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Commentary on the Practice of Medicine (7): Above and Beyond

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A POINT OF NO RETURN

This is the seventh article of a series. I have written about the prescription of iodine and selenium, the use of the word anti-aging, the misuse of the expression adrenal fatigue, and so on. You might have questioned yourself: “Are these really her problems? No big deal". True, there are problems far bigger than mine. But, because they caused so much damage along the way, they turned out to be far bigger than I realized. What are we going to “allow” to happen in the medical world with no sign of protest or disagreement? And for how long? Well, honestly, there’s no reward feeling of being a doctor if these things do happen. Our freedom “to be” is getting so limited that we may all become diseased somehow. Lately I can’t help seeing myself stressed about what to say and, worse, about what not to say, especially in social media, once it may be considered "not included in our compendiums, guidelines and textbooks of Medicine" and, hence, subject to judgement. So, the size of the problem doesn’t really matter. A problem is a problem and we do learn from them, but they might freak someone out if they become an endless and weary process caused by harmful and stressful situations. True, they always come at a price and we can just overcome them if we act in the “now" moment. Otherwise, the problems, other than being lessons, will swallow us into diseases, such as digestive problems, considering that these matters are so difficult to digest. In other words, this is a point of no return. And it is not just about me. The idea is a strong feeling of common cause.

ACCUSED AGAIN

This time was the same article 14 of the Brazilian Code of Medical Ethics mentioned on the first two articles of this series. Art. 14. Practicing or indicating medical acts that are unnecessary or prohibited by the legislation in force in the country. Again, nothing to do with prohibition. So, it must have been considered unnecessary. I feel awkward to say, but it was just because I recommend the use of yoghurt at night as it might help to increase insulin-like growth factor-1 (IGF-1) production. Good levels of IGF-1 are considered beneficial in the process of aging, particularly in the elderly to prevent sarcopenia, a progressive and generalized skeletal muscle disorder involving accelerated loss of muscle mass and function that is associated with increased adverse outcomes, including falls, functional decline, frailty, and mortality [1]. However, the mentioned recommendation is not for everyone. I always test the patient’s IGF-1 levels before suggesting the inclusion of yoghurt in their diets. It might not be recommended at all. Also, when I say that I aim to increase IGF-1 levels, I don’t mean to have them high, but medium, once both low and high IGF-1 levels are associated with health problems, such as sarcopenia and cancer, respectively. At last, food allergies and intolerances, as much as the patient’s preferences, are considered once, we do know, “not every healthy food is healthy for you”.

THE JIGSAW PUZZLE

Let’s try to explain this context in an irrefutable and straightforward way, what is not easy, considering the complexity of the signaling pathways in which IGF-1 is involved.

1. IGF-1 is a hormone that manages the effects of growth hormone (GH). Together, IGF-1and GH promote normal growth of bones, muscles and other tissues [2].
2. GH levels in the blood fluctuate throughout the day depending on your diet and activity levels. But IGF-1 levels remain stable. So, IGF-1 test is a useful way to find out if your body is making adequate amounts of GH [2].
3. The IGF-1 test results tend to go down with time the older you get. Importantly, IGF-1levels and insulin-like growth factor-1 receptor (IGF-1R) downstream signaling are suppressed in many chronic disease

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conditions. This is likely to result in muscle atrophy via the combined effects of altered protein synthesis, ubiquitin-proteasome system (UPS) activity, autophagy, and decreased muscle regeneration [3,4].

4. GH stimulates IGF-1 production in the liver and other tissues, and its secretion is characterized by a pulsatile circadian rhythm, with concentrations peaking during night-time hours [5], especially for day-time active subjects [6]. One study showed peaks during the day - at 1200 and 1800 h in men and at 1100 h and 1600 h in women - but the night peaks were also present [7].

5. Branched-chain amino acids (leucine, valine and isoleucine), known as BCAA, and IGF-1 are essential for muscle protein synthesis [8]. A 2019 study published by the Journal of Nutrition, Health & Aging concluded that compromised muscle parameters were associated with low blood values of specific amino acids (essential amino acids, BCAA and leucine), fatty acids, vitamin D and high homocysteine [9]. Also, BCAA can increase IGF-1 levels in adults [10].

6. Protein intake is essential to maximally stimulate muscle protein synthesis, and the amino acid leucine [11-14] seems to possess a superior effect on muscle protein synthesis compared to other amino acids [15]. Milk, whey protein, and yoghurt are good sources of leucine [16-18].

7. In the Peptide World Congress 2022 set in Las Vegas, Nevada (USA) [19], it was presented many formulas with leucine plus other compounds, such as nicotinamide mononucleotide (NMN) [20] and apigenine [21]. Just to reinforce the importance of leucine in different pathways to optimize health.

Therefore, I tried to make clear the connection between BCAA, leucine, yoghurt, IGF-1 production, night-time peak and protein synthesis, which is well documented.

FAR MORE THAN PROTEIN SYNTHESIS

As I said in previous articles, I order a thorough nutritional, metabolic and hormonal evaluation before prescribing any dietary recommendation. In our context, we certainly have to previously analyze some important parameters, such as fasting insulin, HDL-cholesterol, triglycerides, us-CRP, 25-OH-vitamin D and calcium levels, before recommending the ingestion of yoghurt for protein synthesis. All the parameters involved must be controlled so that we can make a more assertive prescription. That's what we can call a holistic approach:

A) Insulin and IGF-1 are closely related hormones that control different aspects of growth and metabolism in many organisms [22]. Hyperinsulinemia and insulin resistance may mediate common diseases, such as obesity and cancer progression, via the insulin/ insulin-like growth factor axis [22]. On this matter, it's well investigated the role of chronic low-grade inflammatory response in the pathogenesis of insulin resistance [23-25].

B) Yoghurt is a good source of calcium. While vitamin D has multiple effects on bone and calcium metabolism, the regulation of intestinal calcium absorption efficiency is a critical function for vitamin D [26].

C) Yoghurt is recommended for gut health. It contains live bacteria that could contribute *via* modulation of the gut microbiota to its reported beneficial effects, such as reduced visceral fat mass, reduced body weight gain, lower incidence of type 2 diabetes and changes in gut microbiome, including transient increase of yoghurt-contained species (*i.e. S. thermophilus* and *B. lactis*)" [27]. Also, regular consumption of fermented foods (e.g., kimchi, kefir and yoghurt) may represent a potential avenue to counter the pro-inflammatory effects of gut dysbiosis [28]. Therefore, taking yoghurt at night can indeed be a good habit, as probiotics are usually recommended before bed to give the beneficial bacteria time to colonize in the gut overnight.

D) Last, but not least, although a lot more could be written about this issue, sheep, goat and Greek yoghurt are traditional in the Mediterranean diet, one of the most studied and well-known dietary patterns worldwide, with all its charm, health-related benefits and sustainable life-style model [29-32]. I always recommend my patients to get some inspiration from it.

ABOVE AND BEYOND

Even with so much information about IGF-1, BCAA, leucine, milk, whey protein, yoghurt, night peak, muscle gain, you know, all intertwined somehow, none of my arguments were accepted. But, let's carry on. Do you know the electronic music group Above and Beyond, consisting of the English DJs Jono Grant and Tony McGuinness together with the Finnish DJ Paavo Siljamäki? One of my favorites songs of them starts with "My current mood is gratitude" [33]. Further on they say: "How the sky has been much bluer and my life just so much sweeter". Well, the name of the group and the nice and positive words inspired me to say that all these articles are really one attempt to go "above and beyond" the negative aspects of being a doctor in the XXI century. Let's choose to be grateful and give more value to the noble and sublime opportunity we had to become and work as medical doctors in this journey we call "life". Once more, with love and glory.

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