



# dr paul clayton's

## Health Newsletter

Summer 2010

Fats or carbs?

Resveratrol and other flavonoids

Update on the Hygiene Hypothesis

### Food is a many-splendoured thing ...

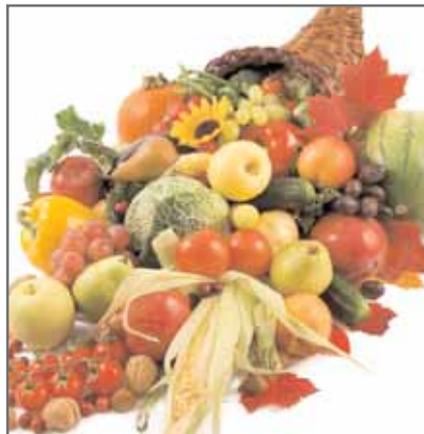
Your diet contains an extremely complex mix of chemicals, and these chemicals not only act at hundreds of different sites in your body (and in your genes), they also act on each other. In fact, the effects that a food ingredient may have on your health cannot be looked at in isolation, because the health impact of one kind of food can be considerably altered by the other items on your plate or in your general diet. Nutrition is, in other words, a non-linear or stochastic science.

For example, even though cholesterol levels are no longer regarded as good risk markers for cardiovascular disease (except by the drug companies), the medical profession was recently taken aback by a powerful study which found that intakes of saturated fat had no effect whatsoever on the risk of heart disease (Siri-Tarino et al '10). This seemed to fly in the face of received wisdom, and then an even more recent study, published in the same journal, found that saturated fats might, in some circumstances, even be protective (Jakobsen et al '10)!

The Jakobsen paper found that in those who reduced their intake of saturated fat and replaced it with refined carbohydrate foods such as white bread and pasta, the risk of heart attacks rose considerably. In fact, in the group with the highest intake of refined carbohydrates, the risk of a heart attack increased by 33 percent for every five percent increase in calorie intake from carbohydrates. In contrast, in those who reduced their intake of saturated fats and compensated by consuming more non-refined carbohydrates (such as whole-grain bread and vegetables), the risk of a heart attack fell significantly.

These findings are in line with previous papers which identified excessive intakes of refined carbohydrates as a significant factor in leading to and exacerbating the Type 2 diabetes and its pre-clinical precursor, the Metabolic Syndrome (ie Accurso et al '08, Volek & Feinman '08). They are beginning to switch the medical profession's attention away from fats and towards carbs as the fount of all evil.

Which is unfortunate, as carbs are far from being the only cause of our multiple health problems!



### ... but should it be organic?

Is organic good for you? Not necessarily, according to the latest science ...

In 2009, a meta-analysis of 162 studies of organic foods found that there were no health benefits associated with eating organic food (Dangour et al '09); and now another, smaller meta-analysis has come up with the same result (Dangour et al '10).

Previous work had shown that the nutritional differences between organic and intensively grown crops were negligible (ie Kristensen et al '08); and, even more damningly for those who think that 'natural' (whatever that is) is best, an illuminating paper from Newcastle University has just revealed that when given the choice, both wild and caged birds preferred conventional to organically grown food due to its enhanced protein content (McKenzie & Whittingham '10).

So is the debate over? Well, not quite ... There are one or two studies that suggest that organic food might produce better health end-points than conventional foods (ie Velimirov et al '10), and there is some work that indicates

that wild-grown plants may outscore conventional plants in terms of antioxidant capacity (ie Halvorsen et al '02). Notwithstanding the above, the science to date just isn't good enough to be conclusive, and much more work will need to be done before the organic case can be confirmed or finally refuted.

I think it only fair to add that some scientists are concerned about pesticide residues in conventional foods (ie President's Panel '09); and favour organic foods from a precautionary principle perspective.

The cost differential of organic is rapidly becoming an issue for increasing numbers of consumers, however, and for many the best option is probably to eat more (conventional) fruit and vegetables, but wash the produce thoroughly before cooking and/or eating.

Dangour AD, Dodhia SK, Hayter A, Allen E, Lock K, Uauy R. **Nutritional quality of organic foods: a systematic review.** *Am J Clin Nutr.* 2009 Sep;90(3):680-5

Dangour AD, Lock K, Hayter A, Aikenhead A, Allen E, Uauy R. **Nutrition-related health effects of organic foods: a systematic review.** *Am J Clin Nutr.* 2010 May 12 (epub)

Halvorsen BL, Holte K et al. **A systematic screening of total antioxidants in dietary plants.** *J Nutr.* 2002 Mar;132(3):461-71.

Kristensen M, Østergaard LF et al. **Effect of plant cultivation methods on content of major and trace elements in foodstuffs and retention in rats.** *J Sci Food & Agric.* 88:2, September 2008, 2161-2172(12)

McKenzie AJ, Whittingham MJ. **Birds select conventional over organic wheat when given free choice.** *Journal of the Science of Food and Agriculture.* 2010; DOI: 10.1002/jsfa.4025

President's Panel '09. [http://deainfo.nci.nih.gov/advisory/pcp/pcp08-09rpt/PCP\\_Report\\_08-09\\_508.pdf](http://deainfo.nci.nih.gov/advisory/pcp/pcp08-09rpt/PCP_Report_08-09_508.pdf)

Velimirov A, Huber M, Lauridsen C, Rembiałkowska E, Seidel K, Bügel S. **Feeding trials in organic food quality and health research.** *J Sci Food Agric.* 2010 Jan 30;90(2):175-82.

Accurso A, Bernstein RK, Dahlqvist A, Draznin B, Feinman RD, Fine EJ, Gleed A, Jacobs DB, Larson G and 15 others. **Dietary carbohydrate restriction in type 2 diabetes mellitus and metabolic syndrome: time for a critical appraisal.** *Nutr Metab (Lond).* 2008 Apr 8;5(1):9

Jakobsen MU, Dethlefsen C, Joensen AM, Stegger J, Tjønneland A, Schmidt EB, Overvad K. **Intake of carbohydrates compared with intake of saturated fatty acids and risk of myocardial infarction: importance of the glycemic index.** *Am J Clin Nutr.* 2010; 91:1764-8

Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. **Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease.** *Am J Clin Nutr.* 2010 Mar;91(3):535-46.

Volek JS, Feinman RD. **Carbohydrate restriction improves the features of Metabolic Syndrome. Metabolic Syndrome may be defined by the response to carbohydrate restriction.** *Nutr Metab (Lond).* 2005 Nov 16;2:31.

# Which carbs are the “good” carbs?

There are three kinds of carbohydrates in our foods.

Best known are the **digestible carbs** such as the sugars and starches. These are digested in the small bowel and broken down into simple sugars such as glucose and fructose.



Less familiar are the **fermentable carbs** such as inulin, which are not digested but pass intact into the large bowel where they are fermented, and broken down into fatty acids. Because they act as a fuel source for probiotic bacteria, these carbs are often known as **prebiotics**.

A third group of **structural carbs**, which we consume in much smaller amounts, includes such valuable compounds as the yeast-derived 1-3, 1-6 beta glucans. These and other structural carbs are absorbed intact into the body and exert a range of specific effects such as enhancement of immune function.

It is only the first category of digestible carbohydrates that impact on blood sugar levels, and it is only these that are linked to an increased risk of diabetic and cardio-vascular problems.

The fermentable carbohydrates, in marked contrast, are associated with improved health and life extension. According to a recent French study (sponsored by the excellent Belgian company Orafiti), rats fed on a diet

supplemented with prebiotics extended their average life-span by over 30% (Rozan et al '08). This was pretty much in line with the biochemical findings; the supplemented animals also had lower body weight, cholesterol and plasma triglycerides compared to rats fed the control diet. It is also a fair bet that these findings are relevant to humans; there is a plethora of literature indicating that a higher intake of prebiotic fibres is osteo-, cardio- and chemo-protective.

Even more persuasively, the idea that prebiotic carbohydrates are good for us because they are what we were 'designed' to eat fits the archaeological records. According to archaeologist Jeff Leach of the Paleobiotics Lab in New Mexico, "As our early ancestor moved from the rainforest to the parched savannah-woodlands of subtropical Africa, subsurface tubers, rhizomes, corms, and perennial bulbs, many rich in prebiotics, would have been a ready and important source of energy."

Studies have shown that inulin-rich plants dominated the dietary intake of our ancestors in many regions, with about 60 per cent of the calorific intake coming from such sources (Gibson et al '05). This would equate to a total dietary fibre intake of between 250 and 400 grams every day, with between 50 and 100 grams of inulin.

The modern, highly processed diet contains substantially less than 10 grams of prebiotic carbohydrates per day, and there is strong evidence that this is a major contributor to today's high incidence of bowel and liver cancer.

Is inulin a panacea? Hardly. I will just cite one paper at this point to point out, yet again, the importance of food combinations. A fascinating Japanese study has just showed that while the symptoms of the inflammatory bowel disease ulcerative colitis do not respond significantly to either prebiotics or probiotics, they do respond very positively to a combination of the two (Fujimori et al '09).

Fujimori S, Gudis K, Mitsui K, Seo T, Yonezawa M, Tanaka S, Tatsuguchi A, Sakamoto C. A randomized controlled trial on the efficacy of synbiotic versus probiotic or prebiotic treatment to improve the quality of life in patients with ulcerative colitis. *Nutrition*. 2009 May;25(5):520-5

Gibson G, Leach J, van Loo J. Inulin and other prebiotic fibers in the Paleolithic Diet. *Biosciences Microflora*, 2005, Vol. 25, pp. 1-8

Rozan P, Nejdi A, Hidalgo S, Bisson JF, Desor D, Messaoudi M. Effects of lifelong intervention with an oligofructose-enriched inulin in rats on general health and lifespan. *Br J Nutr*. 2008 Dec;100(6):1192-9.

## Putting inulin back into the food chain

Inulin, commonly extracted from Jerusalem artichokes or chicory root, is an inexpensive and versatile food ingredient which can be used to replace fats and sugars in a range of foods.

Recent German research has shown that inulin can be used to replace up to a quarter of the fat in processed meats such as sausages, reducing calories without affecting palatability (Nowak et al '10).

Similarly, a range of new and improved snack foods has just been developed at the University of Sao Paulo. Researchers here showed that it was possible to remove (unhealthy) trans fats from snack foods and replace them with inulin; an admirable substitution that had the highly desirable side effect of also reducing the snacks' glycemic index by 25% (Capriles et al '09) while leaving the taste and texture of the products unaffected.

This would be a convenient and cost-effective opportunity to improve public health. Large numbers of consumers will

not switch to salads, whatever health advisors say, but will stick to sausages and snack foods.

Don't, however, hold your breath. Unless made on a large scale, these advanced bangers and snack bars cost up to 30% more than standard products; and as the current regulatory system does not allow the manufacturers to talk about the health benefits of the improvements, they will not be available commercially any time soon.

Jerusalem artichokes



Capriles VD, Soares RAM, Silva MEM, Areas JAG. Effect of fructans-based fat replacer on chemical composition, starch digestibility and sensory acceptability of corn snacks. *Int J Food Sci Tech* Oct 2009; 44(10), 1895-1901

Nowak B, von Mueffling T, Grotheer J, Klein G, Watkinson B-M. Energy Content, Sensory Properties, and Microbiological Shelf Life of German Bologna-Type Sausages Produced with Citrate or Phosphate and with Inulin as Fat Replacer. *Journal of Food Science* (Nov-Dec 2007), 72(9): S629-S638

# Resveratrol - from grapes to apes?

Resveratrol, a fascinating compound found inter alia in grapes, red wine and peanuts, is a front-runner in the age extension stakes and as good an example of the health benefits of nutrition as you are likely to find anywhere.

A phytoalexin (plant defence compound) used by grapes and peanuts to ward off fungal attack, resveratrol first came to public attention when David Sinclair and his team from Harvard reported that resveratrol was able to increase the lifespan of yeast cells (Howitz et al '03).

Sinclair's group found that resveratrol could activate a gene called sirtuin1 (Sirt1 – the yeast equivalent was Sir2), which is also activated during calorie restriction in a number of species including monkeys. Since then studies in nematode worms, fruit flies, fish, and mice have linked resveratrol to longer lives.

Other studies with resveratrol have reported anti-cancer effects, anti-inflammatory effects, cardiovascular benefits, anti-diabetes potential, weight loss, energy endurance enhancement, HRT effects, eye health and protection against Alzheimer's.

Here are a few examples of recent resveratrol pre-clinical findings with their theoretical (and as yet unproven) health benefits:

**1. Resveratrol prevents the accumulation and multiplication of fat cells** (Fischer-Posovszky et al '10).

*Theoretical benefit:* May aid weight control, prevent obesity and Type 2 diabetes.

**2. Resveratrol stimulates the regeneration of cells that line healthy blood vessels** (Hamed et al '10).

*Theoretical benefit:* May prevent atherosclerosis and hypertension.

**3. Resveratrol improves blood flow to the brain** (Kennedy et al '10).

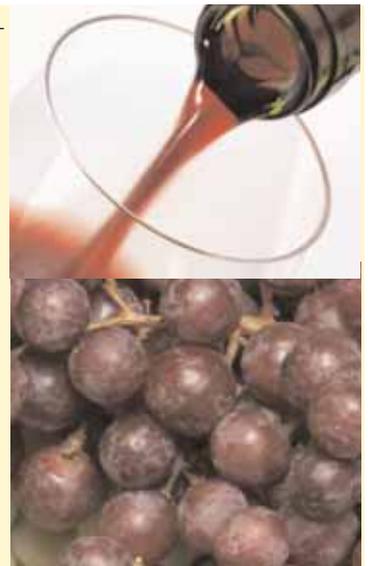
*Theoretical benefit:* May protect against dementia.

**4. Resveratrol is an alternative to HRT** which protects against breast cancer (Sakamoto et al '10).

*Theoretical benefit:* Safer HRT therapies.

**5. Resveratrol prevents formation of abnormal blood vessels in the retina** (Khan et al '10).

*Theoretical benefit:* May prevent loss of vision in diabetes and senior citizens.



So should we all be swallowing resveratrol pills? In my view this would be an unnecessary, expensive and unproven strategy. Despite all the promising pre-clinical work with resveratrol there have been very few clinical trials, so we don't really know much about the clinical effectiveness of this compound. In fact, a study of resveratrol carried out by Pfizer recently reported a negative result (Pacholec et al '10).

Nor do we know enough about safety; the supplements currently on the market offer doses of 30 to 150 mg, which are far in excess of dietary levels.

Resveratrol is not even unique. Similar molecules occur widely in the diet, such as the **curcuminoids** (derived from the spice turmeric), the **catechins** (in green and black tea), **quercetin** (in apples and onions), and **fisetin** (in mangoes); and all of these phyto-nutrients appear to have the ability to activate Sirt1 (Kang et al '08, Chung et al '10). The **flavonols** in cocoa probably have similar effects, and many more related compounds occur in a wide range of fruits, vegetables and other plant foods.

Sadly, this does nothing to support the government's inane 5-a-day propaganda, an approach so timid that while it confers slight cardiovascular benefits, it has hardly any impact on our terrible cancer statistics at all (Boffetta et al '10).

To achieve real protection from the degenerative diseases, the historical evidence shows that we would need considerably higher intakes of phytonutrients (Clayton & Rowbotham '09). These levels are so high that few would be able to obtain the recommended levels of phytonutrients from diet alone.

There is therefore a strong case for supplementation with broad spectrum phytonutrients, containing the appropriate levels of flavonoids and a range of other polyphenols.

Boffetta P, Couto E, Wichmann J and 48 others. **Fruit and vegetable intake and overall cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC).** J Natl Cancer Inst. 2010 Apr 21;102(8):529-37

Clayton P, Rowbotham J. **How the mid-Victorians worked, ate and died.** Int J Environ Res Public Health. 2009 Mar;6(3):1235-53

Chung S, Yao H, Caito S, Hwang JW, Arunachalam G, Rahman I. **Regulation of SIRT1 in cellular functions: Role of polyphenols.** Arch Biochem Biophys. 2010 May 5

de Boer VC, de Goffau MC, Arts IC, Hollman PC, Keijzer J. **SIRT1 stimulation by polyphenols is affected by their stability and metabolism.** Mech Ageing Dev. 2006 Jul;127(7):618-27.

Fischer-Posovszky P, Kukulus V, Tews D, Unterkircher T, Debatin K-M, Fulda S, Wabitsch M. **Resveratrol regulates human adipocyte number and function in a Sirt1-dependent manner.** Am J Clin Nutr 2010, 92, 5-15

Hamed S, Alshiek J, Aharon A, Brenner B, Roguin A. **Red wine consumption improves in vitro migration of endothelial progenitor cells in young, healthy individuals.** Am J Clin Nutr 2010, Volume 92, Pages 161-169

Howitz KT, Bitterman KJ, Cohen HY et al. **Small molecule activators of sirtuins extend Saccharomyces cerevisiae lifespan.** Nature. 2003 Sep 11;425(6954):191-6

Kang SK, Cha SH, Jeon HG. **Curcumin-induced histone hypoacetylation enhances caspase-3-dependent glioma cell death and neurogenesis of neural progenitor cells.** Stem Cells Dev. 2006 Apr;15(2):165-74.

Kennedy DO, Wightman EL, Reay JL, Lietz G, Okello EJ, Wilde A, Haskell CF. **Effects of resveratrol on cerebral blood flow variables and cognitive performance in humans: a double-blind, placebo-controlled, crossover investigation.** Am J Clin Nutr. Published online ahead of print, doi:10.3945/ajcn.2009.28641

Khan AA, Dace DS, Ryazanov AG, Kelly J, Apte RS. **Resveratrol regulates pathologic angiogenesis by a eukaryotic elongation factor-2 kinase-regulated pathway.** Am J Path July 2010, Volume 177, Pages 481-492

Pacholec M, Bleasdale JE et al. **SRT1720, SRT2183, SRT1460, and resveratrol are not direct activators of SIRT1.** J Biol Chem. 2010 Mar 12;285(11):8340-51

Sakamoto T, Horiguchi H, Oguma E, Kayama F. **Effects of diverse dietary phytoestrogens on cell growth, cell cycle and apoptosis in estrogen-receptor-positive breast cancer cells.** J Nut Biochem. Published online ahead of print: doi: 10.1016/j.jnutbio.2009.06.010

## That D'arned vitamin again

I probably talk too much about vitamin D, but here we go again. I am obsessional on this subject because of the stupidity of the regulators, who ban effective vitamin D supplements and insist on a RNI (Recommended Nutrient Intake) so low that it contributes to a flood-tide of unnecessary illness and death due to heart disease, cancer, auto-immune disease, infections and osteoporosis.

In fact, new research from Sunlight, Nutrition, and Health Research Center in San Francisco calculates that inadequate levels of vitamin D may be causing about 37,000 premature deaths in Canada every year, and costing the country 14 to 15 billion dollars (Grant et al '10). These results, if extrapolated to the UK, indicate that low vitamin D levels contribute to 75,000 premature British deaths per year; and conversely, that properly designed supplements could save over £200 billion in healthcare costs per year across the European Union!

According to the San Francisco team, "The results of this study strongly suggest that the personal and economic

burden of disease (in Canada) could be significantly reduced if the mean serum 25(OH)D level was increased from its current level of 67 nmol/L to the optimal level of 105nmol/L."

Osteoporosis Canada agrees. According to their most recent recommendations, published in the conservative Canadian Medical Association Journal (Hanley et al '10), adults under the age of 50 should be taking up to 1,000 International Units of vitamin D and people over 50 should be taking supplements up to 2,000 IU.

Will sanity break out? The Institute of Medicine (IOM) is conducting a review of vitamin D science and is due to deliver its findings this summer. Many expect the IOM to recommend RDIs significantly above the current levels of 400IU, and possibly as high as 2000 IU. The IOM may also revise upper safe levels (USLs) with some saying 10,000IU per day reflects the scientific literature. This would be a very cost-effective way of improving our mediocre public health.

Grant WB, Schwalfenberg GK, Genus SJ, Whiting SJ. An estimate of the economic burden and premature deaths due to vitamin D deficiency in Canada. *Molecular Nutrition & Food Research* 2010 March 29th. Published online ahead of print, doi: 10.1002/mnfr.200900420

Hanley DA, Cranney A, Jones G, Whiting SJ, Leslie WD, Cole DE, Atkinson SA, Josse RG, Feldman S, Kline GA, Rosen C. Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada. *CMAJ*. 2010 Jul 19

## The lethal peanut – update on the Hygiene Hypothesis

The reported rate of peanut allergy in children more than tripled from 1997 to 2008, according to a recent survey (Sicherer et al '10). Researchers in the US conducted telephone interviews with 5,300 households during 2008, representing 13,534 individuals.

They found that 1.4 percent of children were reported to have peanut allergies, compared to 0.4 percent in 1997. And 2.4 percent of children were reported to have peanut and/or tree nut allergies in 2008, compared to 0.6 percent in 1997. Lead researcher Scott Sicherer said: "There is an alarming increase in peanut allergies, consistent with a general, although less dramatic, rise in food allergies among children in studies reported by the CDC."

The researchers cautioned that their study had limitations due to its self-reported nature, but pointed out that their findings were consistent with those from other countries that used different methods, including Canada, Australia and the United Kingdom. They suggested that the increase in allergies was due to the old idea that our home environments have become cleaner, leading to weaker immune systems as we are exposed to fewer germs.

The old 'Hygiene Hypothesis', however, is being replaced by more specific models of allergy. These models focus on two agents that have been removed from our diet, due to changes in food technology and the progressive sterilisation of the food chain. These two agents are **intestinal worms** and **yeasts**.

Both have a very specific impact on the innate immune system, directing it to increase the ratio of TH1 to TH2 cells

in the adaptive immune system (ie Baran et al '07). A high TH1 / TH2 ratio protects against allergy; a low TH1 / TH2 ratio facilitates it. Removing yeast and worms from our diet has lowered the TH1 / TH2 ratio, and made us very much more prone to allergy.

The remedy is obvious; to reduce the flood-tide of allergy we must put either worms, or yeast, back into the food chain. Most people would prefer yeast! Or at least, the purified extracts of yeast such as Wellmune (as in ImmunoShield) that have been shown to enhance immune function in a number of trials (ie Biothera '10).

Peanuts



Baran J, Allendorf DJ, Hong F, Ross GD. Oral beta-glucan adjuvant therapy converts nonprotective Th2 response to protective Th1 cell-mediated immune response in mammary tumor-bearing mice. *Folia Histochem Cytobiol*. 2007;45(2):107

Biothera '10. [http://www.biotherapharma.com/healthcare/Exp\\_Biology\\_2010.htm](http://www.biotherapharma.com/healthcare/Exp_Biology_2010.htm)

Sicherer SH, Muñoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. [http://www.jacionline.org/article/S0091-6749\(10\)00575-0/abstract](http://www.jacionline.org/article/S0091-6749(10)00575-0/abstract)

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