METABOLIC SYNDROME, OBESITY AND VITAMIN D DEFICIENCY

FUNDAMENTAL METABOLIC LINK RECENTLY DISCOVERED

The first article mentioning such a link has been published in May 2004 by the *American Journal of Clinical Nutrition* (Chiu, et al. 2004). The study had enrolled 126 healthy, glucose-tolerant subjects and results have shown that **25-hydroxy-vitamin D** levels were positively correlated with ***insulin sensitivity*** index, leading to the following conclusion: "Subjects with hypovitaminosis D are at higher risk of ***insulin resistance*** and the ***metabolic syndrome***" (Chiu, et al. 2004). Data have quickly started to accumulate soon after. An article published in May 2005 by the *European Journal of Clinical Investigation* tells us how clinical trials and observational studies demonstrate that **calcium** and **vitamin D** deficiencies increase the risk of malignancies, of chronic inflammatory and autoimmune diseases, and of metabolic disorders such as ***hypertension*** and ***metabolic syndrome*** (Peterlik and Cross 2005). Compared to the traditional vitamin D functions in bone health and in mineral fixation, a much more widespread role has been attributed to **vitamin D** as early as in 2006, due to the identification of vitamin D receptors in plenty of other tissues (Martini and Wood 2006).

Since 2007, multiple articles have flourished about **vitamin D** deficiency, ***metabolic syndrome***, ***obesity,*** and ***diabetes*** type 2. **Vitamin D** and **calcium** insufficiency may negatively influence ***glycemia*** (Pittas, et al. 2007). **25-hydroxy-vitamin D** level is inversely associated with 10-year risk of ***hyperglycemia***, with ***insulin resistance***, and with ***metabolic syndrome*** (Forouhi, et al. 2008). Low-circulating **vitamin D** concentrations may be associated with an increased prevalence of ***metabolic syndrome*** (Reis, et al. 2007). This last study also suggests a link between an increased risk of ***metabolic syndrome*** and elevated **parathormone** levels in older men, knowing that parathormone levels generally provide the mirror image of vitamin D levels as this is how the body tries to deal with the resulting lack of **calcium** (Reis, et al. 2007).

A specific study has been carried out in 2007 to evaluate the increased prevalence of vitamin D deficiency among morbidly obese patients (body mass index of 40+). It shows that 61 % of morbidly obese patients presenting a ***metabolic syndrome*** suffer from **vitamin D** deficiency compared to 33 % of those who did not achieve the criteria for metabolic syndrome (Botella-Carretero, et al. 2007). Another study published in 2007 concerned 217 obese children where 25-hydroxy-vitamin D levels correlated negatively with ***body mass index***; more than half of the obese children were **vitamin D** insufficient and almost half of the insufficient group suffered from severely low **vitamin D** levels (≤ 10 ng/ml) (Smotkin-Tangorra, et al. 2007). In February 2008, a huge epidemiological study collected from 6,810 British subjects aged 45 has shown an inverse association between **vitamin D** levels and ***metabolic syndrome*** (Hypponen, et al. 2008).

Identical findings have been published in July 2009 among 3262 middle-aged and elderly (50-70) Chinese individuals: low **vitamin D** levels are significantly associated with ***metabolic syndrome*** or ***insulin resistance*** (Lu, et al. 2009). In February 2010, another survey performed among 324 middle-aged Korean subjects led to exactly the same conclusions, i.e. a strong inverse association of serum **vitamin D** levels with both ***metabolic syndrome*** and ***hypertension*** (Kim, et al. 2010). In June 2010, a new study has provided the same conclusions after measuring the **25-OH vitamin D** level in 542 Arab Americans where insufficiency is associated with ***metabolic syndrome*** and ***insulin resistance*** (Pinelli, et al. 2010).

Taking into account the emerging role of vitamin D in glucose homeostasis and insulin release, we cannot be surprised by the accumulation of "observational data strongly support[ing] the role of **vitamin D** deficiency in the pathogenesis of ***type 2 diabetes***" (Chowdhury, et al. 2009). Therefore, as the relationship may be mediated at least partially through incident ***diabetes type 2***, low serum concentrations of **vitamin D** have been associated with increased risk for ***cardiac events*** (Penckofer, et al. 2008). According a publication issued in January 2009, prospective cohort studies suggest that **25-OH-vitamin D** deficiency is associated with ***cardiovascular diseases*** and with ***mortality*** over follow-up (Michos 2009).

This has been confirmed through another study published in April 2009 by the *Saudi Medical Journal* and conducted on 119 type 2 diabetic patients from Iran, showing a strong link between **vitamin D** deficiency and high ***body mass index*** ($p = 0.003$), ***metabolic syndrome*** ($p = 0.05$), and increased ***highly sensitive C-reactive protein*** ($p = 0.009$) (Bonakdaran and Varasteh 2009). Linking further on **vitamin D** levels and cardiovascular disease, a study has been published in July 2010 showing the positive association between **vitamin D** (as well as **parathormone**) disruption and ***carotid intima-media thickness*** (as well as ***metabolic syndrome*** prevalence) (Richart, et al. 2010). In a meta-analysis published in March 2010, ten observational studies and nine randomized control trials concerned with the association between vitamin D levels and blood pressure have been identified; eight observational studies and three randomized control trials supported an inverse association between **vitamin D** and ***blood pressure***, which shows the need for more research (Feneis and Arora 2010).

As **vitamin D** deficiency appears to be highly prevalent and because of the purported links with ***diabetes*** as well as with ***cardiovascular disease***, correcting **vitamin D** levels in order to prevent and even treat ***diabetes*** represents a "promising field to explore" (Baz-Hecht and Goldfine 2010). Already a few clinical trials suggest beneficial impact of vitamin D supplementation in prediabetes, such as improved insulin secretion and sensitivity, but most of these studies present significant limitations and it is still a little bit too early to provide evidence-based recommendations (Barengolts 2010).

Some authors even suggest that it would be possible to reverse the increasing epidemics of ***obesity*** by improving the **vitamin D** status as they consider that ***metabolic syndrome*** represents the expression of a "winter metabolism" leading to the accumulation of fat mass, certainly an interesting concept of human hibernation (Foss 2009). A meta-analysis published in March 2010 has shown that high levels of vitamin D among middle-age and elderly populations are strongly associated with significant decreases in cardiovascular disease, in type 2 diabetes and in metabolic syndrome (Parker, et al. 2010). If that relationship proved to be causal, treating those populations with vitamin D has a tremendous potential.

A Chinese team has recently found that supplementing ***1,25-dihydroxy-vitamin D*** improved the **insulin resistance** in muscle cells, but of course these conclusions only apply *in vitro*, at least for the moment (Zhou, et al. 2008). Despite the limitations of our current knowledge, we can only agree with this article published in May 2010: "increasing evidence suggests that the provision of a simple, well-tolerated, and inexpensive correction of vitamin D insufficiency favorably affects the morbidity and mortality of cardiovascular disease along with the prevention of the most common chronic degenerative diseases" (Mascitelli, et al. 2010). Indeed, some data already support a possible role of **vitamin D** insufficiency in ***Parkinson disease*** (Evatt, et al. 2008). We therefore agree with Penckofer's title: "*Let the sunshine in*"!

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