truly humanity's double-edged sword[(21)]. For without them, our species would likely have never evolved the complex cultural and technological innovations which allowed our departure from the hunter-gatherer niche. However, because of the dissonance between human evolutionary nutritional requirements and the nutrient content of these domesticated grasses, many of the World's people suffer disease and dysfunction directly attributable to the consumption of cereals[(21)].

## Dietary fat, essential brain nutrients and health

Substantial evidence now indicates that to prevent the risk of chronic disease, the absolute amount of dietary fat is less important than is the type of fat[(35)]. Fatty acids fall into one of three major categories: *1*) saturated fatty acids, *2*) mono-unsaturated fatty acids and *3*) polyunsaturated fatty acids (PUFAs). Essential PUFAs required by all mammals are not produced within the body, and must come from the diet and occur in two biologically important families, omega-3 and omega-6 (Table 1). The most prominent omega-6 fatty acids in the human diet are the highly unsaturated fatty acid (HUFA) ARA found in aquatic foods and animal meat and the PUFA linoleic acid (LA) found in foods including seeds, nuts and their oils (Table 1) which can be converted into the HUFA ARA by enzymes. Existing USA and UK recommendations to increase the consumption of EPA/DHA to 1 g day$^{-1}$ and 0.5 g day$^{-1}$ for those with and without existing cardiovascular disease respectively[36, 37] include consumption of shore-based foods e.g. shellfish and not just mainly pelagic oily fish e.g. mackerel and salmon[38] and high strength DHA + EPA oils. Much of the evidence upon which these guidelines are based, however, comes from supplemented intakes of preformed EPA/DHA at levels in excess of 1 g day$^{-1}$ and ~3.5 g DHA/ EPA day$^{-1}$ has been recommended by some for current USA diets[39]. The high requirement for DHA/EPA can likely be reduced to one-tenth of that amount by consuming less energy per meal and less energy per day (i.e. low-energy-dense food and drinks - - see Table 2) (compare [39] with [40]). Major dietary sources of the omega-3 PUFA ALA include seed oils (Table 1), which can be converted to EPA and then DHA by enzymes. However, the conversion of ALA through to the EPA and DHA is inefficient and may be an evolutionary consequence resulting from the ubiquitous presence of DHA + EPA HUFA containing foods in the food chain of our human ancestors, thus reducing the importance of the *de novo* synthesis pathway[41].

The cardio-protective effects of DHA/EPA have been recognized for over 50 years with the low incidence of mortality rate from CHD (coronary heart disease) in Greenland Eskimos, a population consuming a high fat diet, but rich in DHA/EPA[42]. In Greenland, coronary heart disease is almost undetectable[43, 44], while globally cardiovascular diseases account for 30% of all deaths[25]. The totality of evidence for the positive effects of DHA and EPA from aquatic food and fish oil products on various outcomes of cardiovascular disease is almost incontrovertible, according to the review by Griffin[45]. However, others state that DHA, EPA and ALA do not have a clear effect on total mortality, combined cardiovascular events, or cancer [e.g. 46]. The section of the Cochrane study[46] regarding cardiovascular disease has been formally rejected by the Society for the Study of Fatty Acids and Lipids[47]. A more recent review highlights the important cardio-protective effect of DHA/EPA in the secondary prevention of sudden cardiac death due to arrhythmias, but suggests caution to recommend dietary supplementation of PUFAs to the general population, without considering, at the individual level, the intake of total energy and fats[40]. The current review suggests that the real value of DHA and EPA in the primary prevention of cardiovascular disease starts, crucially, with adequate maternal consumption of DHA and EPA (dependant on energy intake and availability of co-factors) before the inception of pregnancy and continues with adequate intake of DHA and EPA during pregnancy and lactation and throughout the life of the new born child. The slow progressive injury to human tissues that eventually becomes cardiovascular disease and premature death becomes irreversible overtime[48, 49]. Thus, secondary prevention of cardiovascular disease using DHA/EPA dietary interventions may not repair all the damage already done to human tissues by the lack of DHA and EPA and other factors in the diet earlier in life. It is important to note that if DHA and EPA fish oils undergo oxidation it may attenuate their beneficial effects[50]; bioactive-packaging made from nanomaterials can help to control the oxidation of food stuffs[51]. Further, the excessive consumption of anything may cause disease or premature death, even omega-3[e.g. 52, 53, 54].

In the United States, during the ninety year period from 1909 to 1999, a striking increase in the use of seed oils occurred. Specifically, per capita consumption of salad and cooking oils increased 130%, shortening consumption increased 136% and margarine consumption increased

410%[55], which directly increased daily energy intake due to their high energy-density (Table 2). These trends occurred elsewhere in the World and were made possible by the industrialization and mechanization of the oil-seed industry[56]. The trend towards an increase in daily energy intake was exacerbated by the excessive human consumption of energy-dense cereals, seeds and nuts, and as meat from grain fed cattle, poultry and other livestock became the norm in the Western diet over the past 100 years[23, 57].

The top predicted causes of death and disability Worldwide for 2020 (ischemic heart disease and unipolar major depression) and three top causes in developed regions (ischemic heart disease, cerebrovascular disease and unipolar major depression)[58] all seem linked to a lack of preformed DHA and EPA in the diet and excess food energy (imbalance between the expenditure/intake of energy). The close interaction between omega-3 (including DHA/EPA) and omega-6 (including GLA, DGLA and AA) fatty acids on the ability to modify inflammatory markers, production of PGI2, PGE1, PGI3, LXs, resolvins[59], neuroprotectins, NO (nitric oxide), nitrolipids, and the action of statins (HMG-CoA reductase inhibitors) and glitazones (PPARs agonists) on essential fatty acid metabolism and NO explains the relationship between various fatty acids and CHD and stroke[60]. Uncontrolled excessive production of pro-inflammatory mediators over prolonged periods of time is associated with heart attacks, thrombotic stroke, arrhythmia, arthritis, asthma, headaches, dysmenorrhea (menstrual cramps), inflammation, cancer and osteoporosis[61, 62] and the American Heart Association urged putting more omega-3 HUFAs into daily diets[63]. However, most epidemiologic cohort studies found no association between DHA and EPA intake and cancer risk[64-66]. But, inverse associations with breast cancer have been reported in Chinese and Japanese women having omega-3 HUFA intakes up to forty times greater than Western intakes[67-69]. A large cohort study on breast cancer suggested that women with the lowest DHA and EPA intake but highest omega-6 PUFA intake (highest energy intake/excess food energy? – 20-30% of dietary fatty acids undergo betaoxidation to acetyl-CoA to enter the Kreb's cycle generating ATP[40]) could benefit from increasing their omega-3 HUFA intake[70]. Another study[67] found a direct association between omega-6 PUFA intakes (energy intake/excess food energy?) and breast cancer risk confined to women having the lowest intakes of omega-3 HUFAs. Such observations are consistent with the effect of the absolute amount of omega-3 fatty acids on the biosynthesis of anti-inflammatory 3-series eicosanoids[45]; AA derived 2-series tumor promoting eicosanoids and/or decreased synthesis of anti-inflammatory and beneficial eicosanoids most likely being an underlying mechanism for cancers such as colon, breast, kidney and prostate cancer [71-73]. Tumor cells undergo apoptosis on exposure to certain fatty acids (especially in response to DHA, EPA and GLA) due to an increase in intracellular free radical generation and the formation of lipid peroxides[60]. Further studies are required to better explain the Worldwide variations in the incidence of cancer which may be linked to differences in diet and lifestyle.

Additional evidence showed important actions of omega-3 HUFAs in brain function[74]. DHA is an important component of human retinal and brain membranes and has been shown to play a role in the cognitive development of infants[75-77]. Poor maternal health and nutrition before and during pregnancy disadvantages fetal development with permanent mental and cognitive deficits[78] and behavioural dysfunction[79, 80] with a risk of heart disease, diabetes and stroke in later life - prenatal programming[81, 82]. Maternal nutrition before and during pregnancy is an independent risk factor for low birth weight and poor pregnancy outcome [83-87]. A diet high in omega-6 PUFAs is generally thought to be associated with an increased risk of preterm delivery[88]. Increasing evidence suggests that depression, bipolar disorder, behavioral disorders and cognitive impairment in later life (dementia) also relate to a lack of DHA and EPA in the human diet [(reviewed by 89)]. Supplementation with a combination of both DHA and EPA (or consumption of aquatic-based foods) is likely to be more effective than use of either alone [(90)]. There is increasing evidence that the reasons for brain disorders are related to the replacement of aquatic-based foods by land-based foods[(80, 91, 92)]. Thus, it is especially important to eat a diet rich in essential brain nutrients DHA, EPA, I, Fe, Cu, Zn and Se (aquatic foods) before the inception of pregnancy, during pregnancy and breastfeeding and to give it to young infants (e.g. in baby food) to ensure optimal brain development and help prevent mental ill-health. The regular consumption of essential brain nutrients should continue throughout life because although the brain recycles its constituents rather than relying on imports, the process is not 100% efficient and the continual loss needs to be replaced by some import.

The growing awareness of the importance of DHA and EPA omega-3 fats is evident from the single major personal health change recommended by the health and nutrition division members of the American Oil Chemists' Society: to eat more fish and take an omega-3 supplement [(93)]. The fats and oils from aquatic based-foods contain high contents of these beneficial omega-3 fatty acids but increased consumer demand has also increased strain on the ability of the World's fisheries to meet demand from wild capture. Many consumers are choosing fish oil supplements or are eating foods that have been complemented with fish oils instead of consuming aquatic foods directly. However, removing undesirable odours, flavours and contaminants is expensive. In contrast, oils derived from land plants such as soybean are inexpensive and contaminant free. Given the potential benefits to the environment with regards to over-fishing and the health prospects of increased consumption of these healthy fatty acids, producing these fatty acids in oilseeds is a desirable and worthy goal (except for the high-energy density of oils (and fats) which may be reduced using nanotechnology[94]). Molecular biology now allows the engineering of oilseeds for the production of DHA and EPA omega-3 HUFAs in a seed oil with an omega-3:6 ratio 1.5:1 (a ratio close to that of many fish oils)[41]. A bread containing nanocapules of DHA/EPA omega-3 fatty acids is being sold in Australia as Tip-Top Bread[94].

Increasing human consumption of DHA, EPA and ALA omega-3 fats and by humans eating less food energy per meal (e.g. a 2000-kcal daily diet consumed in six smaller energy portions - breakfast, brunch, lunch, afternoon tea, dinner and supper, rather than three large portions) to lower transient short-lived meal-induced oxidative stress[95-97], inflammation, proliferation and impaired nitric oxide[98-102], ultimately could have far-reaching effects on health and well-being. However, appreciating the nutrients essential for brain development[4, 5], the addition of I, Fe, Cu, Zn and Se to daily diets including DHA and EPA rich engineered seed oils with reduced levels of toxic factors and anti-nutrients (e.g. phytic acid) that impact bioavailability and utilization of nutrients and increased levels of factors that enhance bioavailability of essential nutrients[103, 104], would have even greater positive implications for human mental health in addition to helping prevent diet mediated inflammatory diseases. Further, for their physiological/beneficial action(s) PUFAs need many co-factors such as folic acid, vitamin B12, vitamin B6, vitamin C, tetrahydrobiopterin (H4B), zinc, magnesium, calcium, L-arginine, and small amounts of selenium and vitamin E[105]. Hence, it is essential that these co-factors should also be provided in adequate amounts to bring about the beneficial action of omega-3 and omega-6 fatty acids. Although principally a lack of DHA and EPA and excess food energy link diet to cardiovascular disease and premature death, evidence gleaned over the past three decades now indicates that virtually all so-called diseases of civilization arise from a complex interaction of multiple nutritional factors directly linked to the replacement of ancestral foods by the excessive consumption of novel Neolithic and Industrial era foods, along with other environmental agents and genetic susceptibility [c.f. 33].

## Energy-density

Refined grain and sugar products nearly always maintain much higher energy densities than unprocessed fruits and vegetables. In the typical USA diet, sugars with a high energy density (HFCS 42, HFCS 55, sucrose, glucose, honey, and syrups) now supply 18.6% of total energy, whereas refined cereal grains with a high energy density supplies 20.4% of energy[33]. Soybean oil 8.8 kcal $g^{-1}$ (data calculated from USDA National Nutrient Database for Standard Reference), appears to deliver 20% of all calories in the median USA diet, with ~9% of all calories from LA alone[55]. Within the past twenty years, substantial evidence has accumulated showing that long term consumption of high-energy-dense (>2 kcal $g^{-1}$[106]) foods can adversely affect metabolism and health[107-109]. Hence, 39% of the total energy in the typical USA diet is supplied by foods that may promote the causes of insulin resistance [110-115]. In addition to high-energy-dense carbohydrates, other elements of Neolithic and Industrial Era foods may contribute to the insulin resistance underlying metabolic syndrome diseases. Milk, yogurt and ice cream are highly insulinotropic, with insulin indexes comparable with white bread[116]. It is known that omega-3 PUFAs are of benefit in type 2 diabetes by decreasing insulin resistance[117]. Diseases of insulin resistance include obesity, type 2 diabetes and hypertension.

The global epidemic of obesity-associated diabetes is a symptom of the modern diet and lifestyle, in which food is plentiful and exercise is optional. Type 2 diabetes accounts for 90% of all diabetes cases around the World[29]. Obesity and sedentary lifestyles closely linked with this type of diabetes[29] are both modifiable and even preventable risk factors. A healthy diet-plus-exercise is most effective for preventing diabetes mellitus[118]. Unfortunately, in modern societies, it is often easier to persuade people to take a pill, than to persuade them to change their diet and lifestyle for the long-term. Diet induced metabolic syndrome may extend to other chronic illnesses and conditions that are widely prevalent in Westernized societies, including: myopia[119], acne[120], gout[121], polycystic ovary syndrome, epithelial cell cancers (breast, colon, and prostate), male vertex balding, skin tags and acanthosis nigricans[109]. Although sugars and grains with a high-energy-density now represent a dominant element of the modern urban diet, these foods were rarely or never consumed by average citizens as recently as two hundred years ago[33]. Diseases of insulin resistance are rare or absent in hunter-gatherer and other less westernized societies living and eating in their traditional manner[14, 122, 123].

The finding that persons with a low-energy-dense (<1.6 kcal $g^{-1}$) diet had the lowest total intakes of energy, even though they consumed the greatest amount of food has important implications for promoting compliance with prescribed dietary regimens[106]. A reduction in liquid calorie intake has been found to have a stronger effect than has a reduction in solid calorie intake on weight loss[124]. Of the individual beverages, only intake of sugar-sweetened beverages (SSBs) was significantly associated with weight change[124]. A diet plan that severely restricts the amount of food a patient consumes will likely lead to feelings of hunger and have unfavourable influences on the patient's satisfaction with the diet and long-term compliance. Overweight and obese patients may develop paradoxical nutritional deficiency from eating high-energy foods with a poor nutrient content. The impact of sedentary lifestyles and availability of energy-dense food in modern societies is undeniable, but substantial individual differences in body weight persist, suggesting that individuals respond differently to the 'obesogenic' environment[125]. Psychometric measures of child appetite and child weight suggest that appetitive trait profiles may not only promote obesity but also protect against it and will include both genetic and environmental influences[125] which require further investigation.

High energy density (c.f. Table 2) and low nutrient density (Table 3) which characterise diet in developed countries are major targets that must be overcome. 2000 kcal day$^{-1}$ = 334 g of chocolate (70-85% cocoa), 353 g peanuts, 496 g cheddar cheese, 554 g Kellogg’s® Corn Flakes, 1681 g chocolate milkshake, 2325 g mussels, 2439 g cod, 4444 g fresh orange juice or 8695 g spinach (data calculated from USDA National Nutrient Database for Standard Reference). Nanotechnology or molecular biology may be able to engineer high-energy-dense foods abundant in the modern diet to maintain lower energy densities (<1.6 kcal g$^{-1}$) while looking and tasting the same as before modification to aid public acceptance and reduce any insulinotropic properties with potential positive effects on metabolism and health.

## Macronutrient composition

In the present USA diet, the percentage of total food energy derived from the three major macronutrients is as follows: carbohydrate (51.8%), fat (32.8%), and protein (15.4%)[33]. Advice for reducing the risk of cardiovascular disease and other chronic diseases has been to limit fat intake to 30% of total energy, to maintain protein at 15% of total energy and to increase complex carbohydrates to 55–60% of total energy (e.g. 126). Both the current USA macronutrient intakes and suggested healthful levels differ considerably from average levels obtained from ethnographic[(34)] and quantitative[(127)] studies of hunter gatherers in which dietary protein is characteristically elevated (19–35% of energy) at the expense of carbohydrate (22–40% of energy)[(34, 127)]. Because protein has > three times the thermic effect of either fat or carbohydrate[(128)] and because it has a greater satiety value than do fat or carbohydrate[(128, 129)], increased dietary protein may represent an effective weight-loss strategy for the overweight or obese. Studies have indicated that fish protein may have a greater effect on satiety compared to other protein sources of animal origin (see 130). Clinical trials have shown that calorie-restricted, high-protein diets are more effective than are calorie-restricted, high-carbohydrate diets in promoting[(131-133)] and maintaining[(134)] weight loss in overweight subjects while producing less hunger and more satisfaction[(135)]. Furthermore, high protein diets have been shown to improve metabolic control in patients with type 2 diabetes[(136-138)]. In obese women, hypocaloric, high-protein diets improved insulin sensitivity and prevented muscle loss, whereas hypocaloric, high-carbohydrate diets worsened insulin sensitivity and caused reductions in fat free mass[(139)]. In numerous population studies, summarized by Obarzanek et al[(140)], higher blood pressure has been associated with lower intakes of protein. An increasing body of evidence indicates that high-protein diets may improve blood lipid profiles[(137, 138, 141-143)] and thereby lessen the risk of diet induced disease.

Improvements in the nutritional value of crop plants, in particular the protein composition has been a major long-term goal of plant breeding programs. Molecular biology has produced transgenic potatoes with about 33% more protein and substantial amounts of essential amino acids including lysine[(144)], which is deficient in many developing countries where diets are heavily based on cereals[21, 103]. Strains of protein-enriched maize have also been created[145]. Some protein based nanotubes are considered food-grade materials[146], which should make their introduction into the human food chain relatively easy and might further facilitate increases in protein composition of currently high carbohydrate foods. The future looks promising to increase protein consumption at the expense of carbohydrate in the human diet, with numerous potential health benefits.

## Micornutrient density

Refined sugars are essentially devoid of any vitamin or mineral (Table 2). Accordingly, the consumption of refined sugar or foods containing refined sugar reduces the total vitamin and mineral (micronutrient) density of the diet by displacing more nutrient dense foods (Table 2). A similar situation exists for refined seed and nut oils (Table 2), except that they contain two fat-soluble vitamins (vitamin E and vitamin K)[147]. Because seed and nut oils and refined sugars contribute ≥36.2% of the energy in a typical USA diet, the widespread consumption of these substances, or foods made with them, has considerable potential to influence the risk of vitamin and mineral deficiencies[33]. At least half the USA population fails to meet the recommended dietary allowance (RDA) for vitamin B-6, vitamin A, magnesium, calcium, and zinc, and 33% of the population does not meet the RDA for folate[33]. Wild foods known to be consumed by hunter-gatherers generally maintain higher micronutrient concentrations than do their domesticated counterparts[13, 148], as does the muscle meat of wild animals[147].

Endemic clinical and sub-clinical iodine deficiency is present in about 20% of humans Worldwide. The global problem of iodine deficiency primarily affects people not regularly consuming shellfish, fish or iodized table salt, without which clinical hypothyroidism, subnormal cognitive development and cretinism would still be the public health dilemma they were prior to iodization of table salt[149]. The scale and impact of endemic iodine deficiency is rivalled only by iron deficiency. Two billion people, over 30% of the World's population are anaemic, many due to lack of iron[150]. Unlike iodine, iron is not yet legislated into the food supply but great efforts are being made to find a simple, cheap, reliable way to provide iron supplements where they are needed. Iron and other key minerals needed for brain development and function (zinc, copper, selenium) are more bio-available from shellfish and fish than from plant-based diets where their absorption is impaired by phytates and other anti-nutrients. Plant based diets rich in staples like cassava or soy (the basis of many vegan and vegetarian food products) are not only a very poor source of iodine but they also contain goiterogens which inhibit iodine absorption[149].

The displacement of more nutrient-dense foods (e.g. aquatic-based foods) by less nutrient-dense novel foods (refined sugars, cereals, seed and nut oils and dairy products) and the subsequent decline in dietary vitamin and mineral density has far reaching health implications, consequences that not only promote the development of vitamin-deficiency diseases but also numerous infectious and chronic diseases[21].

Bio-fortification of novel foods through modern methods of biotechnology/nanotechnology has the potential to help offset essential nutrient deficiencies and improve human health through elevated levels of essential nutrients (including their co-factors[105]), reduced levels of toxic factors and anti-nutrients that impact bioavailability and utilization of nutrients, and increased levels of factors that enhance bioavailability of nutrients[103, 104]. A number of crops, developed with a focus on improving nutritional quality are advancing through regulatory processes towards commercialization[103]. Some examples of nutritionally enhanced crops include cyanogen-free cassava[151]; nutritionally enhanced rice with an elevated level of beta-carotene[152], increased levels of iron and zinc[153], an elevated level of cysteine residues to enhance iron bioavailability and a decreased level of phytates to improve iron and zinc bioavailability[154]; and tomatoes and soybeans with increased antioxidant contents[155]. Food and nutrition products that contain nanoscale additives are already being sold, such as iron in nutritional drink mixes, micelles that carry vitamins, minerals and phytochemicals in oil and zinc oxide in breakfast cereals[51]. Other food nanotechnology products are cooking oils that contain nutraceuticals within nanocapsules and nanoparticles that have the ability to selectively bind and remove chemicals from food ('Nanotechnology in agriculture and food', available at http://www.nanoforum.org). Delivery of fragile micronutrients including their co-factors can be improved through nanoencapsulation[156]. By reducing particle size, nanotechnology can contribute to improve the properties of bioactive compounds (e.g. DHA and EPA), such as delivery properties, solubility, prolonged residence time in the gastrointestinal tract and efficient absorption through cells[157]. Bioactive compounds that are encapsulated into the packaging itself are a promising approach because this would allow the release of the active compounds in a controllable manner[51].

## Acid-base balance

After digestion, absorption, and metabolism, nearly all foods release either acid or bicarbonate (base) into the systemic circulation[158, 159]. Virtually all pre-agricultural diets were net base yielding because of the absence of cereals and energy-dense, nutrient poor foods, foods that were introduced during the Neolithic and Industrial Eras and that displaced base-yielding fruit and vegetables[159]. Consequently, a net base-producing diet was probably the norm throughout most of hominin evolution[159]. The known health benefits of a net base-yielding diet include preventing and treating osteoporosis[160, 161], age-related muscle wasting[162], calcium kidney stones[163, 164], hypertension[165, 166], and exercise-induced asthma[167] and slow the progression of age and disease-related chronic renal insufficiency[168]. Research is required to determine if micro- and nanotechnologies can modify novel net acid producing cereals to become net base yielding foods.

## Salt

The average sodium content (3436 mg $day^{-1}$) of the typical USA diet is substantially higher than its potassium content (2617 mg $day^{-1}$)[169]. The addition of manufactured salt to the food supply and the displacement of traditional potassium-rich foods by foods introduced during the Neolithic and Industrial periods (Tables 3 and 4) caused a 400% decline in the potassium intake while simultaneously initiating a 400% increase in sodium ingestion[13, 22, 170]. The potassium concentrations in vegetables are four and twelve times those in milk and whole grains, respectively, whereas in fruit the potassium concentration is two and five times that in milk and whole grains[147]. The inversion of potassium and sodium concentrations in hominin diets had no evolutionary precedent and now plays an integral role in eliciting and contributing to numerous diseases of civilization[33]. Diets low in potassium and high in sodium may partially or directly underlie or exacerbate a variety of maladies and chronic illnesses, including hypertension, stroke, kidney stones, osteoporosis, gastrointestinal tract cancers, asthma, exercise-induced asthma, insomnia, air sickness, high-altitude sickness and Meniere's Syndrome (ear ringing)[171-181]. The removal of sodium salt from processed foods and bio-fortification of cereals and dairy products with potassium may help alleviate the current sodium-potassium imbalance in the human diet.

## Fibre content

The fibre content (15.1 g $day^{-1}$)[169] of the typical USA diet is considerably lower than some recommended values (25–30 g)[126]. Refined sugars, seed and nut oils, dairy products, and alcohol are devoid of fibre and constitute an average of 48.2% of the energy in the typical USA diet[33]. Furthermore, fibre-depleted, refined grains represent 85% of the grains consumed in the USA and because refined grains contain 400% less fibre than do whole grains (by energy), they further dilute the total dietary fibre intake[33]. Fresh fruit typically contains twice the amount of fibre in whole grains, and non starchy vegetables contain almost eight times the amount of fibre in whole grains on an energy basis[147]. Fruit and vegetables known to be consumed by hunter-gatherers also maintain considerably more fibre than do their domestic counterparts[148]. Diets low in dietary fibre may underlie or exacerbate constipation, appendicitis, hemorrhoids, deep vein thrombosis, varicose veins, diverticulitis, hiatal hernia, and gastroesophageal reflux[182].

Fibre type and quantity are undoubtedly under genetic control, although this topic has received little attention. The technology to modify fibre content and type by micro- and nano-engineering would be a great benefit in persuading the many individuals who, for taste or other reasons, do not include adequate amounts of fibre in their daily diet. For example, fibre content could be added to more preferred foods (e.g. milk, cheese, ice cream, refined cereals and white bread – but these are all novel foods that can currently (without modification) promote the diet induced diseases of civilization) or the more common sources of dietary fibre could be altered for greater health benefits.

## Science communication to the public

The risks of well regulated and rigorously tested food micro- and nanotechnology products that help prevent disease are likely to be insignificant when compared with the magnitude of the current problem of the diet induced disease epidemic. Using bio-nanotechnology (or molecular biology) to engineer foods so they cannot (without excessive consumption) promote diet induced diseases is likely to be of great benefit to mankind. In reality there are already more humans on Earth, than can be sustained by the natural World. However, the consumption of (wild) aquatic-based foods in a sustainable manner should not be discouraged and nanotechnology will probably enhance the production, utilization and food safety of this nutritious resource. Bio-nanotechnology will change society beyond anything that has gone before. This should, but not with any certainty, eventually slow down the spiraling diet induced healthcare costs. Further, today's controversial areas such as nanotechnologies in foods, stem cell research, cloning, gene therapy, human enhancement and biochip implants will become acceptable practice before 2050[(1)].

## Conclusion

Chronic illnesses and health problems either wholly or partially attributable to diet account for the largest burden of chronic illnesses and health problems Worldwide. These diseases (e.g. cardiovascular disease) are epidemic in modern societies and typically afflict 50–65% of the adult population, yet they are rare or non-existent in hunter-gatherers and other less Westernized people. What the World needs is an integrated and sustainable food policy that makes the best, and most appropriate use of the technologies at our disposal. To promote health and help prevent disease the future direction of food production should be towards greater production of anti-inflammatory (DHA, EPA, ALA, LA and AA profile similar to aquatic foods e.g. mussels *Mytilus spp.*), higher protein (~ one third of total food energy intake at the expense of lowered carbohydrate), low-energy-dense, high fibre (25–30 g $day^{-1}$), bio-available nutrient rich (including co-factors), high potassium – low sodium, brain foods (foods rich in preformed DHA, EPA, I, Fe, Cu, Zn and Se - aquatic foods). Micro- and nanotechnologies are already engineering foods for human (and livestock) consumption that may eventually (without excessive consumption) prevent the current diet induced disease epidemic, especially in future generations, by preventing the causal mechanisms of disease. Nanoscience and nanotechnology are new frontiers and their potential cannot be underestimated. There is still an ocean of knowledge about the causal mechanisms of disease that awaits to be discovered, which could further enhance the human desire to increase longevity in optimum health (creating more problems and challenges for society).

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# References

1. Tolfree D, Smith A (2009) Roadmapping emergent technologies. Leicester: Matador
2. Crawford MA, Bloom M, Broadhurst CL, Schmidt WF, Cunnane SC, Galli C, Gehbremeskel K, Linseisen F, Lloyd-Smith J, Parkington J (1999) Evidence for the unique function of docosahexaenoic acid during the evolution of the modern hominid brain. *Lipids* **34**, S39-S47
3. Crawford MA, Broadhurst CL, Galli C, Ghebremeskel K, Holmsen H, Saugstad LF, Schmidt WF, Sinclair AJ, Cunnane SC (2008) The role of docosahexaenoic and arachidonic acids as determinants of evolution and hominid brain development. *Fisheries for Global Welfare and Environment, 5th World Fisheries Congress*, 57-76
4. Cunnane SC (2005) Origins and evolution of the Western diet: implications of iodine and seafood intakes for the human brain. *Am J Clin Nutr* **82**, 483-484
5. Cunnane SC (2006) Survival of the fattest: the key to human brain evolution. *M-S (Med Sci)* **22**, 659-663
6. Innis SM (2007) Fatty acids and early human development. *Early Hum Dev* **83**, 761-766
7. Innis SM (2005) Essential fatty acid transfer and fetal development. *Placenta* **26**, 70-75
8. Birch EE, Garfield S, Castaneda Y, Hughbanks-Wheaton D, Uauy R, Hoffman D (2007) Visual acuity and cognitive outcomes at 4 years of age in a double-blind, randomized trial of long-chain polyunsaturated fatty acid-supplemented infant formula. *Early Hum Dev* **83**, 279-284

9. de Groot RH, Hornstra G, van Houwelingen AC, Roumen F (2004) Effect of alpha-linolenic acid supplementation during pregnancy on maternal and neonatal polyunsaturated fatty acid status and pregnancy outcome. *Am J Clin Nutr* **79**, 251-260
10. Innis SM (2004) Polyunsaturated fatty acids in human milk: An essential role in infant development. *Adv Exp Med Biol* **554**, 27-43
11. Liou YA, King DJ, Zibrik D, Innis SM (2007) Decreasing linoleic acid with constant (alpha)-linolenic acid in dietary fats increases (n-3) eicosapentaenoic acid in plasma phospholipids in healthy men. *J Nutr* **137**, 945
12. Ponder DL, Innis SM, Benson JD, Siegman JS (1992) Docosahexaenoic acid status of term infants fed breast milk or infant formula containing soy oil or corn oil. *Pediatr Res* **32**, 683-688
13. Eaton SB, Konner M (1985) Paleolithic nutrition - a consideration of its nature and current implications. *N Engl J Med* **312**, 283-289
14. Eaton SB, Konner M, Shostak M (1988) Stone agers in the fast lane - chronic degenerative diseases in evolutionary perspective. *Am J Med* **84**, 739-749
15. Williams GC, Nesse RM (1994) Why we get sick: the new science of Darwinian medicine. Times Books, New York
16. Boaz NT (2002) Evolving health: the origins of illness and how the modern world is making us sick. New York: Wiley & Sons, Inc
17. Truswell AS (1977) Diet and nutrition of hunter-gatherers. Health and disease in tribal societies. New York: Elsevier
18. Abrams HL (1979) The relevance of paleolithic diet in determining contemporary nutritional needs. *J Appl Nutr* **31**, 43-59
19. Cohen M (1989) Health and the rise of civilization. London: Yale University Press
20. Cordain L, Gotschall RW, Eaton SB, Eaton SB (1998) Physical activity, energy expenditure and fitness: An evolutionary perspective. *Int J Sports Med* **19**, 328-335
21. Cordain L (1999) Cereal grains: Humanity's double-edged sword. *World Review of Nutrition and Dietetics; Evolutionary aspects of nutrition and health: Diet, exercise, genetics and chronic disease*, 19-73
22. Frassetto L, Morris RC, Sellmeyer DE, Todd K, Sebastian A (2001) Diet, evolution and aging - The pathophysiologic effects of the post-agricultural inversion of the potassium-to-sodium and base-to-chloride ratios in the human diet. *Eur J Nutr* **40**, 200-213
23. Cordain L, Watkins BA, Florant GL, Kelher M, Rogers L, Li Y (2002) Fatty acid analysis of wild ruminant tissues: evolutionary implications for reducing diet-related chronic disease. *Eur J Clin Nutr* **56**, 181-191
24. World Health Organization (2005) Composition of World health expenditures http://www.who.int/nha/pie_chart_%202005.pdf.
25. World Health Organization (2007) Cardiovascular diseases. Fact sheet N°317.
26. World Health Organization (2008) Cancer. Fact sheet N°297.
27. American Cancer Society (2004) Cancer facts & figures 2004. Atlanta: American Cancer Society

28. Danaei G, Vander Hoorn S, Lopez AD, Murray CJL, Ezzati M (2005) Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. *The Lancet* **366**, 1784-1793
29. World Health Organization (2008) Diabetes. Fact sheet N°312.

30. Institute of Medicine (2005) Preventing childhood obesity: Health in the balance. .
31. World Health Organization (2006) Obesity and overweight. Fact sheet N°311.
32. Andlin-Sobocki P, Jonsson J, Wittchen H-U, Olesen J (2005) Cost of disorders of the brain in Europe. *Eur J Neurol* **12**, 1-27
33. Cordain L, Eaton SB, Sebastian A, Mann N, Lindeberg S, Watkins BA, O'Keefe JH, Brand-Miller J (2005) Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr* **81**, 341-354
34. Cordain L, Miller JB, Eaton SB, Mann N, Holt SHA, Speth JD (2000) Plant-animal subsistence ratios and macronutrient energy estimations in worldwide hunter-gatherer diets. *Am J Clin Nutr* **71**, 682-692
35. Institute of Medicine of the National Academies (2002) Dietary fats: total fat and fatty acids. Washington, DC, pp. 335- 432: The National Academy Press
36. Kris-Etherton PM, Harris WS, Appel LJ (2003) Omega-3 fatty acids and cardiovascular disease new recommendations from the American Heart Association. *Arterioscler Thromb Vasc Biol* **23**, 151-152
37. Scientific Advisory Committee on Nutrition (SACN) (2004) Advice on fish consumption: benefits and risks. . Norwich: The Stationery Office
38. Robson A (2006) Shellfish view of omega-3 and sustainable fisheries. *Nature* **444**, 1002
39. Hibbeln JR, Nieminen LRG, Blasbalg TL, Riggs JA, Lands WEM (2006) Healthy intakes of n-3 and n-6 fatty acids: estimations considering worldwide diversity. *Am J Clin Nutr* **83**, S1483-1493
40. Russo GL (2009) Dietary n-6 and n-3 polyunsaturated fatty acids: From biochemistry to clinical implications in cardiovascular prevention. *Biochem Pharmacol* **77**, 937-946
41. Damude HG, Kinney AJ (2008) Engineering oilseeds to produce nutritional fatty acids. *Physiol Plant* **132**, 1-10
42. Sinclair HM (1956) Deficiency of essential fatty acids and atherosclerosis, etcetera. *Lancet* **270**, 381-383
43. Lands WEM, Libelt B, Morris A, Kramer NC, Prewitt TE, Bowen P, Schmeisser D, Davidson MH, Burns JH (1992) Maintenance of lower proportions of (n-6) eicosanoid precursors in phospholipids of human plasma in response to added dietary (n-3) fatty-acids. *Biochim Biophys Acta* **1180**, 147-162
44. Lands WEM (1991) Biosynthesis of prostaglandins. *Annu Rev Nutr* **11**, 41-60
45. Griffin BA (2008) How relevant is the ratio of dietary n-6 to n-3 polyunsaturated fatty acids to cardiovascular disease risk? Evidence from the OPTILIP study. *Curr Opin Lipidol* **19**, 57-62
46. Hooper L, Thompson RL, Harrison RA, Summerbell CD, Ness AR, Moore HJ, Worthington HV, Durrington PN, Higgins JPT, Capps NE (2006) Risks and benefits of omega 3 fats for mortality, cardiovascular disease, and cancer: systematic review. *Br Med J* **332**, 752-760
47. von Schacky C, Harris WS (2007) Cardiovascular benefits of omega-3 fatty acids. *Cardiovasc Res* **73**, 310-315
48. Zieske AW, Malcom GT, Strong JP (2002) Natural history and risk factors of atherosclerosis in children and youth: the pday study *Pediatr Pathol Mol Med* **21**, 213-237
49. Lands WEM (2005) Dietary fat and health: the evidence and the politics of prevention - careful use of dietary fats can improve life and prevent disease. *Ann N Y Acad Sci* **1055**, 179-192
50. Turner R, McLean CH, Silvers KM (2006) Are the health benefits of fish oils limited by products of oxidation? *Nutr Res Rev* **19**, 53-62

51. Sozer N, Kokini JL (2009) Nanotechnology and its applications in the food sector. *Trends Biotechnol* **27**, 82-89
52. Church MW, Jen K-LC, Jackson DA, Adams BR, Hotra JW (2009) Abnormal neurological responses in young adult offspring caused by excess omega-3 fatty acid (fish oil) consumption by the mother during pregnancy and lactation. *Neurotoxicol Teratol* **31** 26-33
53. Lichtenstein AH (2005) Remarks on clinical data concerning dietary supplements that affect antithrombotic therapy. *Thromb Res* **117**, 71-73
54. Iso H, Sato S, Folsom AR, Shimamoto T, Terao A, Munger RG, Kitamura A, Konishi M, Iida M, Komachi Y (1989) Serum Fatty Acids and Fish Intake in Rural Japanese, Urban Japanese, Japanese American and Caucasian American Men. *Int J Epidemiol* **18**, 374-381
55. Gerrior S, Bente L (2002) Nutrient content of the U.S. food supply, 1909-99: a summary report. **US Department of Agriculture, Home Economics report no. 55, Washington, DC**,
56. O'Keefe S (2000) An overview of oils and fats, with a special emphasis on olive oil. United Kingdom, pp 375-97: Cambridge University Press
57. Whitaker JW (1975) Feedlot empire: beef cattle feeding in Illinois and Iowa 1840-1900: Iowa State University Press
58. Murray CJL, Lopez AD (1997) Alternative projections of mortality and disability by cause 1990-2020: Global burden of disease study. *Lancet* **349**, 1498-1504
59. Calder PC (2006) n-3 polyunsaturated fatty acids, inflammation, and inflammatory diseases. *Am J Clin Nutr* **83**, 1505S-1519S
60. Das UN (2008) Essential fatty acids and their metabolites could function as endogenous HMG-CoA reductase and ACE enzyme inhibitors, anti-arrhythmic, anti-hypertensive, anti-atherosclerotic, anti-inflammatory, cytoprotective, and cardioprotective molecules. *Lipids Health Dis* **7**, 37
61. Samuelsson B (1979) Prostaglandins, thromboxanes, and leukotrienes: formation and biological roles. *Harvey Lect* **75**, 1-40
62. Lands WEM (1986) Fish and human health. Orlando, Fla: Academic Press
63. Kris-Etherton PM, Harris WS, Appel LJ, Nutrition C (2002) Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* **106**, 2747-2757
64. MacLean CH, Newberry SJ, Mojica WA, Khanna P, Issa AM, Suttorp MJ, Lim YW, Traina SB, Hilton L, Garland R (2006) Effects of omega-3 fatty acids on cancer risk a systematic review. *JAMA* **295**, 403-415
65. Terry PD, Terry JB, Rohan TE (2004) Long-chain (n-3) fatty acid intake and risk of cancers of the breast and the prostate: recent epidemiological studies, biological mechanisms, and directions for future research
*J Nutr* **134**, 3412-3420
66. Engeset D, Alsaker E, Lund E, Welch A, Khaw KT, Clavel-Chapelon F, Thiebaut A, Chajes V, Key TJ, Allen NE (2006) Fish consumption and breast cancer risk. The european prospective investigation into cancer and nutrition (EPIC). *Int J Cancer* **119**, 175-182
67. Gago-Dominguez M, Yuan JM, Sun CL, Lee HP, Yu MC (2003) Opposing effects of dietary n-3 and n-6 fatty acids on mammary carcinogenesis: the Singapore Chinese health study. *Br J Cancer* **89**, 1686-1692
68. Hirose K, Takezaki T, Hamajima N, Miura S, Tajima K (2003) Dietary factors protective against breast cancer in Japanese premenopausal and postmenopausal women. *Int J Cancer* **107**, 276-282

69. Wakai K, Tamakoshi K, Date C, Fukui M, Suzuki S, Lin Y, Niwa Y, Nishio K, Yatsuya H, Kondo T, Tokudome S, Yamamoto A (2005) Dietary intakes of fat and fatty acids and risk of breast cancer: a prospective study in Japan. *Cancer Sci* **96**, 590-599
70. Thiebaut ACM, Chajes V, Gerber M, Boutron-Ruault M-C, Joulin V, Lenoir G, Berrino F, Riboli E, Benichou J, Clavel-Chapelon F (2009) Dietary intakes of omega-6 and omega-3 polyunsaturated fatty acids and the risk of breast cancer. *Int J Cancer* **124**, 924-931
71. Marmot M, Atinmo T, Byers T, Chen J, Hirohata T, Jackson A, James WPT, Kolonel LN, Kumanyika S, Leitzmann C (2007) Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington, DC: American Institute for Cancer Research
72. Rose DP, Connolly JM (1999) Omega-3 fatty acids as cancer chemopreventive agents. *Pharmacol Ther* **83**, 217-244
73. Schumacher MC, Laven B, Wolk A, Brendler CB, Ekman P (2007) Do omega-3 dietary fatty acids lower prostate cancer risk? A review of the literature. *Curr Urol* **1**, 2-10
74. Salem N, Litman B, Kim HY, Gawrisch K (2001) Mechanisms of action of docosahexaenoic acid in the nervous system. *Lipids* **36**, 945-959
75. Iribarren C, Markovitz JH, Jacobs DR, Schreiner PJ, Daviglus M, Hibbeln JR (2004) Dietary intake of n-3, n-6 fatty acids and fish: Relationship with hostility in young adults - the CARDIA study. *Eur J Clin Nutr* **58**, 24-31
76. Stoll AL, Damico KE, Daly BP, Severus WE, Marangell LB (2001) Methodological considerations in clinical studies of omega 3 fatty acids in major depression and bipolar disorder. *Fatty Acids And Lipids-New Findings* **88**, 58-67
77. Willatts P, Forsyth JS (2000) The role of long-chain polyunsaturated fatty acids in infant cognitive development. *Prostaglandins, Leukotrienes & Essential Fatty Acids* **63**, 95-100
78. Litt J, Taylor HG, Klein N, Hack M, (2005) Learning disabilities in children with very low birthweight: prevalence, neuropsychological correlates, and educational interventions. . *J Learn Disabil* **38**, 130-141
79. McNamara RK, Carlson SE (2006) Role of omega-3 fatty acids in brain development and function: potential implications for the pathogenesis and prevention of psychopathology. *Prostaglandins Leukot Essent Fatty Acids* **75**, 329-349
80. Hibbeln J, Davis J, Steer C, Emmett P, Rogers I, Williams C, Golding J (2007) Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. *Lancet* **369**, 578-585
81. Barker DJ (2007) The origins of the developmental origins theory. *J Intern Med* **61**, 412-417
82. Barker DJ (2004) The developmental origins of chronic adult disease. *Acta Paediatr* **93**, 26-33
83. Doyle W, Crawford MA, Wynn AHA, Wynn SW (1989) Maternal nutrient intake and birth weight. *J Hum Nutr Diet* **2**, 407-414
84. Wynn SW, Wynn AHA, Doyle W, Crawford MA (1994) The association of maternal social class with maternal diet and the dimensions of babies in a population of London Women. *Nutr Health* **9**, 303-315
85. House S (2000) Stages in reproduction particularly vulnerable to xenobiotic hazards and nutritional deficits. *Nutr Health* **14**, 147-193
86. Carlson SE (2001) Docosahexaenoic acid and arachidonic acid in infant development. . *Semin Neonatol* **6**, 437-449

87. Rees G, Doyle W, Srivastava A, Brooke ZM, Crawford MA, Costeloe KL (2005) The nutrient intakes of mothers of low birth weight babies-a comparison of ethnic groups in East London, UK. *Matern Child Nutr* **1**, 91-99
88. Wathes DC, Abayasekara DRE, Aitken RJ (2007) Polyunsaturated fatty acids in male and female reproduction. *Biol Reprod* **77**, 190-201
89. Ruxton CHS, Reed SC, Simpson MJA, Millington KJ (2004) The health benefits of omega-3 polyunsaturated fatty acids: a review of the evidence. *J Hum Nutr Diet* **17**, 449-459
90. Silvers K, Woolley C, Hamilton F, Watts P, Watson R (2005) Randomised double-blind placebo-controlled trial of fish oil in the treatment of depression *Prostaglandins Leukot Essent Fatty Acids* **72**, 211-218
91. Hibbeln J (2002) Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: a cross-national, ecological analysis. *J Affect Disord*, 15-29
92. Hibbeln J, Nieminen L, Lands W (2004) Increasing homicide rates and linoleic acid consumption among five Western countries, 1961-2000. *Lipids* **39**, 1207-1213
93. American Oil Chemists' Society (2003) What the experts eat: the health and nutrition division weighs in with nutrition advice. *Inform (American Oil Chemists' Society)* **14**, 116-117
94. Farhang B (2007) Nanotechnology and lipids. *Lipid Technology* **19**, 132-135
95. Ross R (1999) Atherosclerosis-an inflammatory disease. *N Engl J Med* **340**, 115-126
96. Libby P (2002) Atherosclerosis in inflammation. *Nature* **420**, 868-874
97. Stoll G, Bendszus M (2006) Inflammation and atherosclerosis: novel insights into plaque formation and destabilization. *Stroke* **37**, 1923-1932
98. Roberts CK, Vaziri ND, Barnard RJ (2002) Effect of diet and exercise intervention on blood pressure, insulin, oxidative stress, and nitric oxide availability. Am Heart Assoc. p. 2530-2532
99. Roberts CK, Barnard RJ, Sindhu RK, Jurczak M, Ehdaie A, Vaziri ND (2005) A high-fat, refined-carbohydrate diet induces endothelial dysfunction and oxidant/antioxidant imbalance and depresses NOS protein expression. *J Appl Physiol* **98**, 203-210
100. Nathan C (2008) Epidemic inflammation: pondering obesity. *Mol Med* **14**, 485-492
101. Du XL, Edelstein D, Dimmeler S, Ju Q, Sui C, Brownlee M (2001) Hyperglycemia inhibits endothelial nitric oxide synthase activity by posttranslational modification at the Akt site. *J Clin Investig* **108**, 1341-1348
102. Lands B (2008) A critique of paradoxes in current advice on dietary lipids. *Prog Lipid Res* **47**, 77-106
103. Gilani GS, Nasim A (2007) Impact of foods nutritionally enhanced through biotechnology in alleviating malnutrition in developing countries. *J AOAC Int* **90**, 1440-1444
104. Chassy BM, Hlywka JJ, Kleter GA, Kok EJ, Kuiper HA, McGloughlin M, Munro IC, Phipps RH, Reid JE (2004) Nutritional and safety assessments of foods and feeds nutritionally improved through biotechnology. *Comp Rev Food Sci Food Safety* **3**, 35-104
105. Das UN (2006) Essential fatty acids: biochemistry, physiology and pathology. *Biotechnol J* **1**, 420-439
106. Ledikwe JH, Blanck HM, Kettel Khan L, Serdula MK, Seymour JD, Tohill BC, Rolls BJ (2006) Dietary energy density is associated with energy intake and weight status in US adults. *Am J Clin Nutr* **83**, 1362-1368

107. Liu S, Willett WC (2002) Dietary glycemic load and atherothrombotic risk. *Curr Atheroscler Rep* **4**, 454-461
108. Ludwig DS (2002) The glycemic index physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA* **287**, 2414-2423
109. Cordain L, Eades MR, Eades MD (2003) Hyperinsulinemic diseases of civilization: more than just Syndrome X. *Comp Biochem Physiol A Mol Integr Physiol* **136**, 95-112
110. Rossetti L, Giaccari A, Defronzo RA (1990) Glucose toxicity. *Diabetes Care* **13**, 610-630
111. Delprato S, Leonetti E, Simonson DC, Sheehan P, Matsuda M, Defronzo RA (1994) Effect Of sustained physiological hyperinsulinemia and hyperglycemia on insulin-secretion and insulin sensitivity in man. *Diabetologia* **37**, 1025-1035
112. Thomson MJ, Williams MG, Frost SC (1997) Development of insulin resistance in 3T3-L1 adipocytes. *J Biol Chem* **272**, 7759-7764
113. Zammit VA, Waterman IJ, Topping D, McKay G (2001) Insulin stimulation of hepatic triacylglycerol secretion and the etiology of insulin resistance. *J Nutr* **131**, 2074-2077
114. Boden G, Shulman GI (2002) Free fatty acids in obesity and type 2 diabetes: defining their role in the development of insulin resistance and beta-cell dysfunction. *Eur J Clin Investig* **32**, 14-23
115. McClain DA (2002) Hexosamines as mediators of nutrient sensing and regulation in diabetes. *J Diabetes Complicat* **16**, 72-80
116. Ostman EM, Elmstahl H, Bjorck IME (2001) Inconsistency between glycemic and insulinemic responses to regular and fermented milk products. *Am J Clin Nutr* **74**, 96-100
117. Das UN (2008) Beneficial Actions of Polyunsaturated Fatty Acids in Cardiovascular Diseases: But, How and Why? *Current Nutr Food Sci* **4**, 2-31
118. Madden SG, Loeb SJ, Smith CA An integrative literature review of lifestyle interventions for the prevention of type II diabetes mellitus. *J Clin Nurs* **17** 2243-2256
119. Cordain L, Eaton SB, Miller JB, Lindeberg S, Jensen C (2002) An evolutionary analysis of the aetiology and pathogenesis of juvenile-onset myopia. *Acta Ophthalmol Scand* **80**, 125-135
120. Cordain L, Lindeberg S, Hurtado M, Hill K, Eaton SB, Brand-Miller J (2002) Acne vulgaris - a disease of western civilization. *Arch Dermatol* **138**, 1584-1590
121. Reaven GM (1995) Pathophysiology of insulin-resistance in human-disease. *Physiol Rev* **75**, 473-486
122. Schaefer O (1971) When the Eskimo comes to town. *Nutr Today* **6**, 8-16
123. Trowell HC (1980) From normotension to hypertension in Kenyans and Ugandans 1928-1978. *East Afr Med J* **57**, 167-173
124. Chen L, Appel LJ, Loria C, Lin PH, Champagne CM, Elmer PJ, Ard JD, Mitchell D, Batch BC, Svetkey LP (2009) Reduction in consumption of sugar-sweetened beverages is associated with weight loss: the PREMIER trial. *Am J Clin Nutr* **doi:10.3945/ajcn.2008.27240**,
125. Carnell S, Wardle J (2008) Appetitive traits and child obesity: measurement, origins and implications for intervention. *Proc Nutr Soc* **67**, 343-355
126. Krauss RM, Eckel RH, Howard B, Appel LJ, Daniels SR, Deckelbaum RJ, Erdman JW, Kris-Etherton P, Goldberg IJ, Kotchen TA, Lichtenstein AH, Mitch WE, Mullis R, Robinson K, Wylie-Rosett J, Jeor SS, Suttie J, Tribble DL, Bazzarre TL (2000) AHA dietary guidelines - Revision 2000: A statement for healthcare professionals from the nutrition committee of the American Heart Association. *Circulation* **102**, 2284-2299
127. Cordain L, Eaton SB, Miller JB, Mann N, Hill K (2002) The paradoxical nature of hunter-gatherer diets: meat-based, yet non-atherogenic. *Eur J Clin Nutr* **56**, S42-S52

128. Crovetti R, Porrini M, Santangelo A, Testolin G (1998) The influence of thermic effect of food on satiety. *Eur J Clin Nutr* **52**, 482-488
129. Stubbs RJ (1998) Appetite, feeding behaviour and energy balance in human subjects. *Proc Nutr Soc* **57**, 341-356
130. Borzoei S, Neovius M, Barkeling B, Teixeira-Pinto A, Rossner S (2006) A comparison of effects of fish and beef protein on satiety in normal weight men. *Eur J Clin Nutr* **60**, 897-902
131. Baba NH, Sawaya S, Torbay N, Habbal Z, Azar S, Hashim SA (1999) High protein vs high carbohydrate hypoenergetic diet for the treatment of obese hyperinsulinemic subjects. *Int J Obes* **23**, 1202-1206
132. Skov AR, Toubro S, Ronn B, Holm L, Astrup A (1999) Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *Int J Obes* **23**, 528-536
133. Layman DK (2003) The role of leucine in weight loss diets and glucose homeostasis. *J Nutr* **133**, 261S-267S
134. Westerterp-Plantenga MS, Lejeune M, Nijs I, van Ooijen M, Kovacs EMR (2004) High protein intake sustains weight maintenance after body weight loss in humans. *Int J Obes* **28**, 57-64
135. Johnston CS, Tjonn SL, Swan PD (2004) High-protein, low-fat diets are effective for weight loss and favorably alter biomarkers in healthy adults. *J Nutr* **134**, 586-591
136. Seino Y, Seino S, Ikeda M, Matsukura S, Imura H (1983) Beneficial-effects of high protein-diet in treatment of mild diabetes. *Human Nutrition-Applied Nutrition* **37**, 226-230
137. Odea K (1984) Marked improvement in carbohydrate and lipid-metabolism in diabetic australian aborigines after temporary reversion to traditional lifestyle. *Diabetes* **33**, 596-603
138. Odea K, Traianedes K, Ireland P, Niall M, Sadler J, Hopper J, Deluise M (1989) The effects of diet differing in fat, carbohydrate, and fiber on carbohydrate and lipid-metabolism in type-II diabetes. *J Am Diet Assoc* **89**, 1076-1086
139. Piatti PM, Monti LD, Magni F, Fermo I, Baruffaldi L, Nasser R, Santambrogio G, Librenti MC, Gallikienle M, Pontiroli AE, Pozza G (1994) Hypocaloric high-protein diet improves glucose-oxidation and spares lean body-mass - comparison to hypocaloric high-carbohydrate diet. *Metab Clin Exp* **43**, 1481-1487
140. Obarzanek E, Velletri PA, Cutler JA (1996) Dietary protein and blood pressure. *J Amer Med Assoc* **275**, 1598-1603
141. Wolfe BM, Giovannetti PM (1991) Short-term effects of substituting protein for carbohydrate in the diets of moderately hypercholesterolemic human-subjects. *Metab Clin Exp* **40**, 338-343
142. Wolfe BM, Giovannetti PM (1992) High protein-diet complements resin therapy of familial hypercholesterolemia. *Clin Investig Med* **15**, 349-359
143. Wolfe BMJ, Piche LA (1999) Replacement of carbohydrate by protein in a conventional-fat diet reduces cholesterol and triglyceride concentrations in healthy normolipidemic subjects. *Clinical And Investigative Medicine-Medecine Clinique Et Experimentale* **22**, 140-148
144. Chakraborty S, Chakraborty N, Datta A (2000) Increased nutritive value of transgenic potato by expressing a nonallergenic seed albumin gene from Amaranthus hypochondriacus. *Proc Natl Acad Sci USA* **97**, 3724-3729
145. Glenn KC (2007) Nutritional and safety assessments of foods and feeds nutritionally improved through biotechnology: Lysine maize as a case study. *J AOAC Int* **90**, 1470-1479
146. Graveland-Bikker JF, De Kruif CG (2006) Unique milk protein based nanotubes: food and nanotechnology meet. *Trends in Food Science & Technology* **17**, 196-203

147. First Data Bank (2000) Nutritionist v nutrition software, version 2.3. San Bruno, CA: First Data Bank
148. Brand-Miller JC, Holt SHA (1998) Australian Aboriginal plant foods: a consideration of their nutritional composition and health implications. *Nutr Res Rev* **11**, 5-23
149. Cunnane SC, Plourde M, Stewart K, Crawford MA (2007) Docosahexaenoic acid and shore-based diets in hominin encephalization: a rebuttal. *Am J Hum Biol* **19**, 578-581
150. World Health Organization (2009) Micronutrient deficiencies: Iron deficiency anaemia http://www.who.int/nutrition/topics/ida/en/print.html.
151. Siritunga D, Sayre RT (2003) Generation of cyanogen-free transgenic cassava. *Planta* **217**, 367-373
152. Paine JA, Shipton CA, Chaggar S, Howells RM, Kennedy MJ, Vernon G, Wright SY, Hinchliffe E, Adams JL, Silverstone AL (2005) Improving the nutritional value of Golden Rice through increased pro-vitamin A content. *Nat Biotechnol* **23**, 482-487
153. Vasconcelos M, Datta K, Oliva N, Khalekuzzaman M, Torrizo L, Krishnan S, Oliveira M, Goto F, Datta SK (2003) Enhanced iron and zinc accumulation in transgenic rice with the ferritin gene. *Plant Science* **164**, 371-378
154. Lucca P, Hurrell R, Potrykus I (2002) Fighting iron deficiency anemia with iron-rich rice. *J Am Coll Nutr* **21**, 184S-190S
155. World Health Organization (2005) Modern food biotechnology, human health and development: an evidence-based study. Geneva, Switzerland: World Health Organization
156. Sorrentino A, Gorrasi G, Vittoria V (2007) Potential perspectives of bio-nanocomposites for food packaging applications. *Trends in Food Science & Technology* **18**, 84-95
157. Chen L, Remondetto GE, Subirade M (2006) Food protein-based materials as nutraceutical delivery systems. *Trends in Food Science & Technology* **17**, 272-283
158. Frassetto LA, Todd KM, Morris RC, Sebastian A (1998) Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. *Am J Clin Nutr* **68**, 576-583
159. Sebastian A, Frassetto LA, Sellmeyer DE, Merriam RL, Morris RC (2002) Estimation of the net acid load of the diet of ancestral preagricultural *Homo sapiens* and their hominid ancestors. *Am J Clin Nutr* **76**, 1308-1316
160. Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC (1994) Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* **330**, 1776-1781
161. Bushinsky DA (1996) Metabolic alkalosis decreases bone calcium efflux by suppressing osteoclasts and stimulating osteoblasts. *American Journal Of Physiology-Renal Physiology* **271**, F216-F222
162. Frassetto L, Morris RC, Sebastian A (1997) Potassium bicarbonate reduces urinary nitrogen excretion in postmenopausal women. *J Clin Endocrinol Metab* **82**, 254-259
163. Pak CYC, Fuller C, Sakhaee K, Preminger GM, Britton F (1985) Long-term treatment of calcium nephrolithiasis with potassium citrate. *J Urol* **134**, 11-19
164. Preminger GM, Sakhaee K, Skurla C, Pak CYC (1985) Prevention of recurrent calcium stone formation with potassium citrate therapy in patients with distal renal tubular-acidosis. *J Urol* **134**, 20-23
165. Sharma AM, Kribben A, Schattenfroh S, Cetto C, Distler A (1990) Salt sensitivity in humans is associated with abnormal acid-base regulation. *Hypertension* **16**, 407-413

166. Morris RC, Sebastian A, Forman A, Tanaka M, Schmidlin O (1999) Normotensive salt sensitivity - effects of race and dietary potassium. *Hypertension* **33**, 18-23
167. Mickleborough TD, Gotshall RW, Kluka EM, Miller CW, Cordain L (2001) Dietary chloride as a possible determinant of the severity of exercise-induced asthma. *Eur J Appl Physiol* **85**, 450-456
168. Alpern RJ, Sakhaee K (1997) The clinical spectrum of chronic metabolic acidosis: Homeostatic mechanisms produce significant morbidity. *Am J Kidney Dis* **29**, 291-302
169. U.S. Department of Agriculture (2008) Nutrient Intakes from Food: Mean Amounts Consumed per Individual, One Day, 2005-2006. Agricultural Research Service www.ars.usda.gov/ba/bhnrc/fsrg
170. Cordain L (2002) The nutritional characteristics of a contemporary diet based upon Paleolithic food groups. *J Am Neutraceutical Assoc* **5**, 15-24
171. Miller MM (1945) Low sodium chloride intake in the treatment of insomnia and tension states. *J Amer Med Assoc* **129:**, 262
172. Jansson B (1986) Geographic cancer risk and intracellular potassium-sodium ratios. *Cancer Detect Prev* **9**, 171-194
173. Tuyns AJ (1988) Salt and gastrointestinal cancer. *Nutr Cancer* **11**, 229-232
174. Carey OJ, Locke C, Cookson JB (1993) Effect of alterations of dietary-sodium on the severity of asthma in men. *Thorax* **48**, 714-718
175. Devine A, Criddle RA, Dick IM, Kerr DA, Prince RL (1995) A longitudinal-study of the effect of sodium and calcium intakes on regional bone-density in postmenopausal women. *Am J Clin Nutr* **62**, 740-745
176. Lindseth G, Lindseth PD (1995) The relationship of diet to airsickness. *Aviat Space Environ Med* **66**, 537-541
177. Massey LK, Whiting SJ (1995) Dietary salt, urinary calcium, and kidney-stone risk. *Nutr Rev* **53**, 131-134
178. Porcelli MJ, Gugelchuk GM (1995) A trek to the top: a review of acute mountain sickness. *J Am Osteopath Assoc* **95**, 718-718
179. Antonios TFT, MacGregor GA (1996) Salt - More adverse effects. *Lancet* **348**, 250-251
180. Gotshall RW, Mickleborough TD, Cordain L (2000) Dietary salt restriction improves pulmonary function in exercise-induced asthma. *Med Sci Sports Exerc* **32**, 1815-1819
181. Thai-Van H, Bounaix MJ, Fraysse B (2001) Meniere's disease: pathophysiology and treatment. *Drugs* **61**, 1089-1102
182. Trowell H (1985) Dietary fibre: a paradigm. *Dietary Fibre, Fibre-Depleted Foods and Disease*, 1-20

Table 2

Amount (g) of a selection of foods equivalent to the 119 kcal of energy in one tablespoon (13.5 g) of olive oil (04053)

| Food | g |
|---|---|
| Chocolate bar, 70-85% cocoa (19904) | 20 |
| Peanuts (16087) | 21 |
| Chocolate cookies (18159) | 25 |
| Masterfoods®, Snickers Bar (19155) | 25 |
| Muffin, blueberry (18274) | 30 |
| Cheese, cheddar (01009) | 30 |
| Oats (20038) | 30 |
| Sugars, granulated (19335) | 31 |
| Kellogg's®, Corn Flakes (08020) | 33 |
| Distilled alcoholic drink, 50% abv (14533) | 41 |
| Beef, brisket (13803) | 47 |
| Bread, whole-wheat (18075) | 48 |
| Chicken, with skin (05006) | 55 |
| Ice cream, vanilla (19095) | 58 |
| Pork, loin (10020) | 60 |
| Salmon, Atlantic (15076) | 84 |
| Anchovy, European (15001) | 91 |
| Chocolate milkshake (01110) | 100 |
| Shrimp, mixed species (15149) | 112 |
| Bananas (09040) | 134 |
| Crab, Dungeness (15143) | 138 |
| Mussel, blue (15164) | 138 |
| Red wine (14096) | 140 |
| Cod, Atlantic (15015) | 145 |
| Oyster, Pacific (15171) | 147 |
| Clam, mixed species (15157) | 161 |
| Potatoes (11354) | 172 |
| Apples (09003) | 229 |
| Seaweed, wakame (11669) | 264 |
| Orange juice, freshly squeezed (09206) | 264 |
| Carrots (11124) | 290 |
| Budweiser®, beer (14004) | 290 |
| Cola, soft drink (14148) | 290 |
| Spinach (11457) | 517 |
| Tomatoes, red (11529) | 661 |
| Lettuce (11251) | 700 |
| Drinking water, tap (14411) | N/A |

[1] Entries retrieved from the U.S. Department of Agriculture, Agricultural Research Service, 2007, USDA National Nutrient Database for Standard Reference, Release 21, http://www.ars.usda.gov/ba/bhnrc/ndl are followed by a 5-digit nutrient database number in parentheses. Data were not adjusted for country and seasonal specific differences in nutrient compositions of foods.

Table 1. Estimated fatty acid composition of a range of Aquatic and Land based foods

| Food | Omeag-3 Fatty acids | | | | Omega-6 Fatty acids | |
|---|---|---|---|---|---|---|
| | ALA (18:3ω-3) | EPA (20:5ω-3) | DPA[2] (22:5ω-3) | DHA (22:6ω-3) | LA (18:2ω-6) | AA (20:4ω-6) |
| **Aquatic** | g/100g | | | | g/100g | |
| Mussel, blue (15164)[1] | 0.020 | 0.188 | 0.022 | 0.253 | 0.018 | 0.070 |
| Oyster, Pacific (15171) | 0.032 | 0.438 | 0.020 | 0.250 | 0.032 | 0.038 |
| Shrimp, mixed species (15149) | 0.014 | 0.258 | 0.046 | 0.222 | 0.028 | 0.087 |
| Crab, blue (15139) | 0.000 | 0.170 | 0.000 | 0.150 | 0.012 | 0.055 |
| Salmon, Atlantic (15076) | 0.295 | 0.321 | 0.287 | 1.115 | 0.172 | 0.267 |
| Mackerel, Atlantic (15046) | 0.159 | 0.898 | 0.212 | 1.401 | 0.219 | 0.183 |
| Catfish, channel (15010) | 0.071 | 0.130 | 0.100 | 0.234 | 0.101 | 0.149 |
| Seaweed, wakame (11669) | 0.002 | 0.186 | 0.000 | 0.000 | 0.010 | 0.021 |
| Salmon oil (04593) | 1.061 | 13.023 | 2.991 | 13.232 | 1.543 | 0.675 |
| **Land** | | | | | | |
| Spinach (11457) | 0.138 | 0.000 | 0.000 | 0.000 | 0.026 | 0.000 |
| Kale (11233) | 0.180 | 0.000 | 0.000 | 0.000 | 0.138 | 0.002 |
| Carrots (11124) | 0.002 | 0.000 | 0.000 | 0.000 | 0.115 | 0.000 |
| Potatoes, white (11354) | 0.010 | 0.000 | 0.000 | 0.000 | 0.032 | 0.000 |
| Chickpeas, cooked (16057) | 0.043 | 0.000 | 0.000 | 0.000 | 1.113 | 0.000 |
| Mung beans, cooked (16081) | 0.009 | 0.000 | 0.000 | 0.000 | 0.119 | 0.000 |
| Milk, 3.7% fat (01078) | 0.053 | 0.000 | 0.000 | 0.000 | 0.083 | 0.000 |
| Cheese, cheddar (01009) | 0.365 | 0.000 | 0.000 | 0.000 | 0.577 | 0.000 |
| Butter, unsalted (01145) | 0.315 | 0.000 | 0.000 | 0.000 | 2.728 | 0.000 |
| Egg, whole (01123) | 0.033 | 0.004 | 0.000 | 0.037 | 1.148 | 0.142 |
| Chicken, with skin (05006) | 0.140 | 0.010 | 0.010 | 0.030 | 2.880 | 0.080 |
| Chicken, no skin (05011) | 0.020 | 0.010 | 0.020 | 0.030 | 0.550 | 0.080 |
| Pork, shoulder (10070) | 0.130 | 0.000 | 0.000 | 0.000 | 1.600 | 0.100 |
| Beef, sirloin (13954) | 0.052 | 0.000 | 0.000 | 0.000 | 0.303 | 0.039 |
| Lamb, domestic (17011) | 0.320 | 0.000 | 0.000 | 0.000 | 1.090 | 0.070 |
| Wheat flour, whole grain (20080) | 0.038 | 0.000 | 0.000 | 0.000 | 0.783 | 0.002 |
| Cornmeal, whole grain (20320) | 0.049 | 0.000 | 0.000 | 0.000 | 1.589 | 0.000 |
| Rice flour, brown (20090) | 0.042 | 0.000 | 0.000 | 0.000 | 0.954 | 0.000 |
| Oats (20038) | 0.111 | 0.000 | 0.000 | 0.000 | 2.424 | 0.000 |
| Kellogg's®, All-Bran (08001) | 0.150 | 0.000 | 0.000 | 0.000 | 1.960 | 0.000 |
| Kellogg's®, Corn Flakes (08020) | 0.020 | 0.000 | 0.000 | 0.000 | 0.300 | 0.000 |
| Kellogg's®, Special K (08067) | 0.096 | 0.000 | 0.000 | 0.000 | 0.705 | 0.000 |
| Masterfoods®, Snickers Bar (19155) | 0.048 | 0.000 | 0.000 | 0.000 | 2.966 | 0.000 |
| Muffins, blueberry (18274) | 1.234 | 0.000 | 0.000 | 0.000 | 8.469 | 0.000 |
| Bread, whole wheat (18075) | 0.025 | 0.000 | 0.000 | 0.000 | 0.574 | 0.001 |
| Tortillas, corn (18363) | 0.034 | 0.000 | 0.000 | 0.000 | 1.385 | 0.000 |
| Walnuts, english (12155 | 9.080 | 0.000 | 0.000 | 0.000 | 38.093 | 0.000 |
| Peanuts (16087) | 0.003 | 0.000 | 0.000 | 0.000 | 15.555 | 0.000 |
| Pecan nuts (12142) | 0.986 | 0.000 | 0.000 | 0.000 | 20.628 | 0.000 |
| Brazilnuts (12078) | 0.035 | 0.000 | 0.000 | 0.000 | 20.543 | 0.000 |
| Almonds (12061) | 0.006 | 0.000 | 0.000 | 0.000 | 12.061 | 0.000 |
| Sunflower seeds (12036) | 0.060 | 0.014 | 0.000 | 0.000 | 23.050 | 0.000 |
| Sesame seeds (12024) | 0.363 | 0.000 | 0.000 | 0.000 | 20.654 | 0.000 |
| Flaxseed (12220) | 22.813 | 0.000 | 0.000 | 0.000 | 5.903 | 0.000 |
| Apples, with skin (09003) | 0.009 | 0.000 | 0.000 | 0.000 | 0.043 | 0.000 |
| Bananas (09040) | 0.027 | 0.000 | 0.000 | 0.000 | 0.046 | 0.000 |
| Oranges, Florida (09203) | 0.011 | 0.000 | 0.000 | 0.000 | 0.031 | 0.000 |
| Olive oil (04053) | 0.761 | 0.000 | 0.000 | 0.000 | 9.762 | 0.000 |
| Cottonseed oil (04502) | 0.200 | 0.000 | 0.000 | 0.000 | 51.500 | 0.100 |
| Groundnut oil (04042) | 0.000 | 0.000 | 0.000 | 0.000 | 32.000 | 0.000 |
| Corn oil (04518) | 1.161 | 0.000 | 0.000 | 0.000 | 53.515 | 0.000 |
| Soybean oil (04044) | 6.789 | 0.000 | 0.000 | 0.000 | 50.952 | 0.000 |
| Sesame oil (04058) | 0.300 | 0.000 | 0.000 | 0.000 | 41.300 | 0.000 |
| Sunflower vegetable oil (04060) | 0.200 | 0.000 | 0.000 | 0.000 | 39.800 | 0.000 |
| Palm oil (04055) | 0.200 | 0.000 | 0.000 | 0.000 | 9.100 | 0.000 |
| Flaxseed oil (42231) | 53.300 | 0.000 | 0.000 | 0.000 | 12.700 | 0.000 |
| Margarine, 80% fat (04628) | 2.040 | 0.000 | 0.006 | 0.000 | 22.252 | 0.000 |
| Benecol®, light spread (04687) | 2.187 | 0.000 | 0.000 | 0.000 | 9.724 | 0.000 |
| Peanut butter (16097) | 0.083 | 0.000 | 0.000 | 0.000 | 14.715 | 0.000 |

[1] Entries retrieved from the U.S. Department of Agriculture, Agricultural Research Service, 2007, USDA National Nutrient Database for Standard Reference, Release 20, http://www.ars.usda.gov/ba/bhnrc/ndl are followed by a 5-digit nutrient database number in parentheses. Data were not adjusted for country and seasonal specific differences in nutrient compositions of foods. [2]DPA (docosapentaenoic acid ω-3) is an intermediary between EPA and DHA.

Table 3. Examples of the estimated vitamin and mineral content of refined and unrefined sugar, a seed oil, shellfish, land-based meat, a vegetable and a fruit

| | Units /100g | Food | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Sucrose[1,2] (19335) | Molasses[3] (19304) | Sunflower oil (04060) | Mussel, blue (15164) | Oyster, Pacific (15171) | Beef, grass fed (13047) | Broccoli (11090) | Apples, with skin (09003) |
| Vitamin C | mg | 0 | 0 | 0 | 8.0 | 8.0 | 0 | 89.2 | 4.6 |
| Vitamin B-12 | µg | 0 | 0 | 0 | 12.00 | 16.00 | 1.97 | 0 | 0 |
| Niacin | mg | 0 | 0.930 | 0 | 1.6 | 2.010 | 4.818 | 0.639 | 0.091 |
| Riboflavin | mg | 0.019 | 0.002 | 0 | 0.210 | 0.233 | 0.154 | 0.117 | 0.026 |
| Thiamine | mg | 0 | 0.041 | 0 | 0.160 | 0.067 | 0.049 | 0.071 | 0.017 |
| Folate | µg | 0 | 0 | 0 | 42 | 10 | 6 | 63 | 3 |
| Vitamin B-6 | mg | 0 | 0.670 | 0 | 0.050 | 0.050 | 0.355 | 0.175 | 0.041 |
| Vitamin A | µg[4] | 0 | 0 | 0 | 48 | 81 | 0 | 31 | 3 |
| Calcium | mg | 1 | 205 | 0 | 26 | 8 | 12 | 47 | 6 |
| Iron | mg | 0.01 | 4.72 | 0.03 | 3.95 | 5.11 | 1.99 | 0.73 | 0.12 |
| Magnesium | mg | 0 | 242 | 0 | 34 | 22 | 19 | 21 | 5 |
| Phosphorous | mg | 0 | 31 | 0 | 197 | 162 | 175 | 66 | 11 |
| Potassium | mg | 2 | 1464 | 0 | 320 | 168 | 289 | 316 | 107 |
| Sodium | mg | 0 | 37 | 0 | 286 | 106 | 68 | 33 | 1 |
| Zinc | mg | 0 | 0.29 | 0 | 1.60 | 16.62 | 4.55 | 0.41 | 0.04 |
| Copper | mg | 0 | 0.487 | NA | 0.094 | 1.576 | 0.063 | 0.049 | 0.027 |
| Manganese | mg | 0 | 1.530 | NA | 3.400 | 0.634 | 0.010 | 0.210 | 0.035 |
| Selenium | µg | 0.6 | 17.8 | NA | 44.8 | 77.0 | 14.2 | 2.5 | 0.0 |

[1] Entries retrieved from the U.S. Department of Agriculture, Agricultural Research Service, 2007, USDA National Nutrient Database for Standard Reference, Release 20, http://www.ars.usda.gov/ba/bhnrc/ndl are followed by a 5-digit nutrient database number in parentheses. Data were not adjusted for country and seasonal specific differences in nutrient compositions of foods. [2]Sucrose is a refined sugar. [3]Molasses is unrefined sugar. [4]Vitamin A units in retinol activity equivalents (RAE).

Table 4. Estimated Sodium and Potassium composition of a range of foods available in most developed countries

| Food | Sodium mg/100g | Potassium mg/100g |
|---|---|---|
| Salt, table (02047)[1] | 38758 | 8 |
| Shrimp, mixed species (15149) | 148 | 185 |
| Salmon, chinook (15078) | 47 | 394 |
| Salmon, chinook smoked (15179)* | 2000 | 175 |
| Spinach (11457) | 79 | 558 |
| Bananas (09040) | 1 | 358 |
| Wheat flour, whole-grain (20080) | 5 | 405 |
| Bread, whole-wheat (18075)* | 472 | 248 |
| Milk, 3.7% fat (01078) | 49 | 151 |
| Cheese, cheddar (01009)* | 621 | 98 |
| Butter, unsalted (01145) | 11 | 24 |
| Butter, salted (01001)* | 576 | 24 |
| Pork, shoulder (10070) | 65 | 302 |
| Pork, salami (07071)* | 2260 | 378 |
| Kellogg's®, Corn Fakes (08020)* | 723 | 79 |
| Kellogg's®, Special K (08067)* | 721 | 196 |
| Masterfoods®, Milky Way Bar (19135)* | 167 | 124 |
| Margarine, 80% Fat (04628)* | 654 | 18 |
| Benecol®, light spread (04687)* | 670 | 4 |
| Soy sauce (16123)* | 5637 | 217 |
| Peanuts, dry roasted (16390) | 6 | 658 |
| Peanuts, dry roasted (16090)* | 813 | 658 |

[1] Entries retrieved from the U.S. Department of Agriculture, Agricultural Research Service, 2007, USDA National Nutrient Database for Standard Reference, Release 20, http://www.ars.usda.gov/ba/bhnrc/ndl are followed by a 5-digit nutrient database number in parentheses. Data were not adjusted for country and seasonal specific differences in nutrient compositions of foods. * indicates the addition of sodium salt to the food.