

THE POST GRADUATE TRAINING BOARD
of the
NATIONAL INSTITUTE OF MEDICAL HERBALISTS

Continuing Professional Development Seminar

Nutritional Supplements

Seeing through the marketing hype to use them appropriately and effectively

Birmingham and Midlands Institute, Birmingham

8th March 2014

A one-day seminar led by

Sarah Firnberg MNIMH

**Supplements – cutting
through the hype**

Saturday 8th March 2014

Sarah Firnberg MNIMH

Timetable

AM

FIRST SESSION 10 – 11

SECOND SESSION 11.30 – 1

PM

FIRST SESSION 2 – 3.15

SECOND SESSION 3.45 - 5

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Who am I?

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Introduction

- Working at Anne Walker’s clinic I was impressed with fast results.
- Experienced the benefits myself (especially Magnesium and chromium)
- If you’re asking your patients to part with their money and buy them, you need to be confident you are giving them good advice.
- Many factors dictate the efficacy of the supplement.

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Nutritional supplements

- A minefield of variation and confusion.
- More knowledge might leave you with more unanswered questions
- Sometimes there’s no “right” answer. But there are plenty of wrong or poor answers and that’s what I’m hoping to help you avoid.

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Synopsis for the day

- This morning
 - Malnutrition in the uk, symptoms of deficiency and associated diseases
 - Supplement marketing, and issues surrounding choice.
 - Supplements most commonly used in practice
- This afternoon
 - Issues surrounding choice in more depth
 - Specific areas of confusion (Vit A, CoQ, Vit E, B12, etc)
 - Safety & interactions

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Do we Need supplements?

- Food is always better!
 - **real foods contain a host of nutrients that vitamin pills do not.** And we need these other nutrients — often more than the vitamin itself — for healing, prevention of disease and cellular function.
 - In real food, vitamins exist within a complex of interwoven, interactive and interdependent nutrients.
- Vitamin C is not the same as an orange or an acerola cherry; vitamin A is not the same as liver or carrots, vitamin B is not the same as brewer's yeast or rice bran.

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Widespread deficiency.

- Diet and nutrition studies consistently find us deficient in many nutrients, even by the most conservative estimates.
- In 1997, for example, a report by the European Commission into nutrient intake in European Union Member States concluded that "for almost all vitamins, minerals and trace elements, there exist one or more population groups with intakes below nationally recommended levels."

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Nutritional Deficiencies

- According to the most recent statistics
 - Magnesium intakes were below the LRNI in 9% of men and 13% of women between 19 -64.
 - Iodine: almost 70 per cent of teenage girls in the UK are deficient.
 - Many studies confirm widespread vitamin D deficiency.

1. Henderson L, Irving K, Gregory J, Bates C, J, Prentice A, Perks J, Swan G, Farron M. The National Diet and Nutrition Survey: adults aged 19 to 64 years. Volume 3: Vitamin and Mineral intake and urinary analyses. TSO (London 2003)
2. 1. Vanderpump M, et al. Assessment of the UK iodine status: a National Survey. Endocrine Abstracts 2011;25 OCB.8
3. 2. Vith N, et al. Randomized comparison of the effects of the vitamin D3 adequate intake versus 100 mg (4000 IU) per day on biochemical responses and the wellbeing of patients. Nutrition journal 2004;3:3 [http://www.nutritionj.com/content/3/1/3]

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Why are we so deficient?

- **Chronic Stress:** emotional, physical and spiritual
- **Processed foods** in the diet: Synthetic ingredients tax the body
- **Refined sugar.** The average person consumes at least 140 pounds of sugar a year which robs the body of its vitamin B stores, magnesium and chromium stores.
- **Drugs & alcohol:** both recreational and prescription drugs deplete vitamins and minerals
- **Toxins:** poisons in the environment and personal care products deplete vitamin B complex, along with other nutrients (required for de-toxing).
- **Malnutrition.** Most people are malnourished because they are not eating the right kinds of foods.
- **Northern latitude** (vitamin D deficiency).

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Why are we so deficient cont.

- Food is less nutritious:
 - Modern agriculture depletes soil of valuable nutrients which aren't replaced., storage etc
 - Food has been selectively cultivated to be sweeter, starchier and less colourful
 - Dandelion vs spinach, Garden apples vs Golden delicious. Yellow sweetcorn vs anthocyanin rich traditional /wild strains.
- Storage – a cabbage can be stored for up to 10 months!
- Transport over long distances
- Cooking – Few foods eaten raw. Cooking, particularly microwave destroys, many nutrients, and the enzymes required for assimilating those nutrients – eg pasteurised milk

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Poor digestion & assimilation

- Growing number of digestive issues – compromises ability to absorb nutrients.
 - IBS
 - Crohn's
 - Colitis
 - Coeliac & gluten intolerance
- Many patients on acid inhibiting drugs (ppi's) – associated with increased nutrient deficiency.
- Greater need for the nutrients required to repair damage and calm inflammation.

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**Sweetcorn: GMO vs Non-GMO
2012 study**

	GMO	Non-GMO
Calcium	6,130 ppm	14 ppm
Magnesium	113 ppm	2 ppm
Manganese	14 ppm	2 ppm

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Symptoms of Nutritional Deficiency

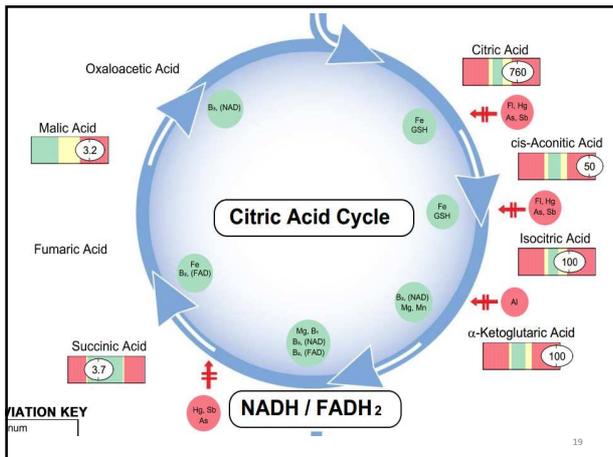
- See appendix p. 1.
- Book recommendation:
 - Signs and Symptoms Analysis from a Functional Perspective. By Dicken Weatherby ND (2nd Edition. Bear Mountain Publishing 2004) Available from Amazon.

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Chronic disease and nutrition

- Cardiovascular disease
 - Cancer
 - Diabetes
- All associated with deficiency in nutrients such as Anti-oxidants, EFA's, Magnesium, B vitamins, vitamin D.
- Poor gut health associated with inflammation and poor absorption
(see appendix for many more)

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How to Choose your brand

The two big issues we are going to cover during the remainder of this morning are

- Marketing hype
- The issues which affect quality and suitability

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Fact of Hype?

- Esther C has 4 times the bioavailability of "regular" vitamin C
- "Beware: Many Vitamin C Supplements Contain These 6 'Red Flags'" Try my new supplement instead...
- Altrient C is the first choice of people who *really* understand bioavailability
- dihydroquercetin functions as a vitamin C "supercharger" Studies demonstrate that dihydroquercetin acts to inhibit the oxidation of vitamin C . . .

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Some facts about vitamin C

- See appendix p.4

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Don't take everything at it's face value

- Is regular ascorbic acid good enough . . . Well plenty of research suggests it successfully enhances immunity.
- Are other forms better – well, possibly. Mixed ascorbates, or vitamin C presented as a powdered food (eg acerola cherry).
- What about liposomal? – An interesting relatively new technique. Very expensive, Some evidence of effectiveness

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Beware of clever self promotion

- American celebrity doctors like Dr Mercola (DrMercola.com) – will blind you with science until you are in no doubt that *only* their supplements will work.
- “Novel preparations” (like EsterC for example), appear to quote research specific to *their brand* when in fact, it's generic research.

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Multi's

- There is such a plethora on the market!

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Incredible variety – Where do you start?

- Mens
- Womens
 - Young women
 - Menopausal women
 - Pre-conception and pregnant
- Sports
- Joints
- Specialist (blood sugar, adrenal, joints etc)

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Where do you start?

- Start with the client – what do they want / need
 - Energy?
 - Anti-inflammatory
 - Young woman – maybe needs plenty of iron. Do they get lots of UTI's? – Look at Viridian's multi!
 - Man – needs lots of zinc
 - Menopausal – minerals and B vitamins
 - Adrenal burnout / anxiety / stress? Lots of B vitamins
 - Terrible blood sugar control? B vits + chromium + magnesium
- Get to know a small range of your favourites

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Form & size of supplement

- Powder / liquid / capsules / tablet / transdermal / spray / sub-lingual
 - Depends on
 - the nutrient in question.
 - The person in question
 - Elderly – difficulty taking tablets
 - Finds swallowing difficult
 - Maybe more effective delivery (eg vitamin B 12).

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Advantages of liquids / powders

- Ease of use for people who dislike tablets
- Easier to take larger quantities
- Good for children – can often be sprinkled on food.
 - Watch out for additives: Sugar, artificial sweeteners, colouring, artificial flavouring
 - Some nutrients can be destroyed by heat.
 - **NB:** Storage may be an issue – a damp steamy environment can cause problems (eg kitchen or bathroom).
 - Check ease of use, and how well they dissolve
 - Must be familiar with the taste before recommending
 - Eg Fish oils (!),
 - Never recommend something you don't like yourself?

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Size and shape

- Many people dislike large tablets
- Some people find round tablets hard to swallow.

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Strength

- RDA's vs optimal dose.
- The RDA's are widely considered inadequate. They define the level below which deficiency disease occurs: eg. The Vitamin C level below which scurvy occurs.
- They do not define the level optimal for good health.

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Official Definitions

- **RDA:** Recommended Daily Amount - The average amount of the nutrient, which should be provided per head of a group of people if the needs of practically all members of the group are to be met. (Average for a group of people). I.e, the amount below which specific diseases may occur – eg scurvy, or beri beri.
- **RDI:** Recommended Daily Intake - The amounts sufficient, or more than sufficient, for the nutritional needs of practically all healthy persons in a population. (Food as actually eaten).
- **EAR:** Estimated Average Requirement - (mean) of a group for a particular nutrient or for energy.
- **RNI:** Reference Nutrient Intake - The amount of a nutrient (mean + 2SD), which is sufficient for almost all individuals. It exceeds the requirement of most people and habitual intakes above RNI are almost certain to be adequate.
- **LRNI:** Lowest Recommended Nutrient Intake The amount of a nutrient or energy (mean - 2SD), which is sufficient for only a few individuals. Habitual intakes below the LRNI by an individual will almost certainly be inadequate.
- **DRV:** Dietary Reference Values - A general term (statistical concept), which covers all the figures of EAR, RNI, and LRNI. It includes guidance on high intakes, and is presented as average requirements for the population as a whole.

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“100% of all RDA's”

Does this mean it's good?

- RDA for vitamin C (healthy adults) is 75 - 90 mg. This amount will prevent scurvy. However, it is not the amount thought necessary by nutritionists for optimal health.
- This is the case for most RDA's – consider vitamin D . . .

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Vitamin D: RDA and deficiency

- The RDI for vitamin D at present is 15mcg / 600 iu per day. However, research suggests that this level is too low to redress deficiency and prevent chronic disease.
 - (10mcg = 400 iu)
- The National Diet & Nutrition Survey 2003: “The majority of people (analysed by urinary analytes) fell consistently short of even the RDA”

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[Public Health](#). 2010 Jun;124(6):350-9. doi: 10.1016/j.jpuhe.2010.03.003. Epub 2010 Apr 21.

Addressing vitamin D deficiency in Canada: a public health innovation whose time has come.

[Schwalfenberg GK](#)¹, [Genius SJ](#), [Hiltz MN](#).

[Author information](#)

Abstract

There is disturbing evidence of widespread vitamin D deficiency in many population groups, particularly within nations at high latitude. Numerous recent studies in the scientific literature associate vitamin D deficiency with a colossal increase in morbidity and mortality. Since Canada is at higher latitude, this review assesses the vitamin D status within the Canadian population. This review was prepared by assessing available medical and scientific literature from Medline, as well as by reviewing several books and conference proceedings. A standard 25(OH)D level of 75-80nmol/l or more was used to indicate vitamin D sufficiency. Between 70% and 97% of Canadians demonstrate vitamin D insufficiency. Furthermore, studies assessing 25(OH)D levels of vitamin D at 25-40nmol/l reveal that many Canadians have profoundly deficient levels. Repletion of vitamin D3 with 2000IU/day for those not receiving judicious sun exposure and those with no contra-indications would likely achieve normalized levels in more than 93% of patients, without risk of toxicity. Explicit directives regarding vitamin D assessment and management are urgently required.

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NB:

The majority of the Canadian population live in a more southerly latitude than the UK

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Dosage levels

- A good supplement should reflect the fact that
 - Some nutrients are used up more quickly than others (for example, the B vitamins – 50mg of each one, does not accurately reflect the body's usage)
 - Many RDAs are set at unrealistically low levels (eg., Vitamin C, D etc)
 - Some nutrients may be toxic at doses above the RDA (eg., synthetic Vitamin A, iron).

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Biochemical individuality

- Like herbal medicine, supplements should be recommended on an individual basis. There is no "one size fits all" with, eg multi's – you need to familiarise yourself with a range.
- Eg Multi's for (to name just a few)
 - Adrenal fatigue (lots of B vits and vit. C)
 - Men (lots of zinc)
 - Poor blood sugar control (B vits, Chromium)
 - Menopausal women (minerals and B vits)
 - Pregnant women (lots of iron, vitamin A)

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No multi will contain everything

- Certain minerals are very bulky (Calcium, Magnesium). They leave little room for other nutrients.
- Some companies get around this by recommending large daily doses – up to 6 tablets per day – at lower doses, other nutrients may be low.
- But beware of giving your patient too many different supplements. Sometimes multiple doses from the same pot is easier than having to open lots of different pots.

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Bio-availability

- Refers to the degree to which a nutrient becomes available to the target tissue after it has been administered
- Minerals, for example, are notoriously hard for the body to absorb in both food and supplement form. Typical absorption rates range from 10-45% (Various processes, such as amino-acid chelation, can increase absorption).

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Bio-availability

- Also affected by
 - Additives
 - Capsules
 - Gelatine coatings
 - Binders
 - Fillers
 - Sugars
 - Colours and flavours
 - Poor breakdown of tablet or capsule

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Absorption also influenced by nature of the preparation

- Transdermal – could be effective for the elderly (sprays, baths etc).
- Sublingual – useful for maximum absorption of certain nutrients (eg Vitamin B12).
- Oil based medium for oil soluble nutrients (eg vitamins D, E, A, K and Co Q-10).
- Capsules usually more bio-available than pills (not compressed, no binders or coating)
- “natural” ingredients more bio-available than synthetic – more familiar to the body

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Lipophilic

- Interesting newish technology – nutrient bound to phospho-lipids to enhance trans-membrane absorption. Eg lipophilic vitamin C
 - Claimed to be “as good as intravenous”
- Expensive
- Very little research on lipophilic supplement preparations.

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Miscellised (emulsified)

- Fat soluble nutrients are sometimes presented in this form.
 - Breaking down of fats for better absorption (transport through membranes). This job is normally performed by bile, however, taurine (a precursor to bile) or lecithin can help.
 - Emulsification forms micells
 - In supplements, the micellisation is done by chemicals.

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Micellised vitamins

- Lutein and zeaxanthin, essential to replenish the macula, require being emulsified or broken down to the micellised state in order to enter the bloodstream for transport by high-density lipoprotein (HDL)

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Form of the nutrient Natural vs Synthetic

- Synthetic forms are often synthesised from non-organic sources. They are often crystalline, and not well recognised by the body.
- Natural forms are derived from food sources and thus more familiar to the body.
- Natural may contain co-factors, enzymes, bioflavonoids and other phytochemicals that enhance the performance of the nutrient.

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Natural vs Synthetic

- Synthetic nutrients are
 - Cheaper
 - Have longer shelf life
- BUT
 - They are poorly absorbed
 - Quickly excreted
 - Maybe less effective
 - Made from unsavoury ingredients.
 - In the worst cases –toxic

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Common Synthetic forms

A good rule of thumb: things which end in ~ate or ~ide are synthetic forms

- **Vitamin A:** Acetate and Palmitate
 - **Vitamin B1 (Thiamine):** Thiamine Mononitrate, Thiamine Hydrochloride
 - **Vitamin B2 (Riboflavin):** Riboflavin
 - **Pantothenic Acid:** Calcium D-Pantothenate
 - **Vitamin B6 (Pyridoxine):** Pyridoxine Hydrochloride
 - **Vitamin B12:** Cobalamin
 - **PABA (Para-aminobenzoic Acid):** Aminobenzoic Acid
 - **Folic Acid:** Pteroylglutamic Acid
 - **Choline:** Choline Chloride, Choline Bitartrate
 - **Biotin:** d-Biotin
 - **Vitamin C (Ascorbic Acid):** Ascorbic Acid
 - **Vitamin D:** Irradiated Ergosterol, Calciferol
 - **Vitamin E:** dl-alpha tocopherol, dl-alpha tocopherol acetate or succinate
- NOTE:** The "dl" form of any vitamin is synthetic.

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- See appendix p.7 for chart of synthetic forms of nutrients (to be avoided?)

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Organic chelate vs mineral form

- Mineral form is usually cheaper (cf Mg oxide and Mg Citrate), but often not as bio-available and there may be negative effects (eg Mg oxide can cause diarrhoea). If it doesn't say – it will almost certainly be the cheapest option.

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Food state

- “Natural” ingredients in the form of dried fruits or vegetables.
 - Whole plant supplied
 - Co-factors present

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Nutrients which work as families

- Vitamin E.
 - tocopherols – alpha, beta, delta and gamma.
 - tocotrienols - also alpha, beta, delta and gamma.
- Look for "mixed tocopherols" or "mixed tocopherols and tocotrienols." An isolated form of one part of a nutrient can easily throw the other parts off balance. (More about this later)

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Active nutrient or precursor?

- Some vitamins can be 'made' in the body from precursor molecules. For example, the body can convert beta-carotene into vitamin A. The body can make vitamin D from exposure to sunlight by converting cholesterol into vitamin D.
- Can your body use it just the way it is, or does it need to go through some sort of conversion process?
 - Vitamin B6 for example, is known as Pyrioxal-5-phosphate (P-5-P) in its active, ready-to-be-metabolized form.
 - Many other nutrients may be presented in precursor forms (Co-Q10, precursors are also called provitamins and are inactive until they are converted into vitamins by the body. Examples are choline, inositol, coenzyme Q10, alpha-lipoic acid, beta-carotene, quercetin, other flavonoids)
 - Only higher quality brands will invest the resources to provide the active forms of nutrients when possible.

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Raw ingredients – where do they come from

- Iodine from seaweed – is it radioactive seaweed from Japan?
- Vitamin D3 – (typically from sheep wool lanolin) – is it full of insecticide? D2 is derived from fungi – but is it equally bioavailable?
- Ascorbic acid (Vit C) derived from corn – is it GM corn and is that a problem?
- Fish oils – from a sustainable source? How well are they purified?
- Krill oil – is it ethically acceptable?
- Worth choosing a company whose integrity you can trust

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Supplements most commonly used in practice

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Most common supplements

- Multi
- Magnesium
- EFA's
- Pro-biotics
- Vitamin D
- CoQ 10
- Digestive enzymes

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Supplements most commonly used in practice

- Multis
- Comparison of multis
 - General all purpose multi
 - Gender specific
 - Specific to certain conditions

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Multi vit / min

- Centrum – has mainly 100% RDI's
 - Does this mean it's good?

See Centrum vs Multigenics Multi Appendix p.11

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Multi's

- There are no standardized definitions for multis and the composition varies widely.
- Minerals like calcium, magnesium, potassium, and phosphorus are very bulky, and
- In order for multis to contain therapeutic levels of these minerals, large dose levels may be recommended (eg 6 per day)

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Multi vitamin / mineral

- Such a variety
- Depends who it's for and what you hope to achieve by it.
- Find a selection of "favourites" suitable for different conditions
 - Blood sugar regulation
 - Menopause
 - Stress / energy

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Magnesium

- Magnesium RDA = 375mg/day, but the evidence shows that dietary and supplemental intakes for magnesium for most people are consistently below the RDA.
- Evidence suggests that intake at levels higher than the RDA are beneficial. Generally around 300mg/day.
- It is crucial that the public prioritises magnesium intake from the diet and supplements in order to curb the chronic disease burden linked to metabolic syndrome, diabetes and heart disease.

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Magnesium cont.

- Magnesium is an essential mineral, contained in whole grains, leafy green vegetables, legumes and nuts. It acts as a cofactor in hundreds of enzymatic reactions in the body. A considerable body of evidence indicates that a higher intake of dietary magnesium may favourably affect a cluster of metabolic and inflammatory disorders including:
 - Insulin resistance
 - hypertension
 - dyslipidemia
 - type 2 diabetes
 - metabolic syndrome
 - cardiovascular disease

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Many research papers show benefits health benefits of magnesium

- See appendix p. 14 -

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Magnesium

- The balance between calcium and magnesium is important. Where Ca consumption is high, Mg needs are high.
- Protein, phosphorous and vitamin D status also influence Mg requirement.
- Magnesium is required for energy metabolism. Where this process has broken down (eg insulin resistance), Mg needs are very high.

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Elemental Mg vs Mg compounds

- What does the figure for Total magnesium on a supplement label mean?
- 500mg Magnesium Citrate = 80mg Mg, 420mg citrate.
- Quality manufacturers always make this distinction between the quantity of magnesium present and the quantity of the rest of the compound.
- Poor quality manufacturers often do not!

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Benefits of magnesium cont

- Headaches and migraines
- Cramps and muscle tension
- Tremor
- Cancer
- FM
- PMT
- Reduction in risk of gall stones and kidney stones
- Etc etc . . . Many studies, many benefits

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Magnesium
See appendix p.15

- Different forms
 - Oxide
 - Citrate
 - Malate
 - Fumerate
 - EAP
- Transdermal vs oral
- Tablets / powders /

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Omega 3 EFA's – evidence of benefits in many diseases. See appendix p. 17

- All aspects of Cardiovascular disease
- Reduces inflammatory bio-markers
- Auto-immune disease
- Muscular skeletal disease
- Mental Health
- Blood sugar regulation
- Cancer

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Omega-3 continued

- Omega-3 fatty acids, found in coldwater fish (and fish oil), perilla and flaxseed oils
- Contain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are usually lacking in the typical Western diet
- Although EPA and DHA can be synthesized in the body from ALA, but EPA and DHA synthesis may be insufficient under certain conditions and for most people that consume Western diets.

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Why Omega 3

- The modern diet typically contains disproportionate levels of omega-6 fats. In fact, some Western diets consist of 20 parts of omega-6 to only one part of omega-3. For optimum health, the ratio of omega-6 to omega-3 fatty acids should be between 1:1 and 4:1.

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Omega 3 – quality matters

- Quantity
 - Fish Oil x 1000mg - meaningless
 - How much EPA and DHA is there? That's what matters.
- Purity
 - It is important that the manufacturer describes the purification process and gives details of levels of toxins present.

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Omega 3 – quality matters

- Manufacturing process – can really effect how well the supplement is tolerated
 - Enzymatically treated?
 - Is the oil chemically broken down before being reconstituted? (Many brands do this) resulting in much poorer quality.

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Pro-biotics

- Which strains – are they human appropriate?
- “Do not need to be put in the fridge”? – don’t believe it. All probiotics are living organisms which degenerate if they are not refrigerated.
- How many CFU’s (colony forming units). Ie, how many billion bacteria.
- Added pre-biotics?
- Packaging – needs to protect from moisture and light.

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Vitamin D

- Oil based medium or not?
- D2 or D3
- Need magnesium / calcium
 - What about AdCal?
 - Need vitamin K2
 - Need boron for bone health

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Anti oxidants

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**Oxidative stress leads to disease
(why we need anti-oxidants)**

Metabolism, stress, inactivity, poor sleep, pollution, inflammation and EMF's can stress the weak bonds between cells, causing them to break, and leaving them short of an electron in the outer shell.

The resultant unstable atoms are

Free Radicals

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Oxidative stress

- Free radicals are driven to find an electron – and will do so at the first chance . . . Leaving another free radical.
- Constant swapping of electrons can cause permanent cellular damage which can result in Cancer or other chronic disease. (cf rust or browning apple – cells decay).
- This damage is known as

Oxidative Stress

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- we have three main internal “onboard” antioxidant systems that take care of most of the normal oxidative damage when we are healthy, unstressed and eating well (catalase, superoxide dismutase and glutathione). But these systems can fall short when we are under stress, eating too many sugars and other carbs, trans and hydrogenated fats, or drinking alcohol.

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Role of anti-oxidants

Anti-oxidants can donate an electron without becoming a free-radical!

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ORAC

- Anti-oxidants are measured by the ORAC scale.
- However, their value declines the more they are processed ([Baolin Xu and Sam K. C. Chang](#), 2009, *J. Agric. Food Chem.*, 2009, 57 (11), pp 4754-4764)
- So our patients may benefit more from fresh local raspberries than, eg dried acai berries.

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Areas of confusion

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Areas of Confusion

- Vitamins which work as families
 - Vitamin A
 - Vitamin E
 - B vitamins
 - Niacin vs nicotinamide
- Glutamine vs NAG
- Co-Q10 (ubiquinone vs ubiquinol)
- Selenium (selenomethionine)

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Vitamin A (Retinol)

- Two categories: Retinoids (from animal sources) and Carotenoids (from plants). Precursor to vitamin A in body. Converted by enzymes as required.
- They are chemically quite different and confer different health benefits.

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Retinoids

- Retinol = the whole vitamin A molecule.
 - Can be broken down into smaller components:
 - Retinoic acid (Retin-A) – the active form. Has a key role in embryonic development. However, excessive amounts can lead to birth defects. High amounts are found in retinoid pharmaceuticals used to treat cancer and acne.
 - Retinyl palmitate an ester (chemical) form of retinol (esterified with palmitic acid). Widely Used in skin care products. Similar teratogenic potential as Retinoic acid.

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Retinoids

- Specific immune, inflammatory, genetic, and reproductive-related benefits which can only be obtained from the retinoid forms of the vitamin.
- Particularly important for
 - Fetal growth and childbirth,
 - infancy, childhood growth,
 - night vision,
 - red blood cell production, and
 - resistance to infectious disease.

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Retinoids

- Eye health
- immune system,
- inflammatory system,
- maintenance of epithelial and mucosal tissues,
- growth,
- reproduction,
- bone development,
- creation of red blood cells, and
- production of spermatozoa (male reproductive cells). In food, retinoid forms of vitamin A typically appear as retinyl esters. The body is typically able to convert these retinyl esters into metabolically active forms of vitamin A including retinol, retinal, and retinoic acid.

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Retinoids cont.

- In food, retinoid forms of vitamin A typically appear as retinyl esters. The body is typically able to convert these retinyl esters into metabolically active forms of vitamin A including retinol, retinal, and retinoic acid.

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Carotenoids

- Main role: antioxidant and anti-inflammatory
 - Found in plants
 - Pre-cursor to vitamin A (Retinol) in body. Converted by enzymes as required.
 - Only amount required will be converted – excessive doses avoided.
 - Only source available to vegetarians.
- Responsible for red/yellow /orange colours in eg carrots
- Astaxanthin – responsible for the pink colour in shellfish and salmon. A power anti-oxidant

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Carotenoids

- There are more than 700 naturally occurring carotenoids, Typically, we have around ten different carotenoids in circulation at any time. The best known is beta carotene.
- Beta carotene
 - Acts as powerful anti-oxidant and free radical scavenger

1. Vinson JA, 1991. Beta carotene bio-availability study. Dept of Gastroenterology, Meath and Adelaide Hospitals, Trinity College Dublin.

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Beta carotene cont.

- Protects cells from free radical damage
- Role in formation of blood, bones and teeth
- Essential for normal vision
- Role in skin health (especially relevant for damaged GIT epithelial tissue)
- Best food sources: CLO, liver, eggs, dairy, carrots and orange / red / yellow fruits and veg.

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Other carotenoids

- Sometimes specific carotenoids have a highly specialised application in health.
- For example, the only carotenoids found inside the retina of the human eye are the xanthophylls, lutein and zeaxanthin.

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Vegans and Vitamin A deficiency

- Vegans suffering poor immunity, poor gut health (poor epithelial turnover), poor skin health or poor eyesight – Maybe vitamin A deficiency is the problem. Many people are unable to convert carotenoids to the active retinol form.

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Vitamin A: Two forms.

Retinoids (found in animal foods)	Carotenoids (found in plant foods)	
retinol	Carotenes	Xanthophylls
retinal	alpha-carotene*	astaxanthin
retinoic acid	beta-carotene*	beta-cryptoxanthin*
retinyl esters	gamma-carotene*	canthaxanthin
	delta-carotene	fucoxanthin
	epsilon-carotene	lutein
	zeta-carotene	neoxanthin
		violaxanthin
		zeaxanthin

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Vitamin A and toxicity and side effects

- Almost impossible to overdose through food (except possibly polar bear livers!)
- Carotenoids not associated with toxicity.
- Synthetic retinoids override the body's own control mechanisms and high doses may be associated with side effects and toxicities (Rare)
- **NB:** All of the retinoid compounds have been found to cause birth defects, at relatively low levels.
- Retinoids tend to be very long acting: side effects and birth defects have been reported to occur months after discontinuing retinoid therapy.

• Ross AC. Vitamin A and retinoids. In: Shils M, Olson JA, Shike M, Ross AC, ed. Modern Nutrition in Health and Disease. 9th ed. Baltimore: Lippincott Williams & Wilkins; 1999:305-327.

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Vitamin A toxicity cont.

- Preformed vitamin A is rapidly absorbed and slowly cleared from the body.
- Generally, signs of toxicity are associated with long-term consumption of vitamin A in excess of ten times the RDA (8,000 to 10,000 mcg/day or 25,000 to 33,000 IU/day).
- More research is necessary to determine if subclinical vitamin A toxicity is a concern in certain populations. There is evidence that some populations may be more susceptible to toxicity at lower doses, including the elderly, chronic alcohol users, and some people with a genetic pre
- disposition to high cholesterol.

1. Peniston KL, Teasdale SA. The acute and chronic toxic effects of vitamin A. *Am J Clin Nutr*. 2006;83(2):191-201.

2. Chen A, Hama M, Abbott M, Kusan K. Oral retinoids and pregnancy. *Med J Aust*. 1996;165(3):354-357

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Vitamin E

- Vitamin E is a potent antioxidant. Because it is fat soluble, it offers protection against damage to cell walls throughout the body.
- Vitamin E is often used to help preserve oily foods and supplements.
- Protection Against Heart Disease: Vitamin E helps protect LDL cholesterol from free radical damage. Oxidised (damaged) LDL tends to accumulate in blood vessel walls in the early stages of atherosclerosis.

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Functions of vitamin E

- One or more members of the vitamin E family may:
 - Maintain cell membrane integrity and reduce cellular aging.
 - Act as a free radical scavenger.
 - Maintain healthy platelet aggregation.
 - Promote a healthy nervous system and retina of the eye.
 - Maintain healthy cognitive function.
 - Enhance immune function.

• 1. Clinica (Sao Paulo) 2012;67(2):135-43
• 2. Diabetes Metab Res Rev 2007 Oct;23(7):539-46
• 3. J Nutr 2002 Feb;132(2):374S-377S
• 4. J Am Coll Nutr 2004 Jun;23(3):233-8
• 5. Neurobiol Aging 2002 Sep;23(9):1277-85
• 6. Br J Gen Pract 2003 Jun;53(493):288-90

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Best food sources

- Sunflower seeds
- Almonds
- Swiss chard
- Spinach
- Avacados

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Vitamin E

- Vitamin E is a blanket term for eight different fat soluble nutrients—
 - four different tocopherols (alpha, beta, gamma, delta)
 - four different tocotrienols. (alpha, beta, gamma, delta)
- Different ratios of these compounds are found in different parts of a plant.
 - green parts of a plant contain mostly alpha tocopherol
 - seed germ and bran contain mostly tocotrienols.

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- Best known sub class is alpha-tocopherol. it is among the most intensely studied nutrients. Because of its ability to prevent free radical damage, it may have profound effects on risks of common diseases.
- Average diet, quite deficient in vitamin E

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Tocotrienols

- **Tocotrienols** have shown superior action in maintaining arterial health .
- Shown to support healthy triglyceride levels
- Just 120 mg per day of gamma-delta tocotrienols induced a 28% decline in triglyceride levels in the blood after just one month.
- It's properties due to double bonded structure in the isoprenoid side chain, making it a great scavenger of free radicals.
- Research has shown that tocotrienols display potent neuroprotective properties and in particular alpha-tocotrienol is being touted as the most potent neuroprotective form of vitamin E .

• 1. *Atherosclerosis*. 2005 May;180(1):19-25.
• 2. *J Atheroscler Thromb*. 2010 Oct 27;17(10):1019-32.
• 3. *Free Radic Biol Med*. 2011 Sep 15;51(6):1164-74
• 3. *Wei Sheng Yan Jiu*. 2004 Mar;33(2):243-5.

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How to choose a vitamin E supplement

- Many lower quality supplements contain just alpha-tocopherol.
- According to a University of California study, alpha tocopherol displaces critically important gamma tocopherol in the body. While alpha tocopherol inhibits free radical production, gamma tocopherol is required to trap and neutralize existing free radicals.
- Choose supplements with mixed tocopherols and tocotrienols.

• 1. *J Nutr*. 1985 Jun;115(6):807-13

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Co Q-10 – Ubiquinone or ubiquinol?

- Converts fats and sugars into usable cellular energy
- Production declines significantly with age by up to 72% (eg. In the heart muscle wall);
- Statins reduce plasma CoQ10 by almost 40% in addition to the reduction due to ageing!;
- Ubiquinol appears to have higher bioavailability, and be up to 40% more effective than ubiquinone.

1. *BioFactors*. 1999;9(2-4):291-9.
2. *Mitochondrion*. 2007 Jun;7 Suppl:5168-74.
3. *Exp Gerontol*. 2006 Feb;41(2):130-40.

Ubiquinol vs ubiquinone

- Ubiquinol appears to be absorbed significantly (up to 8 x) faster than ubiquinone.
- Higher levels of ubiquinol remain in circulation longer.
- In studies measuring exercise-induced fatigue, *ubiquinol* was 90% more effective than ubiquinone.
- BUT – ubiquinol is expensive! Bio-availability of the cheaper ubiquinone can be enhanced by emulsification (or miscellisation).

1. *Exp Gerontol*. 2006 Feb;41(2):130-40.
2. *Int J Food Sci Nutr*. 2006 Nov-Dec;57(7-8):546-55.

Selenium

- Toxicity of sodium selenate
- Natural selenomethionine – preferable.

Iron

- Ferrous sulphate vs. food state
- Ferrous sulphate often causes constipation

- NB According to Dr Campbell McBride, Dysbiotic flora will take up iron (often causing anaemia in chronic gut disease). Supplementing can exacerbate dysbiosis in this case.

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Opposition to supplements

- Studies often extremely poor quality.
- Synthetic nutrients .

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Safety

- Very safe . . . however
- Issues with certain toxic, synthetic forms, most notably Selenium . .

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Interactions

- We need to cover our backs
- Must be aware of potential for interactions, and make our patients aware (even if we feel the possibility is slight)
- Use online sources if in a hurry:
- Excellent book: Expensive, but really worth it.
- Herb, Nutrient, and Drug Interactions by M. B Stargrove, J. Treasure and D L McKee. 2008 Mosby Elsevier.

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Side effects / bad response

- Nausea after taking supplements: Check the patient has drunk enough water, and advise them to drink if they feel nauseous.
- Extreme fatigue – Supplements can up-regulate detoxification pathways.

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Conclusion

- I've given you a lot of information here.
- However, with more knowledge, you might find you have more questions than answers . .
- Significant amount of research into the role of specific nutrients in disease, but less research into the best way to deliver these nutrients.
- Common sense judgements may be the way to go. Balancing the considerable advantages of Natural, bio-available supplements against the cost.

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Appendix 1

Different forms of Vitamin C

Vitamin C is available in many forms, and you will find much marketing hype claiming superior quality and bio-availability. Here are some facts about this vitamin . . .

- **Natural vs. synthetic ascorbic acid:** Natural and synthetic ascorbic acid are chemically identical in terms of bioavailability and bioactivity.

However, the mixed ascorbates found in powdered fruit (eg acerola cherry), appear to confer an advantage

- **Different forms of ascorbic acid (powders, tablets, etc.):** The gastrointestinal absorption of ascorbic acid occurs through an active transport process, as well as through passive diffusion.

At low gastrointestinal concentrations of ascorbic acid, active transport predominates, while at high gastrointestinal concentrations active transport becomes saturated, leaving only passive diffusion. In theory, slowing down the rate of gastric emptying (e.g., by taking ascorbic acid with food or taking a slow-release form of ascorbic acid) should increase its absorption. The bioavailability of ascorbic acid appears equivalent whether it is in the form of powder, chewable tablets, or non-chewable tablets. Moreover, bioavailability of ascorbic acid from slow-release preparations has not been found to be greater than that of plain ascorbic acid.

- **Mineral ascorbates:** Mineral salts of ascorbic acid (mineral ascorbates, eg Magnesium ascorbate) are buffered and therefore less acidic. Thus, mineral ascorbates are often recommended to people who experience gastrointestinal problems (abdominal pain or diarrhoea) with plain ascorbic acid. There appears to be little scientific research to support or refute the claim that mineral ascorbates are less irritating to the gastrointestinal tract. When mineral salts of ascorbic acid are taken, both the ascorbic acid and the mineral appear to be well-absorbed, so it is important to take into consideration the dose of the mineral accompanying the ascorbic acid when taking large doses of mineral ascorbates. For the following discussion, it should be noted that 1 gram = 1,000 milligrams (mg) and 1 milligram (mg) = 1,000 micrograms (mcg). Mineral ascorbates are available in the following forms:

Magnesium ascorbate: The recommended dietary allowance (RDA) for magnesium is 400-420 mg/day for adult men and 310-320 mg/day for adult women. The maximum upper level of intake for magnesium from supplements is 350 mg/day.

Sodium ascorbate: 1,000 mg of sodium ascorbate contains 889 mg of ascorbic acid and 111 mg of sodium. Individuals following low-sodium diets (e.g., for high blood pressure) are generally advised to keep their total dietary sodium intake to less than 2,500 mg/day. Megadoses of sodium ascorbate could significantly increase sodium

intake.

Calcium ascorbate: 1,000 mg of calcium ascorbate generally provides 890-910 mg of ascorbic acid and 90-110 mg of calcium. Calcium in this form appears to be reasonably well absorbed. The recommended dietary calcium intake for adults is 1,000 to 1,200 mg/day. Total calcium intake should not exceed the tolerable upper intake level of 2,500 mg/day.

The following mineral ascorbates are more likely to be found in combination with other mineral ascorbates, as well as other minerals. It's a good idea to check the labels of dietary supplements for the ascorbic acid dose as well as the dose of each mineral. Recommended dietary intakes and maximum upper levels of intake (when available) are listed after the individual mineral ascorbates below:

Potassium ascorbate: The minimal requirement for potassium is thought to be between 1.6 and 2.0 grams/day. Fruits and vegetables are rich sources of potassium, so a diet rich in fruits and vegetables may provide as much as 8 to 11 grams/day. Acute and potentially fatal potassium toxicity (hyperkalemia) is thought to occur at a daily intake of about 18 grams of potassium/day in adults. Individuals on potassium-sparing diuretics and those with renal insufficiency (kidney failure) should avoid significant intake of potassium ascorbate. The purest form of commercially available potassium ascorbate contains 0.175 grams (175 mg) of potassium per gram of ascorbic acid.

Zinc ascorbate: The RDA for zinc is 11 mg/day for adult men and 8 mg/day for adult women. The upper intake level of zinc for adults is 40 mg/day.

Molybdenum ascorbate: The RDA for molybdenum is 45 micrograms (mcg)/day for adult men and women. The upper intake level of molybdenum for adults is 2,000 mcg (2 mg)/day.

Chromium ascorbate: The recommended dietary intake for chromium is 30-35 mcg/day for adult men and 20-25 mcg/day for adult women. An upper level of intake has not been determined by the U.S. Food and Nutrition Board.

Manganese ascorbate: The recommended dietary intake for manganese is 2.3 mg/day for adult men and 1.8 mg/day for adult women. The upper level of intake for manganese is 11 mg/day. Manganese ascorbate is found in some preparations of glucosamine and chondroitin sulfate. Following the recommended dose on the label could result in a daily intake exceeding the upper intake level for manganese.

• **Ester-C®:** Ester-C® contains mainly calcium ascorbate, but also contains small amounts of the vitamin C metabolites dehydroascorbic acid (oxidized ascorbic acid), calcium threonate, and trace levels of xylonate and lyxonate. In their literature, the manufacturers state that the metabolites, especially threonate, increase the bioavailability of the vitamin C in this product and that they have performed a study in humans demonstrating the increased bioavailability of vitamin C in Ester-C®. This study has not been published in a peer-reviewed journal. A small published study of vitamin C bioavailability in 8 women and 1 man found no difference between Ester-C® and commercially available ascorbic acid tablets with respect to the absorption

and excretion of vitamin C.

- **Vitamin C with bioflavonoids:** Bioflavonoids are a class of water-soluble plant pigments. Vitamin C-rich fruits and vegetables, especially citrus fruits, are often rich sources of bioflavonoids as well. The effect of bioflavonoids on the bioavailability of ascorbic acid has been examined in two small published studies. In one study synthetic ascorbic acid given in a natural citrus extract containing bioflavonoids (in the ratio of bioflavonoids to ascorbic acid of 4:1), proteins, and carbohydrates, was more slowly absorbed and 35% more bioavailable than synthetic ascorbic acid alone, based on plasma levels of ascorbate over time and 24-hour urinary excretion of ascorbate. In the other study, there was no difference in the bio-availability of 500 mg of synthetic ascorbic acid and that of a commercially available vitamin C preparation with added bioflavonoids, where the ratio of bioflavonoids to ascorbic acid was 0.05:1.

- **Ascorbyl palmitate:** Ascorbyl palmitate is a fat-soluble antioxidant sometimes used to increase the shelf life of vegetable oils and potato chips. It is an amphipathic molecule, meaning one end is water-soluble and the other end is fat-soluble. This dual solubility allows it to be incorporated into cell membranes. When incorporated into the cell membranes of human red blood cells, ascorbyl palmitate has been found to protect them from oxidative damage and to protect vitamin E (a fat-soluble antioxidant) from oxidation by free radicals. However, the protective effects of ascorbyl palmitate on cell membranes have only been demonstrated in the test tube. Taking ascorbyl palmitate orally probably doesn't result in any significant incorporation into cell membranes because most of it appears to be hydrolyzed (broken apart into palmitate and ascorbic acid) in the human digestive tract before it is absorbed. The ascorbic acid released by the hydrolysis of ascorbyl palmitate appears to be as bioavailable as ascorbic acid alone. The presence of ascorbyl palmitate in oral supplements contributes to the ascorbic acid content of the supplement and probably helps protect lipid-soluble antioxidants during storage. The role of vitamin C in promoting collagen synthesis and its antioxidant properties have generated interest in its use on the skin. Ascorbyl palmitate is frequently used in topical preparations because it is more stable than some aqueous (water-soluble) forms of vitamin c

Appendix 2

Natural vs Synthetic Nutrients	
<p>Natural Recognised by the body like food. No toxicity</p> <p>Avoid supplements that use words ending in -acid, -ide, and sometimes -ate or that use the “dl”</p>	<p>Synthetic</p> <p>Many synthetic vitamins are crystalline. Crystals in our blood stream cause damage and mineral accumulation where it isn't needed, like joints.</p> <p>Longer shelf life</p> <p>cheaper</p>
<p>Vitamin A is found in food as beta-carotene, which must be converted into vitamin A by our body. Vitamin A can be toxic in large doses. Beta-carotene allows the body to convert what it needs and discard what it does not as a natural safeguard against damage.</p>	<p>Synthetic vitamin A is retinyl palmitate or retinyl acetate. This synthetic is made from combining fish or palm oil with beta-ionone. Beta-ionone is created using citrus, acetone, and calcium oxide.</p>
<p>Vitamin B1 – Thiamin, is a water soluble vitamin created by plants and bound to phosphate. Digestion uses enzymes to cleave the phosphate from the thiamin</p>	<p>Synthetic Vitamin B1 – Thiamine mononitrate or thiamine hydrochloride is made from coal tar, ammonia, acetone, and hydrochloric acid. It is much less bioavailable (lacking the phosphate) . It is crystalline in structure, unlike plant-based vitamins.</p>
<p>Vitamin B2 – Riboflavin is easily absorbed, stays in the blood stream for long periods of time, and is readily used by the body in many important enzymes.</p>	<p>Synthetic riboflavin is made either with acetic acid and nitrogen or derived from GMO bacteria or fermentation. It has been shown to be both less bioavailable and more quickly removed from circulation (treated as a toxin) .</p>
<p>Vitamin B3 – Niacinamide or nicotinamide is what we find in food and commonly call niacin. The “flushing” caused by this nutrient is responsible for some of its main benefits.</p>	<p>Synthetic Vitamin B3 – Nicotinic acid is created using coal tar, ammonia, acids, 3-cyanopyridine, and formaldehyde. It is less bioavailable.</p>
<p>Vitamin B5 – Pantothenate is the natural version of this essential B vitamin.</p>	<p>Synthetic Vitamin B5 – Pantothenic acid involves isobutyraldehyde and formaldehyde to form a calcium or sodium salt. The alcohol derivative, penthenol, is sometimes used as it is more stable and lasts longer on store</p>

	shelves
Vitamin B6 – Like B1, pyridoxine is bound with phosphate in plants to make pyridoxal-phosphate. This is the biologically active form. Any other form of B6 must be converted into this phosphate combination before our body can use it.	Synthetic Vitamin B6 – Pyridoxine hydrochloride comes from petroleum ester, hydrochloric acid, and formaldehyde. It isn't readily absorbed or converted and has been shown to actually inhibit the action of natural B6 in the body. It also has side effects not normally found with natural food sources of this vitamin.
Vitamin B7 – Biotin is involved in cell growth, fat production, and metabolism.	Synthetic B7 is produced using fumaric acid
Vitamin B9 – This B vitamin exists in food as folate and is very important in the creation and repair of DNA, thus the vital importance of this vitamin before and during pregnancy.	Synthetic Vitamin B9 – Folic acid doesn't exist in natural foods, is crystalline, and is not easily absorbed despite the large amounts that are added to vitamins and supplements. It comes from petroleum derivatives, acids, and acetylene.
Vitamin B12 – Cobalamin B12 is only created by micro-organisms. Our gut flora plays an important role here, and some micro-algae and seaweed species can produce it.	Synthetic Vitamin B12 – Cobalt and cyanide are fermented to make cyanocobalamin.
Choline is often grouped with B vitamins. It is combined with phosphate in nature and is important in cell membranes and keeping fat in check.	Synthetic Choline – Choline chloride or choline bitartrate is made using ethylene, ammonia, and hydrochloric acid or tartaric acid. It is not bound to phosphate.
Vitamin C – (readily available in citrus, red bell peppers, berries, and many more fruits and vegetables). In nature it is combined with flavonoids and phytonutrients that help in its absorption and use.	Synthetic Vitamin C – Ascorbic acid is an isolated vitamin from genetically modified corn sugar that is hydrogenated and processed with acetone. It does not include the flavonoids and phytonutrients which enhance the action.
Vitamin D – Technically this one isn't always thought of as a vitamin since we make it ourselves. Mushrooms, yeast, and lichen produce vitamin D when exposed to sunlight. Humans do too. A daily dose of about 20 minutes of sunlight provides all we need. Vitamin D3 is the kind that comes from our own skin and lichen. Mushrooms and yeast often yield D2.	Synthetic Vitamin D – To mimic the natural production we find in our skin, scientists irradiate animal fat to stimulate vitamin D3 synthesis. They usually use lanolin, the waxy secretions from sheep skin that keeps wool dry
Vitamin E actually refers to 8 different fat soluble compounds and it acts as an antioxidant that protects fats from oxidation. The most biologically active form is found in grains, seeds, and the oils from grains and seeds.	The synthetic dl-alpha tocopherol is created using refined oils, trimethylhydroquinone, and isophytol. It is not as easily absorbed, doesn't stay as long in tissues, and is quickly dispelled like a toxin or unknown chemical.
Vitamin K – This vitamin is important to	Synthetic Vitamin K – Synthetic vitamin

proper blood clotting and some metabolic pathways. It is found in dark leafy greens.	K, menadione, comes from coal tar derivatives and genetically modified and hydrogenated soybean oil, and uses hydrochloric acid and nickel. It is considered highly toxic and damages the immune system.

Synthetic vitamins are isolated or simulated nutrients that do not take into account all the countless phytonutrients that come along with them. Nature is not a select few things isolated from the rest. We are only beginning to understand how many of the lesser known compounds in plants react with one another as we eat them, but we do know humanity has been eating whole foods for a very long time. We have evolved to recognize the whole, not just individual chemicals that have been created to approximate an essential vitamin. before the name. Minerals should be from whole foods as well as often as possible. They are not considered organic materials as they come initially from the earth, but plants incorporate minerals into their systems and combine them with organic compounds. This is how our bodies know them and incorporate them into our systems as well. Minerals are often combined with proteins to form enzymes. Your body is begging you for the vitamins and minerals it knows, loves, and misses terribly. - See more at: <http://www.sunwarrior.com/news/natural-vs-synthetic-vitamins/#sthash.CUtHqt4f.dpuf>

Appendix 3

Excipient chart – just a few of the more common ones.

<u>Bulking agents:</u>	Dicalcium Phosphate Microcrystalline Cellulose calcium diphosphate HPMC
<u>Tablet coating / glazing</u>	Hydroxypropyl Methylcellulose Glycerin Cellulose,
<u>Colouring</u>	Titanium Dioxide (often also a coating) Riboflavin E numbers
<u>Anti-caking</u>	Silicon Dioxide <i>Magnesium Stearate (often present in significant quantity – this is a Trans Fat,</i>
<u>Other</u>	Modified Tapioca Starch Acacia Gum Olive Oil, Sodium Carboxymethyl Cellulose Sucrose, Corn Starch Aspartame

Appendix 4

Centrum Adult Multi - Formulation

Each Tablet Contains:	Quantity	% EU RDA
Vitamin A (RE)	800 µg	100 %
Lutein	500 µg	- **
Vitamin E (α - TE)	15 mg	125 %
Vitamin C	100 mg	125 %
Vitamin K	30 µg	40 %
Vitamin B1 (Thiamin)	1.4 mg	127 %
Vitamin B2 (Riboflavin)	1.75 mg	125 %
Vitamin B6	2 mg	143 %
Vitamin B12	2.5 µg	100 %
Vitamin D	5 µg	100 %
Biotin	62.5 µg	125 %
Folic Acid	200 µg	100 %
Niacin (NE)	20 mg	125 %
Pantothenic Acid	7.5 mg	125 %
Calcium	162 mg	20 %
Phosphorus	125 mg	18 %
Magnesium	100 mg	27 %
Iron	5 mg	36 %
Iodine	100 µg	67 %
Copper	500 µg	50 %
Manganese	2 mg	100 %
Chromium	40 µg	100 %
Molybdenum	50 µg	100 %
Selenium	30 µg	55 %
Zinc	5 mg	50 %

RDA = Recommended Daily Allowance

** No EU RDA established

Energy, protein, carbohydrate, sugar and fat content negligible.

Free from:

- Gluten
- Yeast
- Azo-dyes
- Wheat

Suitable for:

- Adults
- Children over 11

Dose - Take one tablet daily with water, preferably with food.

Metagenics - Multigenics		
Ingredient	Amount	Daily Value
Vitamin A [85% (6375 IU) as beta-carotene [†] and 15% (1125 IU) as retinyl acetate]	7500 IU	150%
Vitamin C (as ascorbic acid)	900 mg	1500%
Vitamin D (as cholecalciferol)	300 IU	75%
Vitamin E (as d-alpha tocopheryl succinate and mixed tocopherols)	150 IU	500%
Thiamin (as thiamin mononitrate)	22.5 mg	1500%
Riboflavin	25.5 mg	1500%
Niacin (as niacinamide and niacin)	315 mg	1575%
Vitamin B ₆ (as pyridoxine HCl)	30 mg	1500%
Folate (as folic acid and calcium L-5-methyltetrahydrofolate ^{††})	600 mcg	150%
Vitamin B ₁₂ (as cyanocobalamin)	150 mcg	2500%
Biotin	150 mcg	50%
Pantothenic Acid (as D-calcium pantothenate)	150 mg	1500%
Calcium (as calcium citrate and microcrystalline hydroxyapatite concentrate)	375 mg	38%
Iron (as iron bis-glycinate)	7.5 mg	42%
Phosphorus (as microcrystalline hydroxyapatite concentrate)	82.5 mg	8%
Iodine (as potassium iodide)	114 mcg	76%
Phosphorus (as microcrystalline hydroxyapatite concentrate)	187.5 mg	47%
Zinc (as zinc citrate)	15.5 mg	104%

Selenium (as selenium aspartate)	150 mcg	214%	
Copper (as copper citrate)	1.5 mg	75%	
Manganese (as manganese citrate)	.75 mg	38%	
Chromium (as chromium citrate)	150 mcg	125%	
Molybdenum (as molybdenum aspartate)	78 mcg	104%	
Potassium (as potassium aspartate)	74.25 mg	2%	
Quercetin	18.75 mg	*	
Betaine HCl	137.25 mg	*	
Choline (as choline bitartrate)	93.75 mg	*	
Inositol	90 mg	*	
Citrus Bioflavonoid Complex	75 mg	*	
<i>para</i> -Aminobenzoic Acid (PABA)	37.5 mg	*	
Mixed Carotenoids (including beta-carotene, alpha-carotene, cryptoxanthin, zeaxanthin, and lutein)	4.28 mg	*	
Gamma Tocopherol (as mixed tocopherols)	100.5 mg	*	Other

Ingredients: Microcrystalline cellulose, cellulose, stearic acid (vegetable), croscarmellose sodium, silica, and coating (water, hypromellose, medium chain triglycerides, hydroxypropylcellulose, and sodium copper chlorophyllin).

Appendix 1:. Evidence for benefits of Magnesium in Human Health

- **Cardiovascular disease .**
 - *Low serum magnesium concentrations are associated with cardiovascular and all-cause mortalityⁱ.*
 - Energy: Heart muscle cells are particularly dense in mitochondria (having as many as 100 times more per cell than skeletal muscle!),The mitochondria require adequate magnesium to produce ATP via the citric acid cycle.
 - Fibrillation: A number of studies have shown magnesium supplementation to reduce atrial fibrillation^{ii , iii , iv},
 - Magnesium can act as a calcium channel blocker^v
 - Magnesium has been shown to reduce hypertension^{vi}
 - Its antispasmodic activity may protect against coronary artery spasm^{vii}
 - Magnesium can protect against thrombosis^{viii}
 - Hypertension. Ann Walker (medical herbalist based in Reading) conducted a very interesting study, where the combined effect of magnesium and hawthorn was found to be greater than the sum of either agents used individually.^{ix}
- **Fibromyalgia:** Magnesium deficiency is common in people with fibromyalgia^{x , xi} and relatively low doses 50 mg, of Magnesium combined with malic acid (magnesium malate), has been clinically demonstrated to improve pain and tenderness in Fibromyalgia sufferers^{xii}
- **Blood sugar regulation. In 2007, a study confirmed that** Magnesium deficiency is common in type 2 diabetics^{xiii}, Research has also shown that type 2 diabetics with peripheral neuropathy and coronary artery disease have lower intracellular magnesium levels^{xiv}. Magnesium supplementation has been shown to reduce fasting glucose levels and to raise HDL cholesterol^{xv} and to improve insulin sensitivity and metabolic regulation in type 2 diabetes^{xvi}.
- **PMS:** Magnesium deficiency is common in women affected by PMS^{xvii} and supplementation has been found to significantly reduce a range of symptoms^{xviii} including fluid retention^{xix}, and, when combined with B6, anxiety-related symptoms^{xx}.
- **Migraines: People who suffer from migraines have been shown to suffer from a significant magnesium deficiency^{xxi , xxii}. And studies have shown migraine occurrence is reduced when sufferers supplement with magnesium^{xxiii , xxiv},**

Magnesium

The proportion of elemental magnesium in the compound does not relate to the bio-availability.

Type	Bio-availability	Benefits
Mg Glycinate	Very good 80%?	a chelated form of magnesium with high levels of absorption and bioavailability.
Mg Fumerate	Good	Fumeric acid is a krebs cycle nutrient with some evidence for benefits in psoriasis.
Mg Citrate	Good. Rapidly absorbed into the GIT.	Magnesium citrate: A commonly used form that has a good bioavailability compared to oxide. Has loosening effect on stool loosening This form is found in many supplements and is a good option for delivering magnesium into the body.
Mg Taurate	Good	L-aurine is a Calming amino acid which promotes cardiovascular health (it is abundant in the heart muscle), and insulin sensitivity.
Mg Oxide Cheapest form.	poor	Found in milk of magnesia products, and many OTC magnesium products. This form has a strong laxative effect. This form will supply the lowest levels of bio-available magnesium
Magnesium chloride / Magnesium lactate	better absorption than magnesium oxide	, which contains five times more magnesium
Mg EAP	Readily bio-available?	Bound to Ethanolamine Phosphate – which in theory is compatible with phospholipids – thus, should cross cell membranes with ease. Little research on this.
Food state Mg		Hydroponically grown vegetable base.
Mg Glycinate		
Mg Sulfate		Epsom salt. The sulphate draws toxins out and the magnesium is absorbed transdermally. Add this to the bath – there is good transdermal absorption. You need a good, large mugfull
Floradix Mg		Mg Gluconate.
Mg Sulphate	Transdermal absorption. Not used orally.	Epsom bath salts.
Mg Aspartate	Better than oxide and	Magnesium Aspartate:. There were some promising clinical trials conducted in the

	citrate.	1960s that found a combination of magnesium and potassium aspartates had a positive effect on fatigue and they reduced muscle hyper-excitability. ² Physiologically this makes sense since both magnesium and aspartic acid are critical players in cellular energy production. This form is not commonly found but has been used for chronic fatigue syndrome.
Mg Theonate	Highly bio-available? Crosses blood brain barrier	Appears to show promising evidence for benefits in Alzheimer's (See very interesting article "Novel Magnesium Compound Reverses Neurodegeneration" at www.lef.org .)

Great preparations for transdermal magnesium absorption.

Epsom salt baths – Dr Natasha Campbell-Mc Bride suggests using ½ to 1 cup of Epsom salts per bath, however others have reported good results from one to two cups per tub. A study by Dr RH Waring revealed that most people found maximal benefit by bathing 2 or 3 times/week, using 500-600g Epsom salts each time. Simply dissolve the salts in hot water first and then fill the tub to about waist deep, as warm as possible. Severe deficiencies can reveal negative reactions, such as irritability or hyperactivity, and this will indicate the need to decrease the amount of salts until they can be better tolerated. You may need to start with as little as one tablespoon of salts, and work up gradually. Epsom salts baths are very calming for most people and it is relaxing to have a bath before bed.

General guidelines recommend soaking for soak 20 minutes or more for optimum benefits and only pat drying so that some of the salts are left on the skin to absorb. If the salts become itchy or irritating on the skin, just rinse it off and dry normally. If the skin feels too dry, use coconut oil to moisturize..

Spray – Mix one part salts and one part hot water and pour into a spray-squirt bottle. Spray directly on the skin.

Homemade lotion –Heat some Epsom salts with a little water to dissolve them (approx. 1 tsbs salts : 3tbs water) Add more water if necessary. Then mix in some coconut oil or aloe vera gel. You may need to experiment with ratios. Apply to skin.

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Epsom Salt Council www.epsomsaltcouncil.org

Report on Absorption of magnesium sulfate (Epsom salts) across the skin Dr RH Waring School of Biosciences, University of Birmingham. B15 2TT, U.K. r.h.waring@bham.ac.uk

Appendix 2: Evidence for benefits of Essential Fatty Acids in Health

Cardiovascular function

- Reduction in cardiovascular risk profile in patients with metabolic syndrome and associated inflammation and auto-immunity^{xxv}
- Reduction in coronary heart disease^{xxvi}
- Lowers blood pressure in dyslipidaemic patients (omega-3 oil derived from flaxseed)^{xxvii}
- Reduction in sudden cardiac deaths, total cardiac mortality and non-fatal cardiovascular events^{xxviii,xxix,xxx}
- Significantly more effective than defibrillators in preventing sudden death^{xxxi}.
- Along with vitamin D, reduction in coronary calcification and plaque growth^{xxxii}
- omega-3 fatty acids improve endothelial function in peripheral arterial disease^{xxxiii}
- Fish oil has a beneficial effect on blood viscosity in peripheral vascular disease.^{xxxiv}
- Fish oil supplementation improves walking distance in peripheral arterial disease^{xxxv}.
- The omega-3 fatty acid docosapentaenoic acid (DPA) reduces the risk of peripheral arterial disease associated with smoking^{xxxvi}.
- Fish and long-chain omega-3 fatty acid intake reduce the risk of coronary heart disease and total mortality in diabetic women^{xxxvii}.
- Higher plasma concentrations of EPA and DPA are associated with a lower risk of non fatal myocardial infarction among women^{xxxviii}.
- Omega-3 fatty acid consumption is inversely associated with incidence of hypertension^{xxxix}.
- The consumption of fish reduces the risk of ischemic stroke in men^{xl} and elderly individuals^{xli}.
- Eicosapentaenoic acid (EPA) may have a therapeutic role in attenuating pulmonary hypertension^{xlii}.

Inflammation and inflammatory conditions

- Omega-3 fatty acid supplementation **reduces inflammatory biomarkers**, erythrocyte sedimentation rate, and interleukin-8 concentrations in cystic fibrosis patients^{xliii}.

Auto-immune

- EPA and DHA have therapeutic value in the treatment of systemic lupus erythematosus^{xliv}.
- Omega-3 fish oil reduces the severity of symptoms in patients with systemic lupus erythematosus^{xlv}.
- Omega 3 fatty acids decrease the severity of autoimmune disorders^{xlvi}.

Muscular skeletal

- Clinical studies have reported that oral fish oil supplementation has beneficial effects in rheumatoid arthritis and among some asthmatics^{xlvii}.
- Omega-3 fatty acids have shown significant therapeutic benefits^{xlviii} and reduction in the need for NSAIDs in patients with rheumatoid arthritis^{xlix}.

Mental Health

- Omega-3 fatty acid supplementation is associated with reduced mania and depression in juvenile bipolar disorderⁱ
- A combination of omega-3 and omega-6 fatty acids as well as magnesium and zinc consumption provide a beneficial effect on attentional, behavioural, and emotional problems of children and adolescentsⁱⁱ.
- Fish oil supplementation has a significant therapeutic effect on children with autismⁱⁱⁱ.
- Omega-3 fatty acids appear to be an effective treatment for children with autismⁱⁱⁱ
- A moderate intake of EPA and DHA may postpone cognitive decline in elderly men^{iv}.
- Omega-3 fatty acids may have a therapeutic effect on postpartum depression^v
- Omega-3 fatty acid supplementation exhibits therapeutic value in the treatment of children with attention-deficit/hyperactivity disorder (ADHD)^{vi} symptomatology.
- Omega-3 fatty acids were shown to be more effective than placebo for depression in both adults and children in small controlled studies and in an open study of bipolar depression^{vii}
- The omega-3 fatty acid EPA is as effective as fluoxetine (Prozac) in treating major depressive disorder^{viii}.
- A diet low in trans-unsaturated fat and rich in omega-3 fatty acids and olive oil may reduce the risk of age-related macular^{lix}
- Higher intake of omega 3 fatty acids may reduce the risk of pneumonia^{lx}.

Blood sugar regulation

- Omega-3 Fatty acids supplementation prevents and reverses insulin resistance^{lxi}
- Omega-3 fatty acids alleviate insulin resistance and fatty liver in obese mice^{lxii}

Other

- Intake of eicosapentaenoic and docosahexaenoic acids from fish may be associated with a reduced prevalence of allergic rhinitis^{lxiii}.
- Nephropathy: Fish oil improves tubular dysfunction, lipid profiles and oxidative stress in patients with IgA nephropathy^{lxiv}
- Omega-3 fatty acids prevent the formation of urinary calcium oxalate stone formation^{lxv}.

- Omega-3 fatty acids are beneficial for children with bronchial asthma^{lxvi}
- Omega 3 fatty acid supplementation may contribute to the prevention of early preterm birth both low-risk and high-risk pregnancies^{lxvii}.
- Primary open-angle glaucoma patients have reduced blood levels of DHA and EPA^{lxviii}.
- Fish consumption is associated with a 63% reduction in prostate cancer - specific mortality^{lxix}
- Diets containing EPA and DHA have an inhibitory effect on breast cancer growth and metastasis^{lxx}.
- Dietary Omega-3 fatty acids may protect smokers against chronic obstructive pulmonary disease^{lxxi}

Appendix 3: Evidence for the benefits of probiotics in health

Although sometimes one particular strain is found to be effective, there is no reason to suppose that other (unstudied strains) might not be equally effective

- Infectious diarrhoea^{lxxii}
- Atopic dermatitis^{lxxiii}, ^{lxxiv} and infantile excema^{lxxv} and atopic dermatitis^{lxxvi}
- Dental caries in children^{lxxvii}
- Constipation^{lxxviii}
- IBS^{lxxix}
- Anti-biotic associated diarrhoea and C-diff^{lxxx}

Specific strains:

Lactobacillus casei Rhamnosis and L Reuteri

- For children with constipation^{lxxxi}
- Reduction in inflammation in Crohn's and UC^{lxxxii}
- Bacterial vaginitis and vaginosis^{lxxxiii}, ^{lxxxiv}

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