dr paul clayton's Health Newsletter

Autumn 2007

The D edition

D is for Disease

I wrote about 'vitamin' D back in the spring and summer, but fascinating and important new research continues to be published. I have been specifically requested by a number of you to re-visit the subject, and now that the days are getting shorter, and we are all becoming more depleted in this vital compound – here we go again.

Starting with D facts …

D is not a vitamin at all!

'Vitamin' D is not a vitamin. Sorry to re-state the blindingly obvious, but the Definition of a vitamin is a compound that is needed in small amounts by the body to maintain good health, cannot be made in the body, and must therefore be obtained from the Diet.

D is certainly essential for good health, but it is made in the body when skin is exposed to sunlight, and it is not present in very many foods. Liver is a good source generally, but although cod liver is the one food that people quote – and rightly so, since it is one of the richest sources of D – it is not one that many eat, other than those masochists who entertain themselves by Drinking cod liver oil.

Depletion and Deficiency

Most people living in the temperate zones are Depleted or Deficient in D, conditions known collectively as hypo-vitaminosis D. As the temperate zones include central and northern Europe, the former Soviet Union, Japan, the northern half of China, the southern half of South America and most of North America above the Mason-Dixon Line, that's a lot of people!

Osteoporosis, one of the Diseases linked to D-insufficiency, affects more than 75 million in the EU, Japan and North America alone.

On a global scale, the number of people whose health is Damaged by a lack of D is probably well over 250 million, making D-related Disease one of the most important causes of ill health and Death today.

It seems absurd that so many should be suffering from a simple lack of sunlight, but we Don't spend as much time in the fresh air as we used to, and are 'Designed' to Do. Our indoor lifestyles, and the thoroughly misguided and counter-productive government campaigns to avoid exposure to sunlight, are killing us.

Disease risks

D Depletion and Deficiency are strongly linked to an increased risk not only of osteoporosis, but also to autism, allergy, Type 2 Diabetes, end-stage renal Disease, a range of cancers including some skin cancers, and autoimmune Diseases such as multiple sclerosis.

This substantial list of problems could easily be avoided if people were advised to take adequate Daily Doses of D, or if more foods were fortified with D. Which brings us to the next problem.

Daily intake values too low

The recommended Daily intake values for D have been Distorted by the profoundly wrong concept of D as a vitamin, and are far too low to protect us from Disease.

The D experts are clamouring for D intake levels to be raised, but for many years now their efforts have been stifled by bureaucratic inertia. As a Direct result, millions of people are suffering unnecessary ill health. Regulatory folk have long cited safety concerns as the main reason we should not increase the recommended Daily values, but …

D is extremely safe

Previous safety values (again, distorted by the false concept of D as a vitamin) are completely and Disastrously wrong; huge Doses of D can be safely taken by almost everyone, and we would all be healthier if we increased our intakes of D ten-fold or more.

In fact, widespread D-fortification of food would probably be one of the single most cost-effective ways of improving public health.

As this would cut Deeply into the profits of the pharmaceutical industry, one has to wonder if the huge sums of money Big Pharma spends lobbying in Brussels, Washington and elsewhere hasn't had some impact on the current sorry state of affairs.

So much for scare headlines and the reckless use of **bold fonts**; now for the science.

In the following sections doses of D are given in micrograms (mcg), rather than the more old-fashioned International Units (IU). For the more nostalgic reader, 1 mcg = 40 IU.

D - Definitions

'Vitamin' D refers to two biologically inactive precursors. These are D3, also known as cholecalciferol, and D2, also known as ergocalciferol. D3 is produced in the skin on exposure to UVB radiation, and is considered to be more bioactive. D2 is originally derived from plants and only enters the body via the diet, from consumption of foods such as oily fish, egg yolk and liver.

D3 and D2 are metabolised in the liver and kidneys to produce 1,25-dihydroxyvitamin D [1,25(OH)2D], the biologically active form.

Hypo-vitaminosis D

As I pointed out previously, the current UK RNI of 7mcg, and the 'tolerable upper limit' of 50 micrograms are both grotesquely inadequate. You make 250 mcg in your own skin by spending half an hour in the sun – and this happens, unsurprisingly, to be the new dose level recommended by the real D experts.

In a recent and important paper, reviewers from the Council for Responsible Nutrition, Mount Sinai Hospital in Toronto and Creighton University in Nebraska, pooled data from 21 clinical trials with vitamin D3 using doses ranging from 10 to 2500 mcg (Hathcock et al '07). This large meta-analysis showed conclusively that doses of 250 mcg are safe and probably effective at reducing the risk of a large number of disease conditions.

Unfortunately, due to our currently meaningless RNI values, hardly anyone is able to get the amount of D they really need. According to the paper's authors, "Unfortified foods, fortified foods, and most dietary supplements, combined, do not contribute to a total exposure anywhere near the recommended vitamin D Upper Limit of 250 mcg per day."

Other scientists who have examined D status in various populations support this damning verdict. In one typical recent paper, researchers measured blood levels of vitamin D in 382 healthy children between six years and 21 years of age living in the northeastern U.S.A (Weng et al '07). After measuring the intake of vitamin D from diet and supplements and evaluating blood levels of vitamin D, the researchers found that 55 per cent of the children had inadequate vitamin D blood levels with the proportion increasing to 68 per cent in winter. Among Afro-American children, whose darker skins impede D synthesis, over 90% were deficient in D.

A study from Britain last year reported almost identical results, suggesting that over 70 per cent of seemingly healthy teenage girls might be vitamin D deficient (Das et al '06); and elderly populations are, if anything, even worse off (Vaqueiro et al '07).

The findings of widespread hypo-vitaminosis D in young children are alarming, as this is the period in people's lives when the little darlings / oiks (*select one*) should be building their bones. A lack of D at this stage means that they are unlikely ever to achieve optimal bone mineral density, and when they reach old age they will be much more vulnerable to osteoporosis.

D-deficiency in the elderly means that the already low peak bone mass will fall below the fracture level even more quickly. The combination of low D during both adolescence and old age means that the current pandemic of osteoporosis can only get worse.

But there is much more to lack of D than fragile bones …

D and Autism

The links between poor D status and disease have just been extended by a provocative paper which makes a persuasive case that lack of D may be behind the huge increases in autism. John Cannell, a psychiatrist at the Atascadero State Hospital in California, says it better than I can (Cannell '07) – so here he is:

"Any theory of autism must take into account its strong genetic basis and its striking epidemiology. The apparent increase in the prevalence of autism over the last 20 years corresponds with increasing medical advice to avoid the sun, advice that has probably lowered levels of activated vitamin D (calcitriol) in developing brains. In animals, severe vitamin D deficiency during gestation dysregulates dozens of proteins involved in infant brain development, increases inflammatory markers in the brain and causes increased brain size and enlarged ventricles, all abnormalities similar to those found in autistic children. Conversely, consumption of vitamin D containing fish during pregnancy reduces autistic symptoms in offspring.

"Autism is more common where there are low levels of UV-B such as the high latitudes, urban areas, areas with high air pollution and cloud cover. Autism is more common in dark-skinned persons and severe maternal vitamin D deficiency is exceptionally common in this group. Estrogen and testosterone have very different effects on calcitriol metabolism, and this could explain the striking male/female sex ratios in autism.

"Finally, children with vitamin-D-deficient rickets show autistic signs that apparently disappear with high-dose vitamin D treatment."

Cannell concludes from this that genetic factors similar to those studied by the Harvard group, plus gestational and early childhood D deficiency, may explain the epidemiology of autism. If so, he says, much of the disease is iatrogenic, brought on by medical advice to avoid the sun; and therefore could be avoided by D supplementation during pregnancy and in infant formula.

D and allergy

Another paper from Harvard Medical School, who are clearly very interested in D at the moment, links low D levels to the explosion in asthma that has occurred over the last 40 years (Litonjua & Weiss '07).

The scientists had already found that higher D intakes in pregnant women reduced asthma risk in young children by as much as 40%, and hypothesised that the increases in asthma are due to reduced sun exposure.

Specifically, they suggested that our increasingly indoor lifestyles have led to reduced D levels, that reduced D levels in pregnant women have impaired the development of normal lung and immune function in infants, and that this has driven the increase in asthma and allergy.

In support of their hypothesis, they point out that D deficiency is particularly common in the obese, in the African American community (particularly in urban and inner-city settings), and recent immigrants to westernized countries; and these are precisely the groups with the highest incidence of childhood asthma.

Like so many of the other scientists whose work is reviewed in this issue of the newsletter, Litonjua and Weiss recommend D supplementation; particularly in pregnancy.

D and Cancer

D has a number of important anti-cancer properties. Acting via the vitamin D receptor (VDR), it inhibits the in vitro proliferation of cancer cells, and induces differentiation and apoptosis. This means that people with superior D status should be protected against cancer, and over the years many studies have indeed found a relationship between latitude and cancer risk, showing that populations with greater exposure to sunlight have a reduced risk of disease. This relationship has been shown for prostate, breast, ovarian and colorectal cancer, but causality has never been proven until very recently, in an American intervention study of the protective effects of vitamin D. I cited this paper in July, but it is so important that I make no apology for repeating it.

The researchers found that post-menopausal women who took large amounts of vitamin D3 were 60 to 77 per cent less likely to develop cancer than a control group (Lappe et al '07). The trial group supplemented their diet for four years with a mere 30 mcg of vitamin D3 per day. This is about 4 times the current recommended daily dose, but still less than the amount you would make on a sunny day. The women were free of known cancers for at least 10 years prior to entering the study; but as some might have entered with undiagnosed cancers, researchers eliminated the first-year results and singled out the last three years of the 4-year period. Now the vitamin D group showed a 77 per cent cancer-risk reduction compared to the non-supplementers.

At almost the same time, a second group at the Samuel Lunenfeld Research Institute in Ontario (another area with high rates of hypo-vitaminosis D) published a very interesting paper which suggested that it is during childhood that sunshine is most protective (Knight et al '07).

The researchers recruited 972 women with newly diagnosed invasive breast cancer and 1,135 randomly selected healthy controls and interviewed them to assess their overall D status, measuring variables such as sunlight exposure (outdoor activity), cod liver oil intake and milk consumption. After adjusting for potential confounding factors, the results indicated that increased exposure to sunlight during adolescence was associated with the highest protection against breast cancer risk later in life, with a risk reduction of 35 per cent. Similar exposures later in life (age 20 – 29) were associated with smaller risk reductions, while no protective effects from vitamin D sources were observed for age 45 – 54.

The researchers concluded that while their results supported the hypothesis that D reduces the risk of breast cancer, its main effects might be exerted early in life, during the period of breast development.

Breast and prostate cancers have a good deal in common, and a third team at Harvard Medical School have just published the results of a fascinating and very productive study on the connections between D levels, genetics, and the risk of prostate cancer (Li et al '07). This was a very complex paper, so I will just summarise its three main findings.

The first of these was that a large proportion of US men have sub-optimal D status (especially during the winter/spring season), and the second was that D plasma levels probably play an important role in preventing prostate cancer progression. But it is the third finding that starts to fit many of the pieces of the jigsaw together, namely the D–gene connection.

There are a number of variants of the 'vitamin' D receptor (VDR), and some of these are less effective than others. Three variants relate to the Fok1 genes; individuals may be Fok1-FF, Fok1-Ff, or Fok1-ff. FF denotes a receptor that is very easily activated by D, Ff is less active, while ff is the least active of all and had already been linked to an increased risk of prostate cancer (Mishra et al '05).

The Harvard team found that in individuals with FF and Ff gene combinations and good D levels, the risks of prostate cancer were significantly lower than in men with ff genes and poor D levels. Improved D status seems to be generally protective, but this study indicates that men with the ff genes should take particular care to sunbathe or to take D supplements.

The ff gene set occurs in 14% of Caucasians, and accounts for a considerable number of at-risk males; but as very few men know their genetic makeup it would seem advisable for all men to increase their D intake. As dark-skinned people generally have lower D status, this helps to explain why Afro-Caribbean men have a significantly higher degree of risk of prostate cancer than white men (Jack et al '07), and why they should be particularly keen on D supplements.

Clearly more work needs to be done on the D–cancer connection, and one study has just been announced which should provide additional answers by 2011 (Trump et al '07).

D and Diabetes

There is quite good evidence that the risk of children developing Type 1 diabetes, which is an auto-immune condition, is increased if their mothers were low in D during the pregnancy (Littorin et al '06).

Now a new meta-analysis has discovered a possible link with Type 2 diabetes also, as supplementation with D and calcium appears to improve blood sugar and insulin levels (Pittas et al '07).

The data showed a relatively consistent association between low intakes of calcium, vitamin D, or dairy foods with Type 2 diabetes. The highest levels of intake were associated with a 64 per cent lower prevalence of diabetes, and a 29 per cent lower incidence of metabolic syndrome (a 'pre-diabetic' condition) among non-blacks.

Although the ways in which D and/or calcium might affect insulin and glucose metabolism are unclear, the authors concluded that combined vitamin D and calcium supplementation might have a role in the prevention of Type 2 diabetes in populations at high risk such as those with glucose intolerance.

If this analysis is borne out by subsequent research, the Pittas paper will prove to be a very important one, as Type 2 diabetes is a huge and growing problem, and the costs of D and calcium supplementation are minimal.

The **Paul Clayton** Newsletter is published quarterly and describes developments in the new field of pharmaco-nutrition – a field 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.

D and Multiple Sclerosis

Yet another Harvard team reports that higher levels of vitamin D may reduce the risk of developing the auto-immune disease multiple sclerosis by as much as 62 per cent (Munger et al '06). This pretty much fits other data which show that D is important in regulating not only the immune system, but specifically that part of the immune system that is about self-recognition.

The researchers report that the main protective effects were observed for people of white ethnicity. When serum vitamin D levels were classified into five groups ranging from lowest to highest, the risk of MS for whites in the highest group was 62 per cent less than for those in the lowest.

Serum D levels were not linked to any effect on MS risk for African Americans and Hispanics, but these groups had significantly lower levels of D than the whites, and the sample sizes were probably too small to detect any trends.

D and Muscle Strength in the Elderly

The last item in our D roundup concerns muscle strength, an important factor in later life as it determines mobility and is strongly linked to well-being and improved survival. There are a number of previous studies linking poor D status to impaired muscle strength; and here too, a new paper (Inderjeeth et al '07) suggests that a lack of D might indeed lead to loss of muscle tone.

It is obvious that hypo-vitaminosis D is responsible for a host of problems, but I am somewhat unconvinced by this one. After all, the fitter and stronger types are the ones who are taking the most exercise, and (probably) getting out the most. So here, it may be that those who are already weak and ill, and getting less sunshine as a result, are producing a false finding. We await further studies!

D and Dialysis

A number of studies have found that D supplementation reduces mortality in end-stage renal disease patients on dialysis. A new paper from Harvard (yet again) has shown that D deficiency is common in dialysis patients, and that the worse the D status the more likely the patient was to die (Wolf et al '07). D supplementation was a highly cost-effective way of reducing mortality, a strategy welcomed by other renal specialists (Al-Aly '07).

D - Safe as Houses

Additional data regarding the true safe upper limit of D can be derived from clinical studies in which high doses were used therapeutically, and without toxicity. For example, the medical condition of hyperparathyroidism has been successfully managed with 1250 to 5000 mcg of D daily (Woodhead et al '80), while rickets may require a daily dosage from 1250 to as much as 7,500 mcg in resistant cases (Eguchi & Kaibara '80).

In one of the best documented clinical cases of D toxicity, a man who took 3,900 to 65,100 mcg of cholecalciferol a day for two years recovered uneventfully after the proper diagnosis, treatment with steroids and sunscreen (Koutkia et al '01). This case demonstrates the extraordinarily high therapeutic index of vitamin D, as the dose ingested over the two-year period is 80 to 13,000 times the current RDA. To put this in perspective, aspirin, one of the pharmaceutical products deemed safe enough to be sold openly, is lethal at 25 to 30 times the therapeutic dose; and even at therapeutic doses kills significant numbers of people by causing gastric bleeding (Lanas et al '05, Cryer '05).

D should be used cautiously in certain medical conditions including primary hyperparathyroidism, sarcoidosis, tuberculosis, kidney disease and lymphoma, as sufferers may develop hypercalcemia in response to any increase in D. They should seek medical advice, as should patients taking digitalis, calcium channel-blockers or thiazide diuretics, before and while taking extra D.

We should keep the D story in perspective. D experts are unanimous – the real health problems related to D are to do with the many millions of people who are not getting enough of it!

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