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Vitamin D – the cure for autoimmune diseases?

Multiple Sclerosis is treatable. Dr Coimbra and his local team of assistant doctors have successfully treated thousands of patients with multiple sclerosis, in many cases reaching a complete resolution of both symptoms and clinical parameters. His therapy essentially relies on one agent: high-dose Vitamin D. The effects are as dramatic as practically blind beginning to see again and people leaving their wheel chairs, provided that does not take too long before the treatment begins. We talked to him about the critical role of Vitamin D in autoimmune diseases.

Dr. Coimbra, how did you get the idea to use Vitamin D on MS and other Autoimmune Diseases?

I did research using laboratory rats to create models of neurological illnesses, with the objective to test new diagnostic possibilities. In this process I found an enormous quantity of published research that has been consistently neglected in medical textbooks and I asked myself why this information had not been applied in clinical practice – as sometimes it has to do with indeed preventively and therapeutically important and basic information. Slowly I became personally convinced that a large number of patients would really benefit from many things that are not discussed at medical conventions and in textbooks simply because they could reduce the consumption of costly pharmaceuticals. At a certain point I was convinced that Vitamin D stimulated the production of neuroregenerative substances in the brain of adults, children, fetuses and embryos, and that Vitamin D is extremely important for the development, function, preservation and regeneration of the nervous system, as well as for the regulation and strengthening of the immune system, among a large variety of fundamental functions for general human health.
This knowledge is still not available in medical texts and the majority of doctors do not know the importance of the Vitamin-D-hormone today. So we began, to administer Vitamin D3 to those that had neurodegenerative illnesses. First I became interested in Parkinson's patients and began to give them Vitamin D3 in physiologically realistic doses.

What do you mean by “physiologically realistic”?

The daily dose that is recommended today, internationally, it's a paltry dose, much below the physiological dose. The physiological dose has been recently recognized to be minimally 7,000 IU daily for adults with normal body mass index, the same amount that one produces in just 10 to 20 minutes of exposure to the sun, depending on the extent of exposed body surface, body position (basking or standing), skin pigmentation, skin age and sun positioning (which changes the amount of UVB – the vitamin D-producing radiation). Sunscreen blocks the body's ability to produce vitamin D, and its use should be delayed until enough vitamin D has been generated. So 10,000 is also a physiological dose, not a super dose. However, most doctors consider this dose potentially toxic. Today the recommended dose is still 600 international units despite being the result of a miscalculation. So, 600 international units are recommended but if a person is exposed to the sun for just 20 minutes, he / she may easily produce 10,000 IU! This is an evident difference between medical practice and up-to-date scientific knowledge.

So, we began to give 10,000 IU to those with neurodegenerative illnesses. One day a Parkinson's disease patient who received 10,000 IU of Vitamin D returned for his second visit, after 3 months of taking 10,000 IU every day and this patient had a vitiligo lesion on his face that had diminished a lot in just a few months of administering 10,000 IU/d. This made me search for information in the medical literature in relation to the effects of Vitamin D on the immune system. I was surprised by the enormous quantity of publications that were already available in 2001-2002.
In line with this first result, I began to give 10,000 IU/d of Vitamin D to patients with multiple sclerosis, which is a major and most common autoimmune illness in neurology, and also the one that has the most devastating effects. That initial daily dose was also given to patients with other autoimmune diseases like psoriasis, lupus, rheumatoid arthritis, etc. We were amazed to see how much better these patients got, although they were not completely disease free. This was the point of departure: the recognition of the great value of Vitamin D in the treatment of autoimmune disorders.

Why does Vitamin D help in autoimmune diseases?

Vitamin D is the largest regulator of activity in the immune system and modifies the functioning of thousands of genes in every cell of the immune system. It's a substance that has no peer.
I'll make a comparison to explain what I mean by saying that so many genes that are regulated in their activity by vitamin D: Imagine a skyscraper with many rooms. Imagine that thousands of doors inside this skyscraper can be locked and unlocked by only one key. So you can compare the skyscraper with every cell of the immune system and imagine that the key is vitamin D.
When there is a deficiency of vitamin D, the sick person can't regulate, which means stimulate or reduce, the activity of thousands of biological functions inside the cells of the immune system - the deficiency of this one substance amounts to a disaster for the immune system! People with vitamin deficiency are vulnerable to several disabling autoimmune disorders like multiple sclerosis, autoimmune polyneuropathy, Guillain-Barré, rheumatoid arthritis, psoriatic arthritis (and psoriasis itself), myasthenia gravis, polymositis and systemic lupus erythematosus – to name only a few.

What exactly does Vitamin D do in the immune system?

Vitamin is a modulator, an immunomodulatory substance, it does not suppress the activity of the immune system in general but it modulates it. And we know that vitamin D suppresses specifically the type of immunological reaction that provokes autoimmune diseases. It is known as "Th17". Virtually all autoimmune diseases are caused by such an aberrant reaction that is not normal, not physiological. Vitamin D is the only substance, for what I know, that is able to selectively inhibit this response, without undermining the other reactions of the immune system. More than this, vitamin D even strengthens the capacity of the immune system to react against viruses, bacteria and other microorganisms. The world pandemic of Vitamin D deficiency synergistically associates with the multiscale mobility networks to enhance the spreading of life threatening infectious diseases like tuberculosis. Tuberculosis is nowadays killing 4,000 people per day worldwide – while Mycobacterium tuberculosis becomes uncontrollably resistant to multiple-drug therapy, as well as to materno-fetal transmission of HIV. Meanwhile, the governments, health systems and international medical community have underestimated the consequences of the world pandemic of vitamin D, leading to avoidable huge and growing annual expenses in health and disability care systems.

The Th17 reaction is caused by overproduction of an "immune messenger" (cytokine) called "interleukin 17". Production of interleukin 17 is a natural phenomenon and is beneficial in adequate, regulated amounts. However, overproduction of interleukin 17 is not a natural phenomenon. And Vitamin D regulates this interleukin 17 production.
So autoimmune diseases are the result of a dysregulated immune system that produces an aberrant immunological Th17 reaction. And Vitamin D is the substance needed to regulate the immune system.

And how does this TH17-reaction get out of hand? Through Vitamin D deficiency?

Patients with autoimmune disorders have a genetically inherited resistance against the effects of Vitamin D. This resistance affects the immunomodulatory actions of vitamin D, and is a partial, not a complete, resistance. Due to this resistance these people are predisposed to develop autoimmune disorders.

The exact mechanism of this resistance is not clear yet. There are various diseases linked to genetic mutations in the vitamin D receptor, making these people resistant to vitamin D. The resistance may also be due to an alteration of the enzymes dealing with the conversion and activation of vitamin D, which are two hydroxylases. So there are many different possibilities: an alteration of the first hydroxylase, of the second hydroxylase, an alteration of the vitamin D receptor itself, and a genetic alteration of the protein that captures vitamin D and carries it along into the bloodstream.
All these genetic alterations may explain the individual resistance to vitamin D and an individual may even suffer from two or three of these issues contributing to his / her resistance to the effects of vitamin D. This is not just a hypothesis: polymorphic changes in one of the two vitamin D hydroxylases (particularly 1-alpha-hydroxylase), or in vitamin D receptor, or in DBP (vitamin D Binding Protein) have been identified and reported in association with autoimmunity.

The effect of such genetically altered vitamin D metabolism on several diseases - not only autoimmune disorders – has been worsened in recent years, possibly due to avoidance of sunlight

exposure and overuse of sunscreens, and prevalence of autoimmune disorders has been increasing.

And what determines which kind of autoimmune disease a patient develops out of this resistance?

Several factors may drive the autoimmune response preferentially against a particular tissue, organ or system. One factor is the inherited features of the immune system, like the major histocompatibility system, the so-called "HLA genotype". Another factor could be infection diseases that challenge the immune system in different ways.

So does Vitamin D resistance inevitably lead to autoimmune disorders?

Some carry this genetic predisposition to autoimmune disorders but do not develop - or have not yet developed - autoimmunity. We believe that something else is necessary in addition to that genetic predisposition to trigger those diseases. The most consistent, I would even say probably ubiquitous triggering factor in relapsing remitting MS, since we have found almost no exceptions among thousands of patients with autoimmune diseases, is a stressful life event, or a prolonged stressful period – for instance, related to professional or familiar environment. It seems to work very similar in most autoimmune disorders.

I am strongly convinced that the increase in autoimmune disease prevalence mainly depends upon three factors: Firstly, the inherited, partial resistance to the biological effects of vitamin D. Secondly vitamin D deficiency, caused by poor exposure to the sun. And thirdly an emotional factor, a triggering factor that leads to the activation of autoimmune diseases in people having the other two predisposing factors. We are not excluding that other factors may also play a role in the process, but even if these factors may actually be contributing to the development of autoimmune diseases, the role they play is a minor one compared to the physiopathologic importance of vitamin D.

After your initial success you developed a fairly simple protocol over the years to treat practically all autoimmune disorders, with mind-blowing result. How does that protocol work?

The treatment basically consists of only one element: Vitamin D3. We need to give very elevated doses of Vitamin D3 to get complete control of the illness. These doses are not equal for all patients; they are specific to each patient and are adjusted to the level of resistance that the patient shows in relation to the effects of vitamin D. We have developed a method to adjust the daily individual doses for each patient, which is done through lab tests. The magnitude of resistance can be evaluated by measuring Parathyroid hormone (PTH).

Why PTH?

Vitamin D inhibition of PTH expression within the cells of the parathyroid gland is one of its biological effects and a good marker as it is one of the ultimate results after a long chain of biological events that include 2 consecutive hydroxylations, serum transportation by DBP and finally VDR activation. So we use the final effect of this chain, which is a reduction in the levels of the parathyroid hormone. It's a way to avoid having to check what actually is the reason for this resistance. It doesn't matter if the reason is this, or that, or if there are multiple concurrent reasons for the resistance to vitamin D. By measuring decrease of the parathyroid hormone levels, we see the final biological effect of all possible causes of resistance to vitamin D acting together. It is a way to optimize our work, to then reach the best biological effect of vitamin D for that individual, regardless of the reason why he has a resistance.

Can you explain how that adjustment works?

When you administer vitamin D, vitamin D inhibits PTH production. Therefore, if I measure hormone levels before starting administering vitamin D and then again after two months of administration of the same daily dose of vitamin D, I can use the reduction of the PTH level as an indicator of the biological response to vitamin D effects. This is exactly the parameter we use to individually adjust the vitamin D dose. We give an initial testing daily dose that has to be sustained for 2-3 months and then measure the extent of PTH inhibition, thereby tailoring the daily dose to achieve a PTH serum level close to its lower limit of the normal range. We avoid complete suppression of PTH production to avoid potentially

toxic doses of vitamin D. I can't suppress PTH causing it to be undetectable because if I did that the patient would be at risk of developing hypercalcaemia and consequent kidney damage. Thus, PTH is also a safety parameter for us, a security level. If I do not suppress PTH, I'm sure I'm not giving a toxic dose of vitamin D. I can balance it to the specific biological resistance to the effects of vitamin D that the individual has for hereditary genetic reasons. Kidney stones (for instance, composed of calcium oxalate) may still occur in a few patients (without hypercalcemia or hypercalciuria) as it may also occur in any other individual bearing a tendency for excessive oxalate production independently on vitamin D therapy. That is another reason why it is so important to maintain a minimal daily hydration of 2,5 litres of water.

PTH-levels are tightly regulated by hormonal feedback loops and mainly dependent on Calcium-levels, just as is the activation of vitamin D. Due to this regulation, there is no direct relationship between 25OHD and 1,25-D levels - is it not too simplistic to use it as the only parameter? Or are these regulations simply overridden by the large doses you administer?

PTH inhibition is an endpoint of one of the multiple effects of vitamin D. The magnitude of PTH decrease in response to a testing dose of vitamin D can indeed be used to reliably assess the individual resistance to the biological effects of vitamin D provided that other variables that significantly influence the PTH level are kept under reasonable control.
Ultimately calcium level (not vitamin D) is expected to be the most important determinant of PTH synthesis – simply because the primary PTH function is the control of calcium levels. Either hypercalcemia or hypocalcemia may cause death, so that serum calcium level has to be strictly kept within a narrow physiological range, and PTH is a major regulator of serum calcium. Therefore, changes of calcium levels can either override or increase the inhibitory effect of vitamin D on PTH synthesis, thereby preventing the use of PTH changes to adjust the dose of vitamin D as to compensate for the specific level of individual resistance (prevent tailoring of vitamin D daily dose).

That is another major reason why patients on high-dose vitamin D therapy have to comply with the recommended diet. If they exaggerate and put themselves into an excessively low-calcium diet, serum calcium will get close to the lower limit of the normal range, in spite of the high level of vitamin D. Consequently, PTH will increase (despite the inhibitory effect of vitamin D) and will decrease the amount of urinary calcium to minimize calcium loss (calcium sparing). In addition, increased PTH will release calcium from bones (using bone calcium to prevent serum calcium from falling below the normal range (using bone tissue as a source of calcium). These PTH-dependent mechanisms cooperate to prevent hypocalcemia under insufficient dietary calcium.
On the other hand, patients that do not comply with the recommended diet and keep taking foods containing excessive amounts of foods containing bioavailable calcium also affect the use of PTH for adjustment of vitamin D intake. As serum calcium gets closer to the upper limit of its normal range due to increased intestinal absorption PTH is inhibited, so that vitamin D is no longer the main inhibitor of PTH production. In such circumstance PTH level becomes low enough to falsely suggest adequate dose of vitamin D to suppress disease activity.

How different are the doses that are needed?

Vastly different. The doses range from 30.000 to over 100.000 IU per day. We usually start with 1000 IU per kilogram of bodyweight and then adjust according to the lab results.

These doses would be considered highly toxic by conventional medicine...

They would be toxic for people who have a normal response to vitamin D – but not in vitamin-d-resistance. It is also important to understand that therapeutic use of Vitamin D3 is very different from preventive use. The therapeutic use of vitamin D3 always requires the guidance and monitoring by a physician with specific training to analyse each particular case and to determine the right dose. Otherwise there may be serious damage to health. People following our protocol also have to eat a very low-calcium diet, with complete restriction of dairy products and drink at least 2,5 litres of water a day. Also urinary and blood calcium have to be carefully monitored. These are measures to protect the kidneys. Apart from that, our patients have to maintain a daily aerobic exercise and obtain periodical dexa-scans to make sure their bones stay healthy.

So far you mainly treat patients with MS. What is the success rate of your protocol on multiple

sclerosis?

In approximately 95% of patients with MS, the disease remains in permanent remission under our protocol. While they keep this high dose, the disease remains inactive, with no new signals, neither clinical nor laboratory, of new lesions. Approximately 5% of patients obtain a partial result; it means that they have improvements but they don't have the complete remission of the disease activity. We are studying the reasons why these 5% can't reach the complete remission of MS. So far we see five main points: The most important one is a high level of stress. Emotional stress can seriously affect the result of this treatment. The other elements that can compromise the success of this therapy are smoking, frequent alcohol drinking, the habit of hot baths, and recurrent (usually urinary tract) infections. This is not specifically related to vitamin D, as those factors in general can accelerate the development of MS, even if the patient is under traditional treatment.

How many patients have you treated with your protocol?

Personally, I've already seen over 1600 MS patients and a similar number of patients with other autoimmune diseases. Five other physicians working in our clinic under my supervision since 2013 may have seen a larger number of patients with autoimmune diseases in total. There are now several doctors worldwide that I have trained and that use our protocol, so total numbers must amount to several thousand patients. One of them (a Portuguese physician trained in 2015) recently told me that his clinic has treated over 400 patients coming from several European countries and Africa.

That is a lot of experience! You also treat many other autoimmune diseases like Psoriasis, Vitiligo, Crohn's... does this treatment work equally well on all those diseases?

Our protocol is a highly effective treatment for all autoimmune disorders that we have dealt with so far. With all these diseases we have managed to have complete control over the disease using the same protocol of treatment. The use of vitamin D in the treatment of autoimmune disorders is not aimed to a specific disease but to regulate the immune system. Under the effect of Vitamin D, the immune system increases the number of the so-called "regulatory T lymphocytes" which regulate the immune response. In the same way, the abnormal Th17 reaction (which is the mechanism implicated in autoimmunity in general) is selectively inhibited by vitamin D. Both these things are extremely important for the control of any autoimmune disorder. So autoimmune diseases like intestinal inflammations, Chron's disease and ulcerative colitis, are cases that we have treated and which have responded completely. The patient lives utterly free from any manifestation and symptoms of the illness and leads a normal life. The same goes for psoriasis and vitiligo – here we have a 95% success rate of complete resolution of symptoms. It is a little different with neurological disorders. We have successfully treated isolated optic neuritis, Guillain-Barré syndrome (GBS), autoimmune polyneuropathy, and severe myasthenia and we can reach 95% of complete suppression of the autoimmune activity here too, but unfortunately that doesn't mean that the older irreversible damages caused by the immune system would subside. Paraplegia settled for years in a MS patient or an established joint deformity in a patient with rheumatoid arthritis is not expected to subside. Symptoms of disease activity like fatigue and signs and symptoms of inflammation (pain, edema, erythema, local heat affecting joints), as well as recently acquired disabilities are expected to subside.

Generally, damages formed up to one year before the beginning of the treatment with high doses of vitamin D almost completely regress.

How do you see your results: Do you think Autoimmune-Disorders can be "healed" or is the only option to keep them in permanent remission?

We do not have an answer for that question yet. We do not talk about "cure". Instead, we have been improving our protocol to optimize effectiveness and safety as to maintain remission in a large number of patients without side effects. Hypothetically, the immune system may eventually "forget" that it had once carried out autoimmune aggressions in some patients after several years without experiencing relapses. Even if that hypothesis turns out to be correct in some patients, several factors may affect the duration of treatment including (1) duration of disease activity prior to the beginning of high-dose vitamin D therapy, and (2) achievement of emotional stability. We cannot exclude the possibility that a large number of patients - maybe most of them - may have to remain on high doses of vitamin D indefinitely to maintain their disease in permanent remission. We anticipate that we will

have to develop laboratorial and clinical criteria to select candidates for reduction of daily doses of vitamin D.

For now, we are really happy for having achieved disease remission and recovery of recent acquired disabilities. It is a major reward. Patients have their lives back. Complete remission is a huge success, given how severe these diseases are. We are able to prove in MS-patients with several consecutive annual MRI scans, that under our protocol recent lesions disappear, and no new lesions or active lesions appear. So given the patient has no permanent disabilities by the time when the treatment begins, he returns to have a completely normal life. The dose of vitamin D has to be maintained and we recommend that the patient comes again after two years for a re-evaluation, and then after two to five years, for a second re-evaluation. We still don' t know for how long the patient needs to maintain this high dose of vitamin D3 and for the moment the treatment is for an indefinite period of time.

Apart from Vitamin D you give two cofactors: Magnesium and Vitamin B2. Can you explain why this is necessary?

The enzymes that convert and activate Vitamin D are dependent on magnesium. As Magnesium deficiency is difficult to diagnose we generally give magnesium to our patients - 100 mg of elementary magnesium four times a day.

These hydroxylases are also dependent on vitamin B2, not directly, but indirectly, because in the stage of vitamin D hydroxylation, the enzymes oxidize, and so before they can convert another molecule, the enzyme must be reduced back - a chemical process called reduction. And this reduction process requires the presence of vitamin B2. About 10-15% of the general population, worldwide poorly absorbs vitamin B2 due to another genetic alteration. This can contribute to vitamin D resistance, because sometimes the hydroxylases will malfunction in absence of an adequate level of vitamin B2. We give high doses of riboflavin (50 mg 4 times a day) to compensate for that deficient absorption and optimize the hydroxylations of vitamin D.

Currently no German clinic offers your protocol, yet we have thousands of patients in desperate need of help. Now detailed instructions for your protocol have been posted online. How do you feel about people now starting your protocol on their own?

Periodic monitoring of laboratory tests like serum levels of PTH, creatinine and calcium, and urinary levels of calcium are required for tailoring the daily doses of vitamin D according to individual resistance to vitamin D. Periodic dexa scans are required to follow and prevent side-effects on bone metabolism. People cannot get or analyse those laboratory tests and results on their own, so we do not recommend following this protocol on your own. A list of European physicians who were trained in our clinic is now available on the internet, unfortunately no German physician yet.
Hopefully your interview will trigger interest. We offer to all practitioners that they can come to our clinic for five days and be trained in the protocol – and they do not pay for that training.

At the moment many practitioners may be hesitant, as no clinical RCTs with your protocol have been conducted – why is that the case?

This question is very important because physicians can't randomize metabolic alterations that cause disease: they are obliged to correct them. If there's one person who has a metabolic disorder diagnosed through laboratory - for example a person with hypothyroidism: a deficiency in thyroid hormones that is potentially lethal and can cause damages to someone's health, if it is not adjusted. I have to correct it. Another example is that of type 1 diabetes, in children that can't produce insulin. Physicians are obliged to correct this deficit and have to administer insulin. So, in those circumstances, when the patient has a metabolic problem, a deficiency, a sort of resistance inherited, in relation to a hormone or a vitamin, the caring physician is ethically obliged to intervene to adjust it. Doing otherwise could be regarded as negligence. So, if you are undertaking a double-blind and randomized research, you are telling me that I will have one group of patients that will treat for example with high doses of vitamin D and a group of patients who will receive placebo; and both doctors and patients involved in this research don't know who are the patients receiving vitamin D and who are receiving placebo. Well, one couldn't do this kind of research with diabetic children, for example. We have never done a randomized double-blind research to know if insulin is suitable for diabetic children!

We have never done and will never do. The same happens with people with hyperthyroidism, since we are forced to give a treatment. A randomized double-blind study will never be done, where a group receives thyroid hormones and the other receives placebo. The same happens in case of a deficiency of vitamin B12. A vitamin B12 deficiency can cause a devastating neurologic disease destroying the spinal cord, so you can't leave a person that suffers from a deficiency of vitamin B12 without treatment, because that would be negligence. You can't leave a person that suffers of pellagra, with a deficiency of niacin (vitamin B3) without treatment, because this can cause diarrhoea, dermatitis and even death. So, you can't leave these persons with treatable deficiencies. If I make a randomized double-blind study, I will be negligent with 50% of my patients. The placebo group will be the victim of medical negligence. This is a very important concept because nowadays the medical community has been taught that all the results published in the literature are not to be considered if they aren't the result of a randomized double-blind study. This is a big mistake.
Especially for nutrients and hormones. So we don't have any randomized double-blind study and we will never do one with any of the patients under our care because of the two great basic principles in medicine, that are taught in all western medical schools around the world. The first principle says not to worsen the state, not to hurt, not to act on your patient in such a way that worsens his clinical state. And the second principle says that the patient has to receive all the possible benefits. Then, if I left a patient with uncorrected vitamin D deficiency (or uncompensated vitamin D resistance) – although aware that vitamin D is a great immunomodulator, probably the most powerful immunomodulatory substance existing in nature - a patient with an autoimmune disease who has an unregulated immune system producing aberrant TH17-immunological reaction, if I leave this patient with deficient levels of the only substance that, selectively and powerfully, is able to inhibit this TH17 reaction and induce the proliferation of regulatory lymphocytes, I will be negligent toward this person. So, I will never do a randomized double-blind study using vitamin D and placebo with persons having autoimmune disease. Why? Because I wouldn’t do this sort of things with my daughter, my wife and I won't do it with my patients. Whenever there is a cause-effect relationship (like vitamin D deficiency or resistance causing autoimmune diseases), the cause has to be removed, or disease activity would be sustained. We have thousands of documented cases that more than demonstrate our concept.

A fundamental issue regarding RCTs is that the therapeutic efficiency of our protocol cannot be tested that way. RCTs require giving the same daily dose of vitamin D to all individuals involved in the experimental group, and the research physician who is supposed to administer the substances has to be blind to what he is giving each patient (placebo or testing substance). In our protocol the caring physician has to calculate (from laboratory data) the daily dose of vitamin D to be given. The result is a wide range of daily doses, each one tailored to the needs of each specific patient as to compensate for his / her individual needs (his / her specific level of resistance to vitamin D). So the caring physician cannot be blind to what the patient is taking.

Another fundamental issue is that there is at least one RCT available where Finish researchers have used 20,000 IU of vitamin D weekly. That is equivalent to less than 3,000 IU per day – much less than the minimal dose of 7,000 IU per day, which is now recognized to be the minimal dose to correct vitamin D deficiency or insufficiency. Nevertheless, they have shown a reduced number of active lesions on the MRI after one year of treatment compared to the placebo group.

We started using vitamin D to treat autoimmune disease for the patients’ sake. Our objective wasn't the research, wasn't to convince anyone but was simply satisfying the second principle of the medical practice: to benefit the patient in the most optimal way. Namely, if the patient has a deficiency of a powerful immunoregulator, known and documented, we have to correct this deficiency. If he has a resistance, we have to increase the dose in such a way that this deficiency is compensated. We have gathered a lot of data during this period, and we got experience with the adjustment of the dose for these patients. We have published preliminary data about vitiligo and psoriasis, as these are the only diseases that we were able to get an approval by the ethical-medical committee of the UNIFESP (our university) to do any research on. We would like it done also for other diseases, but, unfortunately we do not get approval for reasons that many times we don't understand – how can it be unethical to find a treatment that could benefit, in the same way we don't understand how the ethical condition to correct a nutrient-deficiency in a patient could be denied. I am not able to understand this, however the answer has been negative for many diseases. But even if we are not allowed to do research, this hasn't stopped us from continuing to treat our patients according to their interest and we have accumulated great experience and thousands of very well documented cases. And when we will have the possibility, we will solicit an ethical committee to allow us to evaluate these cases retrospectively.

Because you need this approval for scientific publications: If I want to submit a publication to a journal with 2,500 patients treated with high doses of vitamin D, the journal editor will ask us for the approval of the ethical committee - otherwise they will not be able to publish. So first we have to request the ethical committee to approve a revision of the medical records of these patients. With the revision of the medical records we could send the material to a medical journal. Let's hope we don't get problems.

That is mind bogeying (??).

You also have to take into consideration, that MS is a billion-dollar market. The multiple sclerosis therapeutics market alone is expected to be worth around 17 billion dollars in 2017 and 25 billion dollars in 2024. And that is only one autoimmune disease. Vitamin D on the other hand is extremely cheap and non-patentable.

Currently, the pharmaceutical industries have already tested tens of thousands of modified (patentable) molecules of vitamin D under the excuse of getting a drug that would not cause the side effect of high doses of vitamin D (hypercalcemia and its detrimental effects). However, we have been able to use high doses of vitamin D3 without such side effects simply by controlling the amount of dietary calcium, increased hydration and monitoring of PTH level.

Because of the huge amount of money involved in drug marketing, the diffusion of knowledge within the medical community is one of the most strictly controlled of our times. One can easily find an article on that subject by looking for the title “Key opinion leaders: independent experts or drug representatives in disguise?”. It was published in the British Medical Journal (BMJ) in 2008 under the headline “drug marketing”. Interesting to read the letters sent (by doctors) to the editor about that article, as well as watching the two video clip interviews with Kimberly Elliot – who used to work for a pharmaceutical company.

One of the most used tools for controlling medical knowledge is the consistent spreading of the false concept that only RCTs (particularly multicentre RTCs) should be considered as “truly evidence-based medicine” when taking decisions on how best to treat patients. Interestingly, most (if not all) these multicentre RTCs can only be carried out if financially supported by pharmaceutical companies. That concept is fundamentally false. An open-label trial (in which both the researchers and participants know which treatment is being administered) is also valid when there is a dramatic and indefinitely sustained difference between the results of “treatment versus no treatment” or “new treatment versus traditional treatment”. This subject has been discussed, for instance, by Paul Glasziou and colleagues from Oxford University in their article titled “When are randomised trials unnecessary? Picking signal from noise”, published in BMJ in 2007, when the authors provided a list of examples of therapies incorporated to medical practice without RCTs precisely because of the dramatic difference observed (they mentioned “Insulin for diabetes”, sulphanilamide for puerperal sepsis”, etc.). Actually, when the difference is dramatic RCTs become unethical.

Another deceiving concept is that whenever the therapeutic value of a substance is confirmed by RCTs carried out by multiple independent groups of researchers it would be incorporated to clinical practice. Actually it would probably not if the therapeutic agent is too cheap and has the potential of replacing expensive drugs from the market. A good example would be the use of high doses of riboflavin (vitamin B2) for the prophylaxis of migraine: effective, inexpensive and with no side-effects. Nevertheless, rarely prescribed.

What should be the best supplementation for vitamin D? Daily, weekly, monthly or yearly? And why?

We have just started from the assumption that a daily sun exposure is a good rule for people to follow. Vitamin D3 (cholecalciferol) is slowly eliminated from our organism, and we cannot rule out the possibility that we could have achieved the same benefit if we had used weekly administrations (i.e., administering once a week the whole amount that we give daily for 7 days). Since we are giving vitamin D3 to patients with disturbed vitamin D metabolism, we have cautiously tried to minimize the chances of reducing the benefit from the beginning. So, administering vitamin D3 on a daily basis seemed to be a wise decision, since the variation of blood concentration would be minor, possibly producing a more stable benefit. Considering current knowledge on the dynamics of vitamin D

metabolism, we strongly believe that monthly or yearly administrations would be completely inadequate for the purpose of best controlling the activity of autoimmune diseases.

Do you recommend oils or capsules or tablets?

Vitamin D is soluble in oil, not in water. So, when mixed in a lipid vehicle vitamin D is better absorbed and should produce a better effect. A lipid vehicle requires soft gels or oil drops.

One last question. You work with very high doses therapeutically. But what doses do you recommend for prevention in healthy adults?

For healthy people we do not recommend high doses of vitamin D3, but only normal doses up to 10,000 IU per day. That is a completely safe dose as you can easily get these amounts though sun-exposure. Children may receive 1,000 IU per each 5 kg of body weight daily (200 IU per kg of body weight daily).

Thank you very much for this interview!

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