# dr paul clayton's Health Newsletter

**New Year 2007**

Carnosine
Vitamins K+ D
Fish Oil
Probiotics

Dear Readers

Here is a round-up of some of the latest research linking together diet, nutrition and health. It seems that with every passing month, and every hundred or so new research papers that each month brings, the overall picture becomes clearer: your chances of remaining healthy, or becoming ill, are more intimately linked to what you eat than anything else that you do.

In this newsletter, I will report on vitamins D and K, omega 3 fish oils, probiotics, the latest news on green (and black) tea, garlic and onions – and a new compound called carnosine; which unlike most of the health-promoting nutrients I write about is derived from meat.

Let's tackle them in no particular order – but keeping the least-known (carnosine) till last!

## Tea and Cancer

There is already a good deal of work that indicates that tea – both green and black – has anti-cancer effects. This was recently reinforced by a joint American–South Korean study, led by the US Department of Agriculture, and published last month in the Journal of Agricultural and Food Chemistry (Friedman et al '06).

Many of tea's health benefits, including cancer protection and a reduced risk of Alzheimer's, have been linked to the flavonoids found in tea. Green tea contains 30 to 40 per cent of flavonoids, while black tea (green tea that has been oxidized by fermentation) contains between 3 and 10 per cent. But tea contains other good things too, including compounds called theaflavins, and the unusual amino acid l-theanine.

The researchers looked at the effects of each of these in isolation, and then at the effects of a whole tea extract (which is what we drink) against a range of common cancer cell lines. These included breast, lung, prostate and colon cancer cell cultures; and in each case, the tea extracts killed large numbers of the cancer cells, with higher concentrations of tea killing larger numbers than weaker extracts.

"These findings extend related observations on the anti-carcinogenic potential ingredients of tea, and suggest that consumers may benefit more by drinking both green and black teas," wrote lead author Mendel Friedman from the USDA.

Other scientists have shown that the tea polyphenols can reduce the formation of certain carcinogens (d'Ischia et al '06), but it is becoming abundantly clear that these valuable compounds can directly arrest and kill many cancer cells, and force others to redifferentiate; an important process that effectively renders them harmless.

These and other studies have led key researchers at the University of Leicester to recommend large-scale clinical trials of the tea flavonoids in the prevention of prostate and cervical cancers (Thomasset et al '07). Given that tea is pretty safe – especially when compared to the highly toxic anti-cancer drugs currently used – I wholeheartedly agree with them. I would also point out that most soft drinks, unless made with fruit juice, contain none of the anti-cancer compounds outlined above.


Friedman M, Mackey BE, Kim H-J, Lee I-S, Lee K-R, Lee S-U, Kozukue E, Kozukue N. **Structure-Activity Relationships of Tea Compounds against Human Cancer Cells.** *Journal of Agricultural and Food Chemistry* Published on-line ahead of print: ASAP Article doi: 10.1021/jf062276h S0021-8561(06)02276-X

d'Ischia M, Panzella L, Manini P, Napolitano A. **The chemical basis of the antinitrosating action of polyphenolic cancer chemopreventive agents.** *Curr Med Chem*. 2006;13(26):3133-44.

Thomasset SC, Berry DP, Garcea G, Marczylo T, Steward WP, Gescher AJ. **Dietary polyphenolic phytochemicals-promising cancer chemopreventive agents in humans? A review of their clinical properties.** *Int J Cancer.* 2007 Feb 1;120(3):451-8.

## Fish Oil - New benefits?

A new study reports that fish oils can suppress the formation of adipocytes (fat cells), and may thus lead to reductions in body fat.

Not what we have come to expect from an oil (eating oils or fats make us fat, is the common wisdom, because they are so calorie-rich); but the omega-3 fatty acid in question, DHA, is no ordinary oil.

The research team, based at the University of Georgia, added DHA to cell cultures of human pre-adipocytes (cells that grow into adipocytes), at the same concentrations that occur in human plasma after a fish oil supplement. They found that DHA killed off significant numbers of the cells by triggering apoptosis (programmed cell suicide); reduced the accumulation of fat in those cells that survived; and promoted lipolysis, which is the breakdown of fat deposits. This combination of effects, the researchers said, would be expected to lead to weight loss; and indeed, previous studies had shown that fish oils fed to rodents do exactly this.

Verdict: very interesting. I would not rely on a fish-rich diet to make everyone slim, but this adds to all the other evidence that incorporating oily fish in the diet is good for your general health. The problem, however, is that fish stocks are running low, and there isn't enough for everyone.

New strains of GM maize have been bred which produce their own DHA, and this just might be the best political argument for GM crops yet.

Kim HK, Della-Fera M, Lin J, Baile CA. **Docosahexaenoic acid inhibits adipocyte differentiation and induces apoptosis in 3T3-L1 preadipocytes.** *J Nutr.* 2006 Dec;136(12):2965-9.

## Vitamin D and Auto-Immune Disease

A new paper indicates that staying out of the sun may seriously damage your health. A fascinating article in the Journal of the American Medical Association reports on a survey of white US military personnel, in which higher levels of vitamin D were clearly and consistently linked to reduced risk of developing multiple sclerosis (Munger et al '06). The link was particularly strong in younger subjects, and those with the highest vitamin D levels were 62% less likely to develop MS than their colleagues with the lowest vitamin D levels.

The researchers were so struck by the apparently protective effects of vitamin D that they suggested that 'increasing the vitamin D levels in adolescents and young adults, for example by supplementation, could result in an important reduction in MS'.

This is not only a personal but also a public health issue. MS is one of the most common neurological diseases in young adults, affecting some 2 million of them worldwide. And at the time of writing, the pharmaceutical establishment offers no cures for this debilitating and tragic illness; the drugs currently given to MS patients are not only ineffective but also highly toxic.

How very obtuse of us not to have noticed the glaringly obvious and long-known relationship between sunlight exposure and the risk of MS; and how stupid of us not to have moved on from this simple observation to recommending daily outdoors exercise – or, for those living in Northern Europe, vitamin D supplements. Sadly, children today spend less time in the fresh air exposed to sunlight than their parents did, and the medical profession have little faith in, or understanding of, vitamin D.

For example, Munger and her colleagues called for a prevention trial among first-degree relatives of individuals with MS, said to be at higher risk of developing MS, to further investigate the potentially protective role of the vitamin. But at the same time, they concluded that it was still to early to use vitamin D supplements to prevent MS. This seems to me to be wildly over-cautious, given that vitamin D supplements are, unlike the MS drugs, cheap, safe – and increasingly, in circles where they are used, regarded as effective (Gillie '06, Strand '06.)

For the more sceptical among you, vitamin D supplements have already been shown to protect against MS in a mouse model (Nataf '96); and for the more scientifically-inclined, the mode of action has also been pieced together. Vitamin D is essential for the normal functioning of the immune system. When levels of D are too low, auto-reactive T-cells are formed – exactly those cells which cause the damage in MS. When levels of D are normalised, the balance of T cells is restored and autoimmunity is avoided (Hayes et al '97, Cantorna '06).

Munger KL, Levin LI, Hollis BW, Howard NS, Ascherio A. **Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis.** *JAMA* 296, 2832-2838, 200

Gillie O. **A new government policy is needed for sunlight and vitamin D.** *Br J Dermatol.* 2006 Jun;154(6):1052-61. Review.

Strand R: personal communication, 2006

Hayes C, Cantorna M, DeLuca H. **Vitamin D and Multiple Sclerosis.** *Proc Soc Exp Biol Med* 1997; 216:21-27.

Nataf S, Garcion E, Darcy F, Chabannes D, Muller JY, Brachet P. **1,25-dihydroxyvitamin D3 exerts regional effects in the central nervous system during experimental allergic encephalomyelitis.** *J Neuro Exper Neurol* 1996; 55:904-914.

Cantorna MT. **Vitamin D and its role in immunology: multiple sclerosis, and inflammatory bowel disease.** *Prog Biophys Mol Biol.* 2006 Sep;92(1):60-4.

# Vitamin K - what is it good for?

It has long been said that patients taking the blood thinning drug warfarin should not take vitamin K supplements, as these could, theoretically, neutralise the effects of the drug and thereby increase the risk of blood clots. Now, however, a fascinating new prospective clinical study has shown that the truth is far more complicated, and that vitamin K supplements actually help to control and stabilise the anti-clotting effect of warfarin (Sconce et al '06).

It was already known that a low intake of vitamin K was linked to unstable control of anti-coagulation, so this research, carried out at the University of Newcastle, didn't exactly come out of the blue. But what was surprising was how effective the vitamin K supplements were. They helped to stabilise clotting in over half of all the cases studied.

As warfarin use is unpleasant and associated with a high risk of adverse effects (including potentially lethal haemorrhaging), anything that can help to make its effects more predictable, and perhaps cut down on the doses used, is a real breakthrough. Vitamin K supplements should also help to reduce the number of patient visits to hospital for monitoring, and that will be a blessing to many as well.

There are various forms of vitamin K available, but the available data suggest that the most effective is MK-7, a form of vitamin K extracted from fermented soybeans (natto), and sold in Norway and the USA as NattoK2. It is only available on the web at this time. This is due to the bone-headed Eurocrats in Brussels who have decreed that although MK-7 occurs in green and blue cheeses, and is consumed in huge amounts in Japan in natto, it is too risky to be sold to Europeans without exhaustive safety studies.

Regular readers of this newsletter will remember that vitamin K is critically important for health in other ways too. A recent cohort study (Journal of Nutrition, Vol. 136, pp. 1323-1328) reported that postmenopausal Japanese who ate more than four packets of natto per week (equivalent to about 1400 micrograms of MK-7) reduced bone loss at the hip and lower arm by over 80 per cent and 60 per cent, respectively. As if this wasn't enough, vitamin K is also essential for preventing calcification of the arteries, heart valves and other soft tissues.

These findings makes the obtuseness of the EU regulators even more unforgivable; their position on NattoK2 and on many other supplements is now actively harming the health of those whom they are supposedly protecting.


Sconce E, Avery P, Wynne H, Kamali F. **Vitamin K supplementation can improve stability of anticoagulation for patients with unexplained variability in response to warfarin.** *Blood.* 2006 Nov 16; Epub ahead of print.

Kaneki M, Hosoi T, Ouchi Y, Orimo H. **Pleiotropic actions of vitamin K: protector of bone health and beyond?** *Nutrition* 2006; 22:845-852


# Probiotic Toothpaste?

When different kinds of bacteria find themselves in the same location, they may ignore each other, or support each other; but in many cases they will fight each other, competing for the same resources or living space. It is a micro-Darwinian situation, and here – as in the larger world – the strongest survive.

There is good evidence that taking probiotic bacteria can help to maintain a healthy digestive tract by suppressing the growth of 'bad bacteria', and now there is evidence that as far as probiotics are concerned, the digestive tract starts somewhere between the lips and the teeth.

Two studies have just been completed at the University of Florida in which probiotic bacteria were given in oral formulations to healthy young adults. In both cases there was a dramatic fall in the number of strains of bacteria which cause gum disease, the main cause of tooth loss. Numbers of Campylobacter rectus, Porphyromonas gingivalis and Streptococcus mutans fell very significantly; in the case of Campylobacter rectus, numbers were reduced to less than 1% of the pre-treatment values (1).

How do the probiotic bacteria achieve this victory over the disease-causing bacteria? They have a number of tricks up their tiny sleeves. For example, they stick fast to the teeth and gums, displacing pathogens from their docking sites (Haukioja et al '06). And they produce bacteriocins, peptide molecules which act as powerful antibiotics and kill off their bacterial rivals, but which have no effects on mammalian cells.

The company that sponsored the Florida research, Oragenics, is hoping to sell us probiotic toothpaste and chewing gum, but there are obvious alternatives. You could, for example, eat live yoghurt, which – providing it contains the right probiotic bacteria – also reduces the numbers of pathogens, including those that cause dental decay (Caglar et al '05).

Or, if you wanted to be really smart, you could put probiotic-derived bacteriocins into the toothpaste, the chewing gum and indeed any foods at all (O'Connor et al '06). Why might this be a better idea? Because the probiotics are only effective when alive, whereas the bacteriocins are effective indefinitely.

Watch this space; the next generation of toothpastes are just around the corner.



1 Commercial data, not yet published

2 Haukioja A, Yli-Knuuttila H, Loimaranta V, Kari K, Ouwehand AC, Meurman JH, Tenovuo J. **Oral adhesion and survival of probiotic and other lactobacilli and bifidobacteria in vitro.** *Oral Microbiol Immunol.* 2006 Oct;21(5):326-32.

3 Caglar E, Sandalli N, Twetman S, Kavaloglu S, Ergeneli S, Selvi S. **Effect of yogurt with Bifidobacterium DN-173 010 on salivary mutans streptococci and lactobacilli in young adults.** *Acta Odontol Scand.* 2005 Nov;63(6):317-20.

4 O'Connor EB, O'Riordan B, Morgan SM, Whelton H, O'Mullane DM, Ross RP, Hill C. **A lacticin 3147 enriched food ingredient reduces Streptococcus mutans isolated from the human oral cavity in saliva.** *J Appl Microbiol.* 2006 Jun;100(6):1251-60

## Protection from Garlic and Onions

A large scale epidemiological study on over 25,000 Italian and Swiss people has indicated that a high intake of garlic and onions was associated with significantly reduced risks of a wide-range of cancers. Almost 10,000 people with colorectal, ovarian, prostate, breast, renal cell, oesophageal, oral cavity and pharynx cancer, and about 15,000 healthy controls were studied.

"This uniquely large data set from southern European populations shows an inverse association between the frequency of use of allium vegetables and the risk of several common cancers," wrote lead author Carlotta Galeone.

The researchers said that quantification of the garlic intake was very difficult so the intake was classified as high, intermediate and low. Onion intake, on the other hand, was easier and intake was divided into four groups ranging from non-users to people who consumed one portion per day, with a portion defined as 80 grams of onion.

The researchers report that both onion and garlic were associated with significant reductions in the risk of all the cancers studied, with garlic in particular linked to a large risk reduction.

Indeed, people with a 'high' of garlic had an associated risk reduction of 84% for cancer of the oral cavity and pharynx, 88% for oesophageal cancer, 56% for colorectal cancer, 83% for laryngeal cancer, 25% for breast cancer, 73% for ovarian cancer, 71% for prostate cancer, and 38% for renal cell cancer, compared to people with the lowest garlic intake.

People with in the highest intake group for onion (one or more servings per day) had an associated risk reduction of 39% for cancer of the oral cavity and pharynx, 57% for oesophageal cancer, 26% for colorectal cancer, 44% for laryngeal cancer, 10% for breast cancer, 22% for ovarian cancer, 19% for prostate cancer, and 31% for renal cell cancer, compared to people who did not eat onions at all.

Recently also, the European Prospective Investigation into Cancer and Nutrition (EPIC), following 521,457 subjects in 10 European countries, reported that a diet rich in garlic and onions could protect against stomach cancer. An increase in the intake of onions and garlic of 10 grams per day (less than half an ounce) was associated with a 30 per cent reduction in the risk of intestinal gastric cancer.

Galeone C, Pelucchi C, Levi F, Negri E, Franceschi S, Talamini R, Giacosa A, La Vecchia C. **Onion and garlic use and human cancer.** *Am J Clin Nutrition.* 2006 Sep;54(7):396-404.

## Carnosine - a newly discovered nutrient

One of the important ways in which we age and sicken is via the accumulation in the body of AGE; an acronym which stands for Advanced Glycation End-products. These are formed by a combination of oxidative and glycative stress, which is what happens when you eat a diet poor in antioxidants, and with an excessive Glycemic Load. As this is a typical modern diet, the AGE phenomenon is important to all of us.

AGE compounds are decidedly cyto-toxic, and have been shown to trigger cell death in various human cell cultures, such as fibroblasts (Peterszegi et al '06). This type of cell killing involves free radicals, and the scientists found that adding antioxidants to the cell culture provided significant protection against the AGE compounds. Carnosine was one of these antioxidants.

Carnosine, technically a di-peptide, is not only an antioxidant but has now been shown to reduce the formation of AGE compounds in patients (Alhamdani et al '06). It is particularly notable that the Alhamdani paper comes from the University of Baghdad. Amazingly, the scientists there are still capable of doing world-class research, despite the best efforts of Messrs Blair and Bush.

Carnosine not only prevents the formation of the toxic AGE compounds, but is also an important protector of proteins. It protects against protein oxidation, glycation and cross-link formation, a process whereby proteins become stuck together and their function degraded. (The formation of such cross-links is deeply implicated in the development of cataract, hypertension and kidney failure in diabetic and other patients.)

Carnosine even has the ability to break damaging cross-links once they have formed. All this makes carnosine a very important anti-ageing nutrient indeed.

But where does carnosine come from? Unlike almost all the other micro- and phyto-nutrients we go on about, carnosine occurs exclusively in animal tissues; and specifically meat. As carnosine has so many anti-ageing effects, this has lead some to suggest that we should be more carnivorous (Hipkiss '06); a dietary shift which would undoubtedly reduce the excessive glycemic load of the carb-rich diet that so many of us eat today.

In terms of the Sunday lunch, this means more turkey, and fewer potatoes.

Peterszegi G, Molinari J, Ravelojaona V, Robert L. **Effect of advanced glycation end-products on cell proliferation and cell death.** *Pathol Biol (Paris).* 2006 Sep;54(7):396-404.

Alhamdani MS, Al-Azzawie HF, Abbas FK. **Decreased formation of advanced glycation end-products in peritoneal fluid by carnosine and related peptides.** *Perit Dial Int.* 2007 Jan-Feb;27(1):86-9.

Hipkiss AR. **Would carnosine or a carnivorous diet help suppress aging and associated pathologies?** *Ann NY Acad Sci.* 2006 May;1067:369-74.