

Commentary on the Practice of Medicine (10): A Remarkable Ride

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Received July 24, 2023; Revised July 28, 2023; Accepted July 31, 2023

BETWEEN THE LINES

In the mornings I quite often indulge myself in a delightful smoothie prepared with collagen peptides, frozen "açaí" berry pulp, and ripe banana. The vibrant purple hue of the "açaí" berry, a small fruit native to Central and South America, is truly captivating. Indeed, "açaí" enjoys immense popularity in my country. It is rich in anthocyanins - a type of flavonoids - known for their antioxidant properties, particularly beneficial for eye health [1,2]. I buy these small bags with frozen "açaí" pulp from some organic producers nearby and they have the most impressive purple color I have ever seen. As I savor this nutritious blend, I feel like I am not just eating healthy, but, rather, "eating health". The subtle difference in wording holds a stronger connotation - one that goes beyond the mere act of consuming food. I am used to telling my patients that not only the foods themselves, but also the perception of eating something truly nourishing modulate positively our genes. Indeed, a healthy life is all about it: making good choices and enjoying them. Charm and pleasure are essential ingredients in my recipe for that. Although they may not be explicitly found in medical guidelines and textbooks, reading between the lines reveals their significance.

WHAT IS A HEALTHY DIET?

Once again, I found myself facing accusations of violating articles 14 and 18 of the Brazilian Code of Medical Ethics, both of which are connected.

Art. 14. Practicing or indicating medical acts that are unnecessary or prohibited by the legislation in force in the country.

Art. 18. Physicians are prohibited from disobeying the judgments and resolutions of the Federal and Regional Councils of Medicine or disrespecting them.

However, my main purpose in writing these articles is to find an outlet to express my feelings and register what happened to me. I am committed to using this experience to foster a sense of understanding, support, and empathy for others facing similar accusations. Additionally, I saw this as an opportunity to shed light on my work and, hopefully, inspire those who believe in the value of a preventive

approach to life. In the end I am making something creative, positive, constructive, valuable, meaningful and rewarding out of provocative, insensitive, heartless, disrespectful, harmful, and stressful accusations. This time, I faced scrutiny over a seemingly innocuous comment I made about the Zone Diet, a dietary approach developed and advocated by Barry Sears, an esteemed American biochemist. Dr. Sears is renowned for founding and presiding over one of the pioneering biotechnology startup companies in Massachusetts, USA. In simple terms, being in the Zone means to be able to slow down the process of aging by reducing inflammation and increasing the repair of inflammatory damage to the body [3]. The result is decreasing the onset of age-related chronic diseases, resulting in the extension of our health span [3]. The Zone is actually a highly dynamic physiological state that hinges on the dietary choices we make [3]. Dr. Sears's website asserts that our blood can provide valuable insights into whether we are successfully in the Zone or not [3]. In the post, I said that in 2001 I was given a book as a present, "The Wrinkle Cure: Unlock the Power of Cosmeceuticals for Supple, Youthful Skin" [4], written by Dr. Nicholas Perricone, an American dermatologist and anti-aging expert. In his book, Dr. Perricone highly recommended the reading of Dr. Sears's first book, "The Zone: a Dietary Road Map" [5], in order to get additional anti-inflammatory dietary recommendations and improve his antioxidant supplementation plan proposed to revitalize the skin from outside and inside. It was irresistible to buy Dr. Sears's book. Though I wasn't involved in the field of Nutrition at the time, I was genuinely intrigued by the potential of cosmeceuticals, such as vitamin C ester and alpha lipoic acid. Also, the anti-inflammatory, antioxidant, and antiglycant approach proposed by Dr.

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Citation: Stoop IMB. (2024) Commentary on the Practice of Medicine (10): A Remarkable Ride. BioMed Res J, 8(1): 646-650.

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Perricone to slow down, and even reverse, the skin aging process did make sense to me and still does. Yet, it was just a story what I wrote. I could have said that my first encounter with the Zone Diet was while reading Jennifer Aniston's biography, as she is a well-known follower of this dietary approach. It would have been a story just the same. Ultimately, my intention was simply to share an experience that left a lasting impact on me, not to promote any misaligned "agenda". Regrettably, it appears that my sharing was misinterpreted, leading to an unwarranted assumption that I engaged in something unnecessary or prohibited, although the recommendation of an anti-inflammatory diet to help control the levels of inflammation should be considered an obvious, clear, straightforward, well-grounded and safe approach to promote healthy aging. Nonetheless dieting is a fascinating topic to write about once determining what a healthy diet is remains more of a philosophical discussion than an evidence-based inquiry [6]. This was a 2004 statement and it will probably always be true. In fact, it is widely known today that "not every healthy food is healthy for you".

EXPERIENCE COUNTS

Exactly 40 years ago, my journey into the world of medicine began, but I took my first course in Clinical Nutrition only in 2003. One thing that I have come to conclusion is that no diet is good for you if you don't feel good. In other words: if you want to choose a dietary pattern for yourself, the rule number 1 is to be coherent with your perceptions and feelings. Don't go against the flow. Ideally, you'd better be really enthusiastic about it. Then it might be incorporated into your system as your second nature: no great effort should be necessary. Interesting enough, diet, from the Greek word "diaita", means way of life and no doubt everyone should choose his own. Also, you might have read in one of my articles that the XXI Century Medicine is more Personalized [7,8]. It would be contradictory of myself to choose only one dietary pattern for all patients. I refer to the Zone Diet in the same way that I mention the Mediterranean Diet, the Dietary Approaches to Stop Hypertension (DASH) Diet, the Paleo Diet or any other diet [9]. I never pronounced myself as a "Zone Diet only" advocate. To be honest, as far as dieting is concerned, strictiveness of rules is not healthy at all, once being strict may reflect negatively in the expression of our genes. In this case, other problems might come as a consequence of an approach that, in theory, could bring benefits to our lives, that is, to follow inflexibly a recommended healthy dietary pattern.

AN ANTI-INFLAMMATORY, LOW GLYCEMIC-LOAD DIET

The Zone Diet was developed on the concept that the hormonal responses to macronutrients could be orchestrated to maintain key hormones within therapeutic zones and to control the levels of inflammation in the body [6]. In fact, it is proposed basically as an anti-inflammatory, low glycemic-

load diet [6]. The Zone Diet also highlights the importance of AMPK - adenosine 5'-monophosphate (AMP)-activated protein kinase - an enzyme found in every living cell that controls the flow of energy [3]. If AMPK activity is optimized, you live longer [3,10-12]. If AMPK activity is inhibited, you gain weight, develop various chronic diseases at an earlier age, and accelerate your rate of aging[3]. When you are in the Zone, your levels of AMPK are optimal to achieve a longer and better life [3]. Briefly speaking, in my experience the effectiveness of the Zone Diet varies from person to person. It can be great for some people, but not for all, like any other dietary approach. I do like the theory behind it, but, more importantly, it makes me feel good, emotionally and physically balanced. So, it has never been solely a rational choice, but one that I could actually experience with my feelings. All in all, finding the right diet is a process that needs to be guided by both rational assessment and intuitive understanding of what is really good for us. Nutrigenomics and Metabolomics are emerging sciences that have brought valuable insights to our understanding of food choices and personalized prescriptions. These disciplines delve into the intricate interplay between our genetics and the impact of nutrients on our bodies. The integration of Nutrigenomics and Metabolomics has the potential to revolutionize nutrition and healthcare practices. As we uncover more genetic polymorphisms and metabolic pathways, our food choices and prescriptions tend to become increasingly accurate. By harnessing the power of these cutting-edge sciences, we can move towards a new era of precision nutrition.

A 40-30-30 EATING PLAN

The Zone Diet's main recommendation is to balance our offer of macronutrients, that is, carbohydrates (C), proteins (P) and fats or fatty acids (A). Calorie-wise this comes out to a 40% carbohydrate, 30% protein and 30% fat eating plan [13]. It doesn't tell you exactly what to eat, but it is focused on tailoring the right combination of macronutrients at every meal and snacks along the day. The underlying biochemical premise behind this approach is that this combination of P, C and A can actually be crucial to control two hormonal systems that are directly affected by dietary macronutrients: the insulin/ glucagon axis and the eicosanoids system [3]. The insulin/glucagon axis plays a pivotal role in maintaining stable blood sugar levels [5]. On the other hand, the eicosanoids system involves hormone-like compounds derived from fatty acids, which influence various physiological processes, including inflammation and blood clotting [5]. By thoughtfully regulating the interaction between proteins, carbohydrates, and fats, that is, carefully structuring macronutrient intake, the Zone Diet aims to optimize the functioning of these hormonal systems [5]. It further advocates for the use of omega-3 fatty acid supplements which are widely recognized for their numerous health benefits [14-18]. Additionally, regular supplementation of polyphenols is emphasized [17,19-23],

particularly for its protective effects on the gastrointestinal tract, helping promote the interspecies balance of the microbiota community [24]. Notably, polyphenols are also regarded for their involvement in targeting the AMPK signaling pathway, which has emerged as a promising and "novel" anti-aging strategy [12]. Notwithstanding, I am very straight forward towards my patients. I make very simple statements: "You can eat whatever you want and the way you want. I don't really have control on that. What I can really do for you - and I do it very methodically - is to check your body composition (% fat, lean mass and water) and your blood parameters with a thorough nutritional, metabolic and hormonal evaluation. If they are not great (good is not enough), I will let you know and give you the dietary recommendations you need and the supplements that might help you optimize your results and maintain your health and well-being". With these words, I want to make sure that the patients are 100% responsible for their dietary choices. I can only empower them and help them along the way with personalized information and prescriptions tailored to their specific needs. I remind them it is common knowledge that "we make our choices and our choices make us".

A FLEXIBLE EATING PATTERN

Embracing a rigid dietary pattern as an absolute rule is definitely not the best approach to nutrition. Instead, it is essential to combine both scientific knowledge and "common knowledge", but take them as information, while actually putting them into practice requires to be aware of how these dietary recommendations impact our well-being and overall good health. Quantifiable parameters like C-reactive protein, ferritin, glycated hemoglobin, homocysteine, creatinine, blood urea nitrogen (BUN), vitamins, minerals, and others help us assess our health status and conclude whether or not we are doing fine. The Zone Diet is one among many dietary plans we can get inspiration from. Although there has always been a lot of controversy about this macronutrient-based diet, I would like to point out what I like the most about it:

1. It is an anti-inflammatory diet and we do know that a lot of what goes wrong as we age stems from smoldering, low-level inflammation in places like arterial walls and the brain [25]. The importance of chronic low-grade inflammation in the pathology of numerous age-related chronic conditions is clear [25,28-31]. It has been referred to as "the secret killer" [32]. On that account, we could say that the Zone Diet is grounded on the knowledge that diet is able to positively modulate inflammation in the body [26] and is one of the modifiable factors for preventing age-related diseases and preserving good health status as we grow older [31].
2. It is a flexible way of eating that allows for variety. This plan is usually popular with strength and endurance athletes, high intensity cross fit athletes, and those who

are simply looking for steady energy supply throughout the day [32,33]. While some studies may offer critical views, it is crucial to consider research methods and publication dates, as long-term effects often overshadow short-term outcomes, although the combination of foods may be noticed straightaway. For instance: eat one medium-sized raw banana (2C) and compare what you feel when you eat the combination of one warm cooked banana (2C) with two medium slices of low-fat cheese (2P) and one tablespoon of tahini (2A). Be aware of the difference, regardless of any scientific knowledge on nutrition and metabolic pathways. What the Zone Diet emphasizes is that you'd better eat more calories, but combining P, C and A, than eating just C. I feel it's true, other than saying I think it is true.

3. Zone Diet doesn't exclude the recommendations of the charming Mediterranean Diet with its well-known health benefits [34] and those from the Chinese [35,36] and Ayurvedic [37,38] medicines, both rooted in ancient traditions and holistic philosophies. The Zone Diet basically asks you to follow the specific distribution of macronutrients (40:30:30), but it ultimately provides the freedom to choose foods and their preparation methods, although some types of food are recommended only occasionally, especially high-glycemic load carbohydrates and pro-inflammatory fats. By taking inspiration from various dietary plans, including the Zone Diet, individuals can craft a well-rounded approach to nutrition, promoting vitality and long-term health.
4. If a dietary approach has been in the market for almost 30 years, it undoubtedly holds some solid ground. Its endurance over time sets it apart from mere "fad diets" that come and go without substantial support from clinical research. Therefore, it wouldn't be fair to dismiss it as such. On this matter, to underscore its credibility and provide on-going support for clinical research projects on the use of innovative nutritional approaches to reduce inflammation, Barry Sears founded the Inflammation Research Foundation (IRF) in 2003, a Massachusetts non-profit public benefit corporation [39]. The IRF provides certification courses on anti-inflammatory and pro-resolution nutrition throughout the world and I have taken one myself. I guessed this certificate would empower me to talk and write about anti-inflammatory diets, but that was never considered.

Yet, the world of nutrition remains a complex arena where differing viewpoints will continue to coexist. My hope is that we can engage in open and thoughtful discussions about dietary choices, valuing evidence-based insights while respecting diverse perspectives on the path to wellness.

AN EXTRAORDINARY, ORDINARY LIFE

"About time" is a 2013 British-American romantic comedy-

drama film written and directed by Richard Curtis, and starring Domhnall Gleeson, Rachel McAdams and Bill Nighy [40]. A sweet movie, really. Close to the end, it gives us this message: "We're all traveling through time together every day of our lives. All we can do is do our best to relish this remarkable ride" [40]. And that's what I have been trying to do and what I propose to you with my articles. I truly believe that it influences positively the expression of our genes towards health. Don't think you can get away with it. Because you can't. Nobody can. We'd better do our utmost to spread good seeds along the way because it's the only chance we have to get good harvest back. In the medical world too. Make ours a really remarkable ride. With love and glory.

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