



dr paul clayton's

Health Newsletter

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Omega 3 and
Alzheimer's

Vitamin E

Statins

Liver disease

Fish for the brain - Omega 3 in Alzheimer's Disease

Back in 1997, an epidemiological study found that increased fish consumption was linked to a lower risk of Alzheimer's Disease (AD) (Grant '97).

Then in 2005, a pre-clinical study showed that a diet rich in the poly-unsaturated omega-3 fatty acids slowed the progression of Alzheimer's type brain pathology in an aged mouse model (Lim et al '05).

Three years later, a relatively small prospective clinical trial found that small doses of omega-3s lead to some improvements in patients with mild cognitive impairment, although not with Alzheimer's Disease (Chiu et al '08).

This boosted sales of fish oil supplements, and triggered another, larger trial which has just been published – with disappointing results.

According to this study, daily supplements of docosahexaenoic acid (DHA), one of the two omega-3s in fish oil, did not reduce cognitive decline in patients with mild-to-moderate Alzheimer's disease (Quinn et al '10, Yaffe '10).

Here is a prime example of more damn-fool research, using concepts and trial designs more suited to testing drugs than nutritional interventions. The truth is that the biochemical imbalances that have been identified in AD are far too many, and too complex, to be amenable to single, simple input solutions such as a DHA supplement. They are, however, amenable to diet, which contains thousands of different compounds, many of which are known to interact with brain chemistry.

At Columbia University, Professor Nicholas Scarmeas has been studying the relationship between diet and AD for many years. He has published a series of papers that show, unequivocally, that the risk of developing this cruel disease is diminished by the consuming a Mediterranean diet (ie Gu et al '10). This is a diet that contains high levels of a range of bioactive compounds, including the anti-inflammatory flavonoids - which are also strongly linked to

a reduced risk of AD (ie Dai et al '06), and have plausible mechanisms of action (ie Fernandez et al '10, Jonova et al '10)

The current anti-AD drugs are fairly useless, and have a range of adverse effects. If you want to protect yourself or a loved one against AD, the logical way forwards is not drugs, or pharma-style single compound supplements, but by dietary improvement and/or a comprehensive, broad spectrum micro- and phytonutritional support programme. These should contain omega-3s (all of them, not just DHA), which after all play a key role in neuronal defence mechanisms (ie Palacios-Pelaez et al '10); but they must also contain flavonoids and a wide range of antioxidants.

The inclusion of anti-oxidants is critical; omega-3 supplements taken alone, without antioxidants, are oxidised in the body producing toxic and pro-inflammatory lipid oxidation products which shorten life span in pre-clinical models (ie Tsuduki et al '10); and actually exacerbate Alzheimer's (Liu et al '08)!!

No wonder the big Quinn trial failed.



Mackerel - an underrated great-tasting oily fish

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The Paul Clayton Newsletter describes developments in the new field of pharmaco-nutrition, where nature and science are combined to offer non-drug solutions to degenerative disease.

The Newsletters are intended to increase knowledge and awareness of health issues and are for information only.

No health claims for specific products are made or intended and the information should not be used as a substitute for medical advice.

Vitamin E - different strokes

In the last few weeks a meta-analysis published in the British Medical Journal announced that vitamin E supplements may increase the risk of haemorrhagic stroke (where blood flow to a region of the brain is stopped by rupture of the blood vessel) by up to 22% (Schürks et al '10). This news has worried supplementers, and has led many to stop taking vitamin E altogether. Like so many medical reports of the positive or negative effects of supplements, however, this piece of news must be taken with a considerable pinch of salt. In fact, it is downright misleading.

To begin with, the meta-analysis hoovered up trials of both synthetic and natural vitamin E products; a bizarre methodological weakness, because it is well known that the different types (stereo-isomers) of tocopherol have distinct biochemical and biological effects (ie Constantinou et al '09, Han et al '10). This weakness was exacerbated by the decision of the scientists not to include the studies on the effects of full spectrum vitamin E (which combines the 4 tocopherols with 4 tocotrienols), and which as a result has very different effects again (ie Pierpaoli et al '10).



Spinach - high in Vitamin E

A more substantial problem with the study is that the folk who designed the meta-analysis were trying, once again, to isolate the impact of a single nutrient. This doesn't work. The sprawling meta-analysis – in this case involving 115,000 very different people – is just too clumsy and too

wide-scale to see whether vitamin E might be problematic, for example, in those who are just taking a single E supplement.

Vitamin E has been known for years to reduce the ability of the blood to clot when levels of vitamin K are low (Corrigan '79 & '82); and of course, vitamin K depletion is very common UNLESS your supplement also contains vitamin K (NutriShield is one of the few that do this).

If you eat a poor diet (ie a diet depleted in flavonoids, but with excess sodium and pro-inflammatory compounds), which is the case with the typical fast food diet, and are as a result overweight, then you will likely have high blood pressure. In this situation anything that impairs clotting (ie supplements that contain E but no K), will increase the risk of haemorrhagic stroke. In contrast, if you eat a healthy diet and as a result have normal blood pressure (ie Karppanen & Mervaala '08), Vitamin E on its own or in a properly designed supplement will do no harm – and indeed will do you a lot of good.

There is another kind of stroke where blood flow is impeded by blockage, rather than by rupture of the affected blood vessels. This is termed thrombo-embolic stroke, and it is caused by excessively sticky blood platelets or by the formation of clots inside the cardiovascular system. These in turn are often triggered by the development of atheroma, which is often driven by excessive lipid (blood fat) oxidation.

Given the ability of vitamin E to slow the oxidation of lipids in the blood stream (caveat – this is only the case in those who have a good vitamin C status), one would expect vitamin E to offer some protection against thrombo-embolic stroke. Going back to the BMJ meta-analysis, one finds that vitamin E does indeed reduce the risk of this kind of stroke; so the scientists have at least done some of their homework.

The bottom line is that big, pharma-type science (studying a single nutrient in isolation) as reported in the BMJ is a crude and stupid way of studying the subtle and complex effects of micronutrients, which do NOT act individually but in close combination with many other micro- and phyto-nutrients. The BMJ paper gets the headlines, but proves nothing, and does nothing to progress the study of the importance of nutritional support to long term good health.

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Give me an E, please, Bob

A recent study from Yale University School of Medicine found that low blood levels of vitamin E are linked to greater physical decline in free-living older people in Tuscany, Italy (Bartali et al '08). This epidemiological study looked at a raft of micronutrients but only vitamin E showed up as being protective.

"The study provides empirical evidence that a low concentration of vitamin E is associated with subsequent decline in physical function in a sample of older persons living in the community," wrote lead author Benedetta Bartali.

"Although the findings from this epidemiological study cannot establish causality, they provide a solid base that low

concentration of vitamin E contributes to decline in physical function."

"Approximately 15 to 30 mg per day of dietary alpha-tocopherol [a component of vitamin E] is needed to give protection", Bartali said. "This amount can be easily reached through diet, from sources such as almonds, tomato sauce, and sunflower seeds among others." Or from a supplement.

I think that this estimate is broadly correct, although the Tuscan diet has quite good levels of phyto (plant derived) nutrients. For True Brits, a rather larger amount may be needed; together, of course, with a comprehensive micro- and phyto-nutrient support programme.

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Vitamin E - different folks

Avoiding a stroke is surprisingly easy (ie Karppanen & Mervaala '06). But what of those who are already at high risk? A new study suggests that one of the tocotrienols (those forgotten isomers of E which are rarely found in supplements) can prevent nerve cell death in the brain following a stroke.

Tomato sauce - high in Vitamin E

When a stroke occurs, a neurotransmitter called glutamate is released in the affected brain tissues. The glutamate rush is neurotoxic in its own right, but it also activates a harmful enzyme called cystolic calcium-dependent phospholipase A2, or cPLA2. This enzyme in turn produces a burst of arachidonic acid, which kills brain cells. Alpha-tocotrienol has just been shown to inhibit cPLA2, thereby blocking a considerable part of the sequence of events that kills brain cells



after a stroke (Khanna et al '10). These positive effects were observed at low levels of the nutrient, by researchers from Ohio State University.

"Our research suggests that the different forms of natural vitamin E have distinct functions. The relatively poorly studied tocotrienol form of natural vitamin E targets specific pathways to protect against neural cell death and rescues the brain after stroke injury," said Professor Chandan Sen, lead researcher of the study. "We studied an enzyme that is present in the brain, and that is activated after a stroke in a way that causes nerve damage. We found that the enzyme is blocked by very low levels of tocotrienol. So what we have here is a naturally derived nutrient, rather than a drug, that provides this beneficial impact."

The levels of tocotrienol that produced this benefit were very low, and were evident at a concentration easily achieved by supplementation. The researchers said, "On a concentration basis, this finding represents the most potent of all biological functions exhibited by any natural vitamin E molecule." And the protective results were highly significant. Alpha tocotrienol reduced arachidonic acid synthesis by 60%, and increased the number of surviving brain cells four-fold.

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Vitamin E for hearts and lungs

Another paradox. The famous ATBC [Alpha-Tocopherol Beta-Carotene Cancer Prevention] study found that synthetic vitamin E (and beta carotene) increased the risk of lung cancer in smokers (ie Albanes et al '95), and this paper has been used as a stick to beat the supplement industry unmercifully ever since.

Less well-known is a more recent paper, derived from the same group of patients, which showed that smokers with higher dietary levels of (natural) vitamin E had a significantly lower incidence of both cancer and heart disease (Wright et al '06).



The diametrically opposite results from the Albanes and Wright papers were partly to do with different study methods. They might also be due to the many differences between synthetic and natural vitamins; and finally, they may also have been due to the fact that diets rich in all the forms of vitamin E are also likely to be richer in many other protective micro- and phyto-nutrients.

Sunflower seeds - high in Vitamin E

Such different Es

Another new study shows just how different the various forms of vitamin E actually are; and this one highlights the ability of the tocotrienols to protect against cancer (Barve et al '10).

In this study, mice genetically modified to produce a high frequency of prostate cancer were given mixed tocotrienols. Mice given increasing doses of tocotrienols developed significantly lower numbers of tumours; falling from 73% in the placebo group to 38, 33 and 22% in the low, medium and high dose groups.

The study also indicated the mechanism for the protective effect. The mixed tocotrienols suppressed the progression of lesions to fully developed tumours by slowing cell growth and increasing programmed cell death (apoptosis).

The researchers concluded that their findings "further support the potential use of tocotrienols as prostate cancer chemo-preventive agents in humans."



Nuts, especially almonds and hazelnuts, are high in Vitamin E

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Liver longer

The season of good will is approaching, and as it is also a season when many of us drink too much, here is a little coda on nutrition and alcohol. There are no nutritional remedies for bad behaviour, but there are various things you can do to prevent a bad liver.

Livers have become a major public health problem. We are not only drinking too much, but we are also fatter than ever, thanks to our inactive lifestyles and the over-availability of high calorie, nutritionally-impoverished foods.

The result is a huge increase in Alcoholic and Non-Alcoholic Fatty Liver Disease (NAFLD); since 1980, the rate of liver disease in young adults aged between 35 and 44 has increased more than 8-fold (NHS National Archives '10). It has reached the point where hepatology clinics up and down the country are overwhelmed, and there are no longer enough resources (or livers) to go round. In an outburst of public spiritedness, here are some potential prophylactic measures.

There is evidence from a range of sources that the methyl group donor **betaine** offers protection from liver damage, via a number of mechanisms that include the enhanced

metabolism of fats in the liver (ie Kharbanda et al '09, Kathrivel et al '10, Powell et al '10, Varatharajalu et al '10). Fat metabolism in the liver can be further enhanced by cutting down on carbs (Neuschwander-Tetri '10).

Flavonoids offer additional protection, via their antioxidant and anti-inflammatory effects (ie Hou et al '10, Zhao et al '10, Shaker et al '10, Nakbi et al '10). A wide selection of other, mutually supportive antioxidants and anti-inflammatory agents would also be logical.

So if you are going to drink this Christmas, NutriShield would make an ideal chaser!!



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Statin the obvious

New findings show that the cholesterol-lowering statin drugs significantly increase the risk of cataracts, muscle weakness, liver dysfunction and kidney failure (Hippisley-Cox & Coupland '10). They confirm a pattern already familiar to many doctors who prescribe these drugs to vast numbers of patients, as per lucrative treatment guidelines that were heavily influenced by the pharmaceutical industry.

These drugs target LDL cholesterol, but this is an out-of-date and inaccurate biomarker. Most clinical scientists these days regard chronic sub-clinical inflammation of the arteries (known as endothelial dysfunction or ED) as the root cause of atheroma (and hypertension).

If inflammation is present in the arteries, atheroma will form and blood pressure will rise. The factors are intertwined; high levels of cholesterol, combined with low levels of antioxidants and high levels of pro-inflammatory compounds will create pro-inflammatory cholesterol oxidation products, which cause ED. If you do not have ED, however, you can eat cholesterol to your heart's content, as the Victorians did, with no risk of heart disease.

Not only are statins aimed at the wrong target, their idiotic and highly non-specific mechanism (they block

cholesterol synthesis in the liver) means that they have a range of subtle and potentially hazardous effects on many body systems.

After cardiovascular disease, cancer is the next most common cause of death. One of the ways in which cancers beat our defences is by suppressing the immune system, preventing our immune cells from recognising the cancer as foreign and attacking it. A cancer can do this by increasing the numbers of T3-cells, which in turn inhibit the anti-cancer response.

Statins have now been shown to boost numbers of Foxp3 T-cells (Lee et al '10, Kim et al '10); a mechanism which confers a very worrying and potentially extremely serious additional cancer risk (Kobayashi et al '10). More by luck than good management, the statins may have some anti-cancer effects of their own (Lee et al '10), but it is quite appalling how recklessly and fecklessly the drug industry has pushed these drugs on us all.

There is no money in advocating diets. Statins, therefore, will continue to be the best business in town, though they are very far from being the best medicine.

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