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Review Article

Sustainable and personalized nutrition: From earth health to public health

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ABSTRACT

Sustainable nutrition, equaling earth health, involves a personalized approach designed in terms of precision and avoidance of still cogent but unjustified dogmas, equaling public health. For instance, current dietary recommendations continue to dwell on the need to limit as much as possible the intake of saturated fatty acids (SFA), notwithstanding the mounting evidence that the effects of food on health cannot be predicted from the content of single nutrients without considering the overall macronutrient composition and the role of the food matrix. The traditional recommendation to restrict SFA ignores that their effects on health depend on the interaction between naturally occurring food components and those introduced by food processing. It is warranted to modify the still widely promoted dietary guidelines based upon such single nutrients as SFA and instead personalize dietary habits on the basis of the whole pattern of the food matrix. Accordingly, the double edge of malnutrition, that involves deficiency as well as excess and materializes in many individuals throughout their life course, might be tackled by implementing sustainability, with the additional effect of overcoming global inequalities. Within this context SFA may regain their position of tasty and cheap sources of energy to be adapted to each individual lifestyle.

1. Introduction

In the difficult times amidst the SARS-CoV-2 pandemic, the whole world has become more conscious of the importance of primary and secondary prevention. COVID-19 is already having a triple hit on health, education and income, but at the same time this scourge offers tremendous opportunities for reaching the 2030 Agenda and the Sustainable Development Goals. In the frame of the pandemic, the planet gave us the strongest warning that the mankind must change in order to prevent the ongoing worldwide degradation of the ecosystem. At the same time, it has become increasingly clear that COVID-19 has a disproportionate impact on those communities that were already facing disadvantages and discrimination. The impact of the pandemic has been particularly detrimental in people living in areas of high deprivation, and in those with chronic conditions such as diabetes, hypertension and obesity. Inequalities are putting at risk of malnutrition not only children in developing and transition countries but also minorities in high income countries, further contributing to social inequalities in healthcare, disease prevention and treatment that impinge upon this and the next generations [1]. In this context, disease prevention may indeed be the key for mitigating both the COVID-19 syndemic and the burden associated with the issues of sustainable food and nutrition. Food is once more at the core of many of the world's health, environmental, social and economic challenges, as witnessed by the 2020 award of the Nobel Peace Prize to the World Food Programme for the efforts towards bettering not only food availability but also security. The issues – from earth health to public health – are complex and cannot be solved in isolation during the current syndemic that, whether cause and/or effect, is tightly connected to the concept of globalization and climate changes. The ongoing emergency demands a politically correct and holistic switching from globalization to global health, as highlighted even before the spread of SARS-CoV 2 [2]. Sustainable nutrition encompasses the safe supply of adequate food and nutrients to everyone but at the same time involves the preservation of the environment, biodiversity and local

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resources [3].

1.1. Personalized and precision nutrition

Since the 2000s advancements in genotyping technology, coupled with the reduction in the costs of genome sequencing and the more recent advent of digital technologies in healthcare, did initiate a third revolution in medicine. These technologies are creating unprecedented opportunities for primary disease prevention, diagnosis and treatment and for secondary disease monitoring on a personalized basis, both within the health system and beyond. Given the potential for effective public health preventive efforts in postponing the onset of disabilities and reducing healthcare costs, the expectation is that the current 'one size fits all' approach in primary prevention takes advantage of the new technologies in healthcare in order to be more targeted at those in need.

In the context of nutrition science, modern views on food have led to a substantial shift in nutrition research and practice known as *precision nutrition*, which endows the potential to offer multidimensional and dynamic recommendations on the quality and quantity of food [4]. Like precision medicine, precision nutrition aims to understand the effects on health of the complex interplay of genome, microbiome, antibiotic/probiotic use, metabolome, food environment but also of economic, social and behavioral variables, thus allowing a targeted and personalized dietary management with the goal to prevent and treat nutrition-related disorders. Precision nutrition might therefore be considered a subset of precision medicine and an important additional factor in the primary and secondary prevention of such non-communicable diseases as diabetes, neurodegenerative diseases, atherothrombotic cardiovascular diseases and cancer, that all represent a huge global burden for healthcare systems and individuals. All these diseases have common denominators, i.e., a chronic inflammatory state and metabolic derangement, which may be triggered by a genetic predisposition to an impaired physiological response to environmental insults. In this context, the use of polygenic scores for common disease risk assessment [5] represents an important area of progress for public health [6], because if preventive interventions are targeted mainly to those individuals who are going to get an illness, the ensuing focused approach is obviously more efficacious and cost-effective (and also likely more cost-saving) than a traditional one-size-fits-all approach [7]. In the foreseeable future, information from the DNA sequence of individuals is likely to become part of their electronic medical records and thus used to inform their healthcare strategies throughout the whole life course.

The use of artificial intelligence represents an additional tool potentially able to improve precision and prediction accuracy in various clinical settings. The approach based upon the artificial neural network should help to integrate at an individual level the main biological indicators, i.e., basal energy expenditure, metabolic flexibility, microbiome (at the interface between food intake and nutrient absorption) and also metabolome, that involves the quantitative analysis of byproducts of cellular activity, in turn derived from the metabolic pathways of living systems [4]. As an end by-product, smart phone apps might help to translate nutritional recommendations into individual lifestyles [8]. However, reliability and feasibility of personalized nutrition are still challenged by issues requiring further investigation. For instance, manipulation of the microbiome is challenged by the varied ethnicities and geographic localizations, emphasizing once more the close connection between earth and individual health [9] and also indicating that the refinement of the related interventions requires data input from different and well characterized ethnic groups [10]. Unfortunately, the evidence stemming from evaluations on the financial sustainability of such personalized interventions currently limits their implementation even in high income countries, further stressing the negative impact played by social inequalities. Last but not least, even well-defined and well-planned interventions require a high degree of adherence, that depends on the psychological features of each individual [11].

With this background and gaps of knowledge, current evidence on the effectiveness of personalized nutrition is limited to adult populations but is still unknown how children would respond. New efforts from the pediatric communities are warranted to investigate the impact of this approach in children, in a way comprehensive of all the aspects concerning the nutritional status, metabolism and nutritional requirements. Owing to the large number of variables and their implications, emphasis should be given and more efforts directed towards the implementation of highly effective nutrition-specific and nutrition-sensitive interventions able to support, starting from the earliest ages of life, a healthy development at an individual level, that will also impinge upon the levels and quality of health in adulthood.

Consistent with the present and prospective applications of personalized nutrition, social interventions aimed to improve socioeconomical conditions at a population level represent a key goal in order to reach an acceptable degree of effectiveness regarding primary prevention and treatment [12]. The evidence stemming from randomized clinical trials is essential but cannot be the only approach. Interventions on dietary habits also demand to consider food security, cost and environmental sustainability and thus imply a broad concept of wellbeing that encompasses but goes beyond the effects on health. Nutrition and food warrant research programs where medical science (nutrition and health), psychology (how we behave), economy (how resources are used and their impact on wellbeing) and sociology (how social determinants shape human behavior) interact in the frame of an integrated approach.

1.2. The issue of saturated fats: time to change the guidelines?

In adults, the number one global cause of death are atherothrombotic cardiovascular disease. Historically, the so-called lipid hypothesis focused on the detrimental role of saturated fats per se in enhancing the risk of cardiovascular disease. Accordingly, authoritative institutional bodies in the USA as well as in Europe still maintain dietary recommendations focused on saturated fatty acids and suggest to keep their intake as low as possible [13]. On the other hand, the current assessment of disease risk associated with dietary fat consumption emphasizes the confounding nature of the macronutrients that replace saturated fats in diets (for instance carbohydrates, including their various forms and sources) and give broader recognition to the impact played by the food matrix per se and the by whole pattern of food composition as the most productive approach towards an overall healthy diet [14]. For sake of an example, low density lipoproteins (LDL) are made of subclasses of particles with differing cholesterol content and atherogenic properties [15]. Dietary carbohydrates and saturated fats have divergent effects on LDL subclasses, so that a high intake of carbohydrates increases small LDL particles, whereas a high intake of saturated fats does increase larger particles [16]. Small and very small LDL particles are characterized by defective plasma clearance, larger entry and retention into the arterial wall as well as faster oxidation [15]. Current evidence-based effects of SFA on health depend on the interaction of the effects stemming from naturally occurring food components but also of those stemming from the unhealthy components introduced during food processing. A complex food matrix with a high SFA content but also with other nutrients and non-nutritional components (e.g. proteins, micronutrients, phospholipids, probiotics) – as is for instance the case for soft and hard cheese but also for fermented diary products such as yoghurt and kefir – is associated with no increased risk of cardiovascular disease and diabetes [17]. Thus, cogent dietary recommendations should rather emphasize strategies based upon the whole food matrix, to be conveyed to the community as understandable, consistent and robust recommendations on healthy dietary patterns.

Several systematic reviews and meta-analyses recently addressed the saturated fat controversy, i.e., whether or not saturated fat intake is a risk factor for atherothrombotic cardiovascular diseases. The totality of evidence, i.e. meta-analyses or systematic reviews of both observational studies and randomized clinical trials, fails to demonstrate harmful effects of SFA on excessive body weight, metabolic syndrome, type 2 diabetes or cardiovascular disease when compared with diets rich in carbohydrates designed to replace fats [18]. Accordingly, dairy products such as yoghurt and cheese do not exert detrimental effects on serum lipids on the basis of their high content in saturated fat [19], and butter consumption shows relatively small or neutral associations with mortality and cardiovascular disease and even an inverse association with the incidence of diabetes [20]. The beneficial effects of yoghurt and cheese on diabetes and cardiovascular risk are likely related to the whole food matrix and associated nutrients (i.e. protein, calcium, short-chain fatty acids (SFA, i.e., acetic, propionic and butyric acid) but also to peptides and complex phospholipids that are components of the functionally effective membrane-associated receptors. Therefore, while the low-fat versions of these foods might be helpful for overweight and insulin-resistant obese individuals, the full fat versions can be safely used by patients with type 2 diabetes. Interest on the dietary role and metabolic effects of SFA has been recently revamped by epidemiological observations leading to a fresh approach to health and well-being [21]. Furthermore, palm oil rich in palmitic acid was shown to favorably increase HDL cholesterol with no changes in the total cholesterol/HDL ratio [22]. Continuous updating of the evidence stemming from existing reviews, as well as from new systematic narrative reviews are warranted to tackle areas where the role of saturated fat remains unclear. Yet, the totality of current evidence shows that cutting down the intake of saturated fat should be avoided and that dietary recommendations should be rather focused on the choice of the type of food. Future research should also include objective cost-benefit analyses capable to disentangle the role of saturated fat in the context of broad dietary recommendations.

1.3. Focus on palmitic acid: from fetal life through adulthood

Pertaining to saturated fatty acids, in recent years there has been a heated debate on palmitic acid regarding its biological role *per se* [23] but also pertaining to the sustainability of its major plant sources as palm oil. Palmitic acid (16:0) is a saturated fatty acid present in the diet but also endogenously synthesized. Among fatty acids 16:0 has special structural and functional roles during the very early stages of life, for its role in the developing fetus but also for being the main dietary component for energy and storage purposes during lactation [24]. During the fetal life 16:0 is a crucial component of the surfactant of pulmonary alveoli, i.e., a surface-active lipoprotein complex (phospholipoprotein) produced by type II alveolar cells [25]. Proteins and lipids that make up the surfactant have both hydrophilic and hydrophobic regions. By adsorbing onto the air-water interface of the alveoli, with hydrophilic head groups facing water and the hydrophobic tails facing air, the main lipid component of the surfactant dipalmitoylphosphatidylcholine (DPPC) – a phospholipid consisting of two C_{16} palmitic acid groups attached to a phosphatidylcholine head-group – reduces surface tension and facilitates the act of breathing, thus preventing alveolar collapse. The chemically synthesized pulmonary surfactant is included in the WHO Model List of Essential Medicines, the most important drugs needed also in basic healthcare systems.

At birth, the term infant is 13–15% of body fat with 45–50% of 16:0, much of which is derived from endogenous synthesis in the fetus. After birth, the infant accumulates adipose tissue at high rates, reaching the proportion of 25% of body weight as fat by 4–5 months of age [24]. Over this time, human milk provides 10% of the dietary energy as 16:0 in the frame of peculiar triglycerides characterized by 16:0 complexed in the center of the triglyceride molecule [26]. This composition allows better energy absorption while preventing the precipitation of calcium soaps with lipids, thus reinforcing the concept of human milk as a full and complete biological system. In addition, palmitic acid at the sn-2 position of triacylglycerol backbone modulates N-acylethanolamine levels in rat tissues, that possibly explains its effects on lipid and energy metabolism [27]. Furthermore, feeding rats with human and donkey milk, both characterized by a relative high level of triacylglycerol enriched in palmitic acid at the sn-2 position, favourably modified inflammation markers as well as glucose and lipid metabolism due to a modulation of mitochondrial function and efficiency [28]. Assuming that fetal fatty acid synthesis and the peculiar delivery of 16:0 in the human milk did help during the evolution to afford survival advantage to the neonate, it is a timely question whether or not 16:0, i.e., is a non-essential dietary component efficiently synthesized via endogenous reactions, represents an essential component among the exogenous nutrients supplied in the intrauterine phase and the early postnatal period. Optimal ranges of supply and intake need to be established, considering the possibility that during the early stages of life both deficiency and excess may have detrimental effects that to impinge on the overall health of the individual in later life stages.

In adults palmitic acid represents approximately 20–30% of the total fatty acids in our body and therefore a man weighing 70 kg is made on average of approximately 3.5 kg of palmitic acid [29]. Its daily food intake is approximately 20 g and represents around 8% of the total calories [29]. Although often considered to have adverse effects on non –communicable diseases, 16:0 is an essential component of the membrane secretory and transport lipids, because it plays crucial roles on protein palmitoylation and formation of signal molecules and receptors [23]. Specific metabolic conditions related to overweight, visceral obesity and a sedentary lifestyle are often associated to metabolic inflexibility when the inability to efficiently store and use energy substrate may favor a dysregulated de novo lipogenesis and increased endogenous production of palmitic acid [30]. The latter is often associated with an excess of ectopic fat deposition coupled with a lower capability of physical activity, so that a sum of unfavorable conditions takes place stemming from a lower degree of glucose tolerance and insulin sensitivity, that are widely recognized to be key mechanisms for the onset of the metabolic syndrome that predisposes to cardiovascular diseases.

Therefore, dysregulated de novo lipogenesis and dietary SAFA/PUFA imbalance may both lead to the metabolic syndrome, metabolic inflexibility and a dysbiotic microbiome through distinct pathways (Fig. 1). Increased endogenous production of palmitic acid may rise inflammation susceptibility through activation of TLR4 [31] and enhance insulin resistance by ceramide formation [32]. On the other hand, reducing PUFA intake, particularly n-3 highly PUFA, may favor dyslipidemia, hypertension and insulin resistance [33]. Thus, unbalanced body composition and reduced physical fitness might be either cause or consequence of de novo lipogenesis and unbalanced SAFA/PUFA intake. Since these two dysmetabolic conditions often occur concurrently, increased tissue palmitic acid and related deleterious consequences from a dysregulated de novo lipogenesis may be wrongly ascribed to the dietary intake of palmitic acid. The invidual capability to manage the glucose/insulin axis may be considered a major factor in the frame of the concept of energy balance and storage. Indeed, patients with overweight and obesity show considerable interindividual variability in the weight loss response to dietary treatments depending on their insulin resistance and glucose intolerance. In contrast, individual patients are often assumed by clinicians to respond similarly to various diet and exercise prescriptions. Nevertheless, variation in baseline glycemic control in people with overweight and obesity but without type 2 diabetes, such as the presence of normoglycemia or prediabetes, might lead to variable success in weight loss and metabolic responses to dietary treatments [34]. Recent data particularly suggest that a high content of dietary fiber is beneficial for people with prediabetes, due perhaps to fermentation by the microbes and production of short chain fatty acids that favorably influence the individual glucose/insulin axis [35]

2. Conclusions

The perspective of sustainable nutrition offers a novel and holistic approach to the millenarian fight against malnutrition with its double

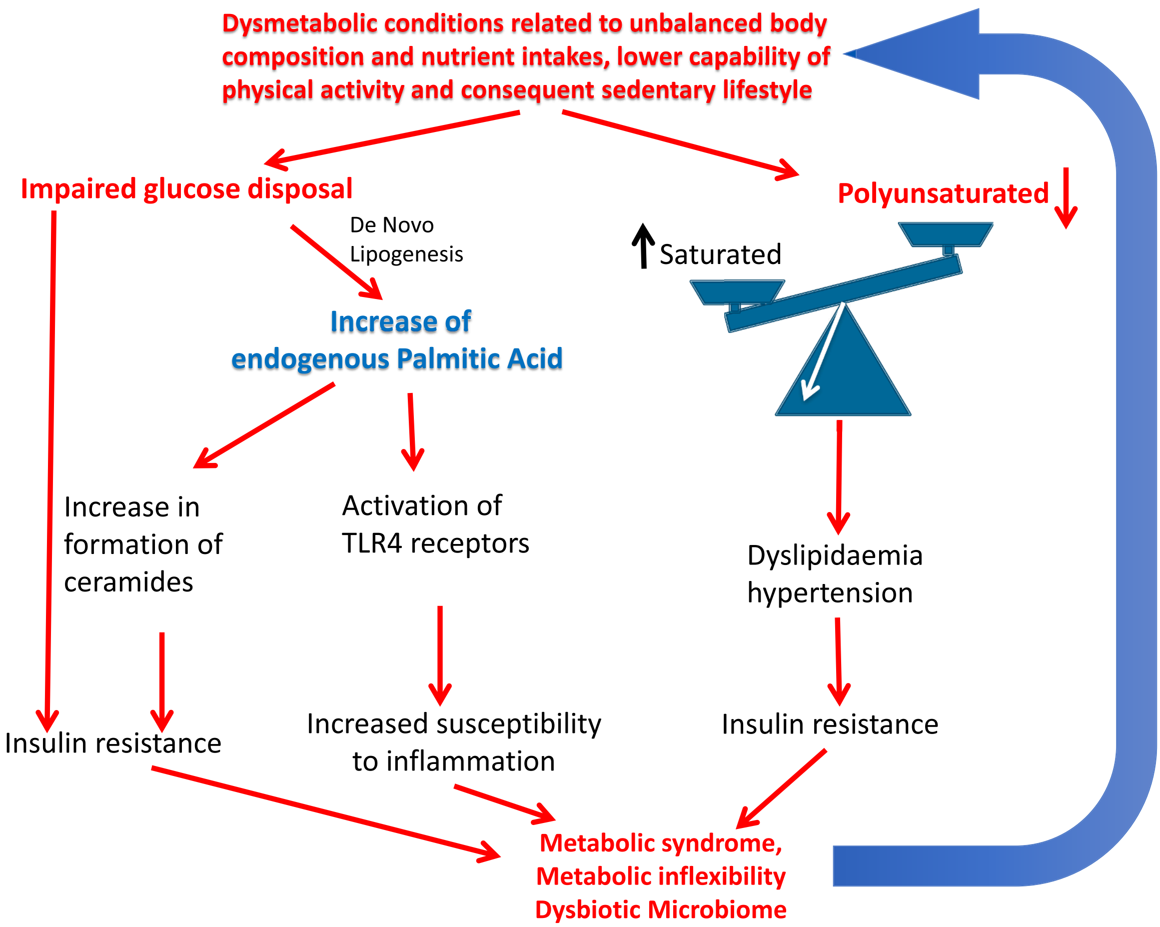

Fig. 1. Pathophysiological consequences of dysregulated de novo lipogenesis and unbalanced dietary PUFA/SFA ratio converge to contribute to the metabolic syndrome, metabolic inflexibility and dysbiotic microbiome, which in the long term result into body composition imbalance and lower capability of physical activity, starting a vicious circle.

edge sword, i.e., inadequate versus excess energy/nutrient intake. This issue was endorsed by Pope Francis in the message that on October 16, 2020 he addressed on the occasion of the World Food Day to Qu Dongyu, director general of the Food and Agriculture Organization (FAO). Due to the ongoing rapid global transition, an increasing proportion of individuals are exposed to different patterns of inadequate nutrition during their life course and face the double burden of malnutrition and overweight as victims of improper dietary habits [36]. In this frame, sustainable nutrition may be able to deliver at a global level a positive message in terms of support to health and well-being for the populations of the planet. New positive messages on saturated fatty acids may offer an alternative as a widely affordable and sustainable source of energy, cheap and tasty. However, interventions are necessary to promote the capability to adapt messages in order to match individual needs to available resources, with the awareness that doing the best for the planet may also be the best in terms of personal health and disease prevention. Thus, food diversity represents the perfect link between sustainable and personalized nutrition (Fig. 2), in the context of the respect of geographical and ethnic variabilities and it should emphasize once more as a healthy way towards more emphasis on the complex human-mother earth diade. Lastly, a warning must be clearly expressed concerning the differences in promoting global health versus dietary interventions in secondary prevention programs, when overt symptoms have already materialized leading to the diagnosis of significant disorders. In these conditions, the holistic/global approach of the EAT commission (3) should be considered apart, and the considerations already mentioned for the glucose/insulin axis (34) taken as prescriptive of an individualized approach.

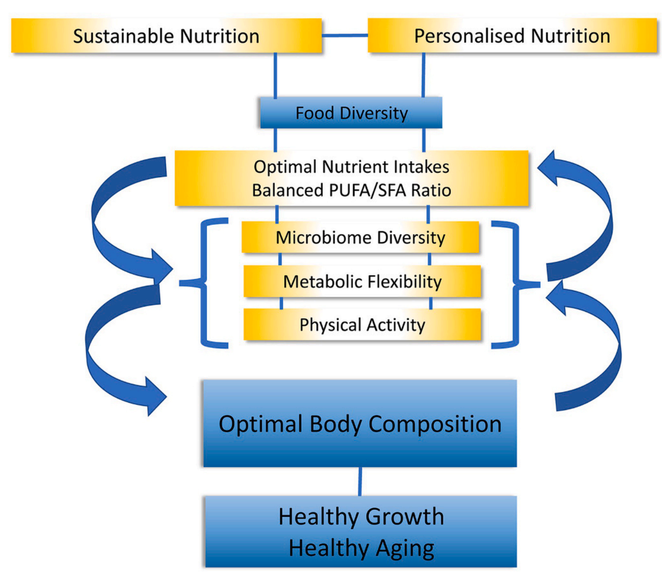

Fig. 2. Food diversity represents a valid strategy for both sustainable and personalized nutrition. Furthermore, it may contribute to maintain the homeostatic control of body composition and thereby healthy growing and aging through the prevision of guaranteeing a balanced nutrient intake, microbiome diversity, metabolic flexibility and physical fitness.

Declaration of Competing Interest

C.A. received research funding from Soremartec Italia, S. Boccia, P. M. Mannucci and A. Astrup are independent members of the Sustainable Nutrition Scientific Board supported by Soremartec. A Astrup is also on Scientific Advisory Board on WW, New York, USA; RNCP, Marseilles, France; Gelesis, Boston, USA, and International Scientific Egg Board, and is currently employed as director at the Novo Nordisk Foundation, Denmark.

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