PERSPECTIVE

Perspective: Darwinian Applications to Nutrition—The Value of Evolutionary Insights to Teachers and Students

Eirik Garnås
Institute of Health, Oslo New University College, Oslo, Norway

ABSTRACT

Evolutionary biology informs us that the living world is a product of evolution, guided by the Darwinian mechanism of natural selection. This recognition has been fruitfully employed in a number of issues in health and nutrition sciences; however, it has not been incorporated into education. Nutrition and dietetics students generally learn very little or nothing on the subject of evolution, despite the fact that evolution is the process by which our genetically determined physiological traits and needs were shaped. In the present Perspective article, 3 examples of topics (inflammatory diseases, nutrition transition, and food intolerance) that can benefit from evolutionary information and reasoning are given, with relevant lines of research and inquiry provided throughout. It is argued that the application of evolutionary science to these and other areas of nutrition education can facilitate a deeper and more coherent teaching and learning experience. By recognizing and reframing nutrition as an aspect and discipline of biology, grounded in the fundamental principle of adaptation, revelatory light is shed on physiological states and responses, contentious and unresolved issues, genomic, epigenomic, and microbiomic features, and optimal nutrient status and intakes. *Adv Nutr* 2022;13:1431–1439.

Statement of Significance: Evolution is not routinely taught or considered as part of study programs in nutrition. The paper specifically addresses this deficiency and suggests areas in which evolutionary biology may be fruitfully employed.

Keywords: evolution, natural selection, nutrition, Darwin, evolutionary medicine, diet, evolutionary health, nutrition transition, mismatch

Introduction

A core axiom of biology is that organisms are adapted to particular environmental circumstances and exposures as a result of evolution via natural selection. Nutrition represents a central feature of the conditions of life for all organisms; hence, Darwin's lessons have obvious implications for the teaching of this subject. Yet, evolution is not regularly taught as part of nutrition programs. In a 2018 survey of 2039 nutrition and dietetics professionals and students, 98% of the 1710 participants who could recall reported having received limited or no information about evolution as part of their education (1). However, the majority were of the opinion that an understanding of evolution can aid in the field of nutrition and dietetics.

These findings are in line with the experiences of this author, who is nutritionally trained and now teaches at a higher education institution. A primary purpose of the educator is to endow students with the best possible tools and practices for making sense of and utilizing the subject at hand. In this sense, it appears amiss to overlook or skip over evolution in nutrition-related affairs.

The theoretical basis and rationale for evolution-oriented nutrition and medicine have been extensively reviewed over the most recent decades (2–17). However, to the author's knowledge, no published report details attempts at incorporating this knowledge into nutritional curricula and teaching. In this paper, 3 examples of the application of evolutionary

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Address correspondence to EG (e-mail: eirik.garnas@oslonh.no).

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insights will be discussed, with the purpose of informing educators (e.g., teachers, clinicians, coaches) and learners (e.g., nutrition and medical students, health professionals, laypeople with a keen interest in nutritional matters) about the usefulness of such insights for the understanding of diet and health.

Inflammatory Diseases

Over the most recent decade it has become clear that inflammation is a central etiological factor in many of the diseases and health disorders of the modern world, including cardiovascular disease, obesity, depression, and Alzheimer disease (9, 10, 18–22). This knowledge is now gradually becoming incorporated into nutrition curricula, largely as a result of the recognition that nutrition is an important modulator of the immunological condition (9, 10, 23, 24). Whereas a healthy diet can contribute to homeostasis, a diet with unfavorable nutritional characteristics can lead to chronic inflammation through a number of mechanisms, such as by causing gut dysbiosis, buildup of arterial plaque, and excess adipose tissue (9, 10, 18, 21, 23, 24).

Inflammation is a conserved response, integral to organismal defense and survival. Through evolutionary thinking, one arrives at the conception that the suite of behaviors and physiological responses commonly seen in conjunction with inflammatory responses serves (or at least served) a Darwinian purpose. This recognition has been used to explain various phenomena and conditions seen in association with inflammation, such as depression (22) and insulin resistance (9). In a classroom setting, this type of adaptationist thinking can help students connect and understand behaviors and symptoms. It serves as a shared starting point for interesting and fruitful discussion.

In my own comprehension and teachings on the matter, I have found basic evolutionary biology to be of great value, particularly with respect to mental disorders and obesity. The latter is of particular relevance to nutrition students and is usually a core theme of study programs in diet and health. By thinking evolutionarily, one moves away from the age-old mantra of "eating less and moving more" into deeper discussions, revolving around ultimate explanations for the physiological and behavioral abnormalities that exist in obesity. As a disorder characterized by low-grade chronic inflammation, one would expect to see symptoms and behaviors associated with increased inflammation, such as fatigue and physical inactivity (25, 26). Once presumably adaptive, such responses could help explain a lack of desire to exercise in the current obesogenic and inflammatory climate by suggesting that inactivity is not solely a cause of obesity but may, in fact, be a result of it. This theory, which is backed by animal studies (27, 28), has obvious implications for health professionals counseling overweight patients, or individuals training to take up such a role.

Nutrition Transition

As part of nutrition and dietetics studies, students learn about nutritional components and their role in health and disease. As a central theme of undeniable importance, one would expect this endeavor to include evolutionary considerations and discussions. However, this is often not the case. Typically, the focus is largely or solely on the physiological effects of the nutrient under scrutiny, as well as experimental investigations of the links between the nutrient and different health outcomes. While useful, such approaches are limited in their scope, and sometimes also yield contradictory results, generating incoherence and confusion. Simply said, under the current paradigm, students learn how things are, but not why they are that way. Physiological responses to nutritional inputs are explored and discussed, often in depth; however, ultimate explanations for the effects are only rarely touched upon. By adding an evolutionary approach to the investigative repertoire, teachers and students can attain a deeper and more complete understanding and appreciation of the matter.

Examples

Omega-3 fatty acids.

Nutrition students learn that the long-chain omega-3 (n–3) fatty acids EPA and DHA are beneficial to brain development and chronic disease prevention; however, the evolutionary rationale for why that is, is generally not conveyed. This undermines the students' ability to recognize the fundamental basis, strength, and validity of what they are learning. For such a recognition to take place, one would arguably have to inform the students about the intake of the fatty acids in human evolution, intertwined with the concept of adaptation.

The discovery that long-chain omega-3 fatty acids, and in particular DHA, are key functional and structural components of human brain tissue suggests that these compounds were a significant part of hominin diets during the evolutionary expansion of the hominin brain, which more than tripled in size during the past 3.5 million years (29, 30). Increased consumption of high-quality energy-dense animal foods, and perhaps over time also cooked underground storage organs (31), provided the necessary substrate to build and fuel a larger, more energy-demanding brain (32, 33).

It has been estimated that human beings are evolutionarily accustomed to a ratio of n–6 to n–3 fatty acids of approximately 1 to 1, while the intake as part of current Western diets is in the range of 10 to 1 to 20–25 to 1 (34). This dramatic shift results from both an increased consumption of n–6 fatty acids and a decreased intake of n–3 fatty acids. Relative to farmed and industrially produced animal foods, the tissue of wild animals generally contains significantly more n–3 PUFAs as a percentage of total fat, but lower quantities of n–6 PUFAs. As an example, in a 2020 Norwegian study, farmed Atlantic salmon was found to have an n–6 to n–3 ratio more than 10 times higher than that of wild salmon (0.7 vs. 0.05) (35). As a proportion of total fat, long-chain n–3 fatty acids constituted 8.9% in the farmed salmon, but 24.1% in the wild variety (35). Similar patterns have been observed in the meats of wild versus domesticated terrestrial animals (36, 37), and this helps account for some of the estimated difference in

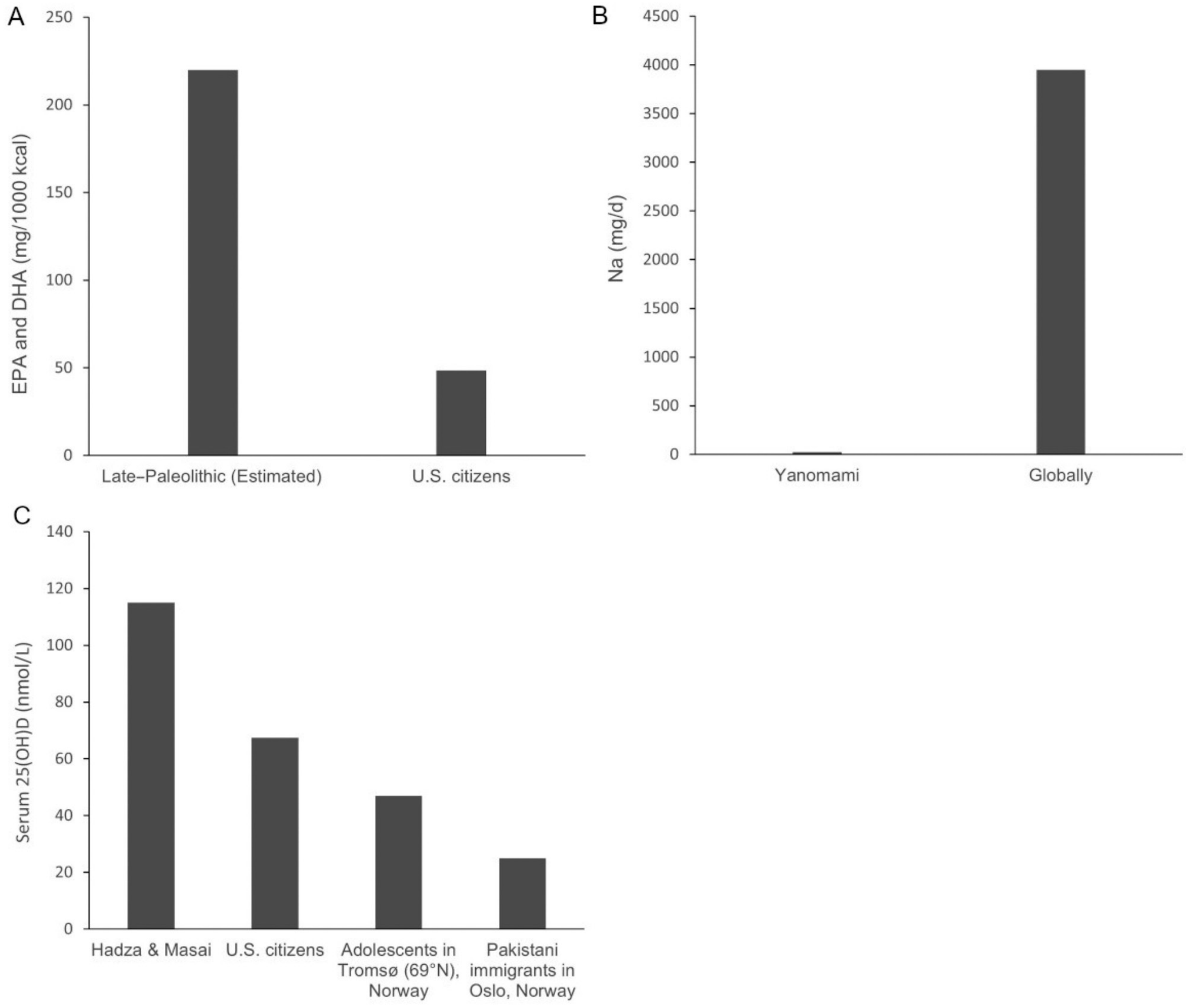

FIGURE 1 (A–C) Intake or status of selected nutrients in different populations relevant to discussions of nutrition transition. All values are statistical means. Data sources: sodium (49, 52), n–3 (102, 103), vitamin D (66–69). 25(OH)D, 25-hydroxyvitamin D.

the n–3 fatty acid content of modern compared to Paleolithic diets (**Figure 1**A). A long-held belief is that human evolution principally occurred in relatively dry, savannah-like environments; however, this assumption has not gone unchallenged, with some researchers proposing a greater significance of land-water ecosystems and marine food sources (12, 38). A higher intake of aquatic foods would have resulted in even higher intakes of n–3 fatty acids, with a larger discrepancy between current and ancestral intake values. Low DHA has been linked with deficient neural and mental development in children, neurodegenerative disease in the elderly, and reduced brain volume across the lifespan (30, 39–41). This can be understood on the basis of evolutionary dietary insights.

Sodium.

In the case of long-chain n–3 fatty acids, there is a general consensus of healthfulness within the nutritional community. However, in certain other cases, varying levels of controversy exist. Here, evolutionary perspective may be of even greater importance, as it can help settle disputes. One such instance is dietary salt. The majority of authors and publications contend that current sodium (Na) intakes far exceed healthful levels, and this is also the position of public health agencies (2, 42–44). However, this stance has not gone unchallenged, with some authors positing that the efforts aimed at markedly lowering dietary salt intakes are misguided (45–48). An evolutionary perspective yields great clarity in this matter by shedding light on the sodium intake levels that have conditioned human genetics and physiology. Information about ancestral and traditional diets suggests that the levels experienced by our naturally living ancestors would have been many times lower than current exposures (3, 42, 49–51). At the far end of the spectrum are the Yanomami hunter-gatherers living in the Amazonian jungle, who have been reported to take in less than one-hundredth of the current global average of approximately 4 g Na/d

(Figure 1B) (49, 52). In combination with the recognition that wild, unprocessed foods are naturally low in sodium, this type of data clearly refutes the notion that we are adapted to high salt intakes. High sodium has been linked with disorders such as hypertension, heart disease, and autoimmunity (42, 44, 53–56)—conditions that are rare or absent among hunter-gatherers and traditional horticulturalists consuming low-salt diets (11, 53).

Vitamin D.

Another instance of discourse concerns vitamin D, which is important for calcium homeostasis and bone mineralization, immune function, and disease prevention (57–59). It is obtained through diet and sunlight and commonly measured as the concentration of 25-hydroxyvitamin D [25(OH)D] in serum. A concentration of 50 nmol/L has been used as a threshold for sufficiency (60, 61). However, a number of vitamin D researchers have proposed, and now operate on the basis of, a higher recommendation (typically >75 nmol/L) (57, 58, 62–65). The contention that increased concentrations are required for function and health is partly based on evolutionary insights. As a species whose evolution largely took place in a warm climate, with considerable UV radiation, one would expect that we are evolutionarily accustomed and adapted to high vitamin D levels. This notion is supported by data showing that traditionally living groups in Africa maintain a mean vitamin D concentration of 115 nmol/L (66), a concentration that greatly exceeds those measured in people living under more industrialized conditions (Figure 1C) (58, 67, 68). Vitamin D deficiency is particularly common and severe among dark-skinned individuals taking up residence in colder areas of the world, where there is less sunlight than closer to the equator (69–71). This is a classic example of mismatch—a core concept in evolutionary medicine that refers to a discrepancy between a trait (in this case, skin color) and an aspect of the environment (in this case vitamin D–generating UV radiation). Skin pigmentation has been under strong selection in recent human evolution (72), with ethnic populations at higher latitudes exhibiting lighter skin tones compared with the dark African complexion. This trait is strongly associated with sun exposure (72), with dark eumelanin-rich skin providing a natural barrier, inhibiting adequate vitamin D synthesis in regions with low levels of UV light (71, 73–75). The case highlights that a recognition of evolutionary adaptation and discordance is critical with respect to identifying nutritional risks and needs of different population groups.

General considerations

In the feeding of other animal species (e.g., zoo animals), randomized controlled trials are not conducted to determine what is an appropriate diet; rather, optimal diet composition is inferred from the animals' nutrition in their natural habitat (76–80). In humans, such an approach is complicated by the fact that hominin evolution occurred (and continues to occur) in a variety of ecological circumstances and niches; hence, the dietary intakes of our ancestors would have varied across time and space. However, Africa is of central importance to our genus and species, as a place of origin and development (81–83). Furthermore, dietary reconstructions and analyses show that both preagricultural and preindustrial diets have a number of characteristics in common that unify them and separate them from modern nutritional practices (2, 9, 11, 84). The commonalities in our dietary past suggest that, although differences pertaining to recent genetic and epigenetic change, personal preference, physical activity levels, and health status, call for some customization on the individual and group level, there exists a shared set of fundamental nutritional requirements for our species.

In contemporary nutrition, nutritional adequacy is frequently confused with nutritional optimality. Modern nutritional science has made significant strides with respect to elucidating the minimal micronutrient dosages required to avoid overt deficiency; however, it is a considerable way off from defining what constitutes an optimal intake. Moreover, it has primarily been concerned only with a small subset of the more than 26,000 distinct biochemicals found in our food (85). Mapping and defining appropriate intake levels of all of these compounds through standard nutritional research procedures is difficult, if not impossible. The Darwinian concept of adaptation, coupled with information about ancestral human diets, may serve as a guiding principle by which to make inferences and generate hypotheses.

As a student, and now as an educator, I have found information about nutritional transitions to be particularly useful with respect to understanding and conveying the broader patterns of diet and health. By gaining insight into these patterns, students attain a more fundamental understanding of nutrition that may better enable them to connect different facts and subjects, discriminate between solid and weak information, and gain confidence in their knowledge. It shifts the focus away from single-nutrient explanations towards a more holistic view in which the organism is connected to the totality of nutritional circumstances and inputs under which its inherited biology evolved.

Food (In)tolerance

Perhaps the most well-known and frequently cited example of dietary adaptation is the fairly recent selection for lactase persistence (86–88). This case clearly highlights the relevance of evolutionary theory to nutrition. In the absence of such knowledge, the concept of adaptation is not well defined and may be taken to mean a range of things more or less inaccurate, vague, and/or crude. Evolutionary biology informs us that adaptation is specific (in this case, involving the enzymatic hydrolyzation of the disaccharide lactose into its constituent parts, galactose and glucose) and occurs at the genetic level as a result of the impact of the relevant allele and trait on organismal reproductive success under the current environmental conditions. A number of genes and traits are involved in mediating the effects of an environmental (e.g., dietary) exposure on the body, health only matters insofar as it affects survival and reproduction, and if the environment

TABLE 1 Engaging the exploratory Darwinian: open-ended questions for educational purposes

Inflammatory diseases	Nutrition transition	Food (in)tolerance
What is the fundamental purpose of the body's inflammatory responses?	How has our dietary environment changed over the past 10 million years?	Is there an evolutionary explanation for food sensitivity and allergy?
What do the characteristics, regulation, and actions of the immune system inform us about our evolutionary past?	What was the impact of the agricultural and industrial revolutions on our diets, and what were the health effects of these changes?	What is the reported incidence of different types of food allergies and sensitivities, and does this incidence track with any environmental exposures?
Which foods and nutritional components have been shown to induce inflammation, and which have been shown to be ameliorating?	What are the primary differences between current Western diets and hunter-gatherer diets, both with respect to food intake and nutritional characteristics?	Which, if any, exposures have been causally linked to food intolerance, and have these exposures changed over time?
Looking at our diet, what are the chief differences between ancestral and modern diets with respect to the proinflammatory potential?	What are the principal health differences between primitive and urbanized groups, and how do these relate to diet?	What drove the evolution of lactase persistence?
How can we reduce the inflammatory load of our current diets and food environment?	What do experimental studies tell us about the health effects of different types of diets, common to different parts of our evolution?	What does the evolution of our diets inform us about what types of foods and nutritional components we presumably tolerate well?
How do inflammatory diseases affect nutritional needs, and is there an evolutionary explanation for this impact?	How did ancestral nutritional environments inform the evolution of our appetite and dietary preferences?	How may the gut microbiota participate in the breakdown of otherwise nondigestible food components, and how can this be explained from a Darwinian point of view?
How does inflammation affect bodily function and behavior, and what could be potential Darwinian explanations for these effects?	What are some unanswered questions with respect to the evolution of the human diet?	What do evolutionary insights inform us about prevention and treatment of food allergies and intolerances?

changes, the characteristic may no longer have the same fitness value. This lends a more nuanced perspective than what is attained through more superficial teachings of the subject of lactose intolerance.

In the new microbiota-heavy nutritional era, evolutionary understanding appears more important than ever. It is now recognized that adaptation may not only take place within the slow-evolving human genome but also within the fast-evolving human microbiome. In the case of lactose intolerance, several studies have investigated this phenomenon, finding that lactose-digesting lactic acid bacteria in the form of fermented dairy products or supplements, and/or lactose feeding, reduce symptoms of lactose intolerance (89–92). Colonic adaptation (i.e., expanded lactose-digesting capabilities of the microbial ecosystem of the large intestine) has been offered as a chief explanation for the improved tolerance in such interventions (92, 93). Such changes are hard to fully grasp and appreciate in the absence of ecological and evolutionary insights.

The importance of this concept is not restricted to lactose, but rather extends into the larger realm of nutrition. This follows from the recognition that lactose is only one of many nutritional substrates that, to varying degrees, are accessed and utilized by members of the resident intestinal microbiota. In particular the broad spectrum of nondigestible (to the human host) carbohydrates found in plant foods are pertinent in this regard, as they constitute the majority of the nondigestible portion of the human diet (94, 95). This group of compounds has been a part of the human diet for millions of years (51, 82, 96); hence, there is no evolutionary reason to suspect that it is not compatible with our biology. However, in irritable bowel syndrome (IBS), intolerance is frequently observed, a recognition that has spurred the use of dietary exclusion protocols [e.g., the low-FODMAP (-fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diet]. While having proved effective for alleviating symptoms in many patients (97), this approach does not address the associated gut dysbiosis that has been documented in IBS (98) or microbiota–diet adaptation. As a matter of fact, stringent exclusion approaches would be expected to undermine such efforts, by robbing beneficial biota of their primary fuel substrates. If one were to apply the adaptation principle invoked in the case of lactose, approaches aimed at microbiota diversification and manipulation appear reasonable and worthy of further investigation, beyond what has already been conducted. Bacterial communities adapted to feeding and cross-feeding on the relevant substances, and that do not cause the generation and accumulation of noxious products, would be required for proper digestion and nutritional utilization. Organisms that have demonstrated digestive capability—for example, in an anaerobic fermented food ecosystem—appear ideal candidates as "probiotics." In this regard, vegetable and/or fruit ferments in which some degradation

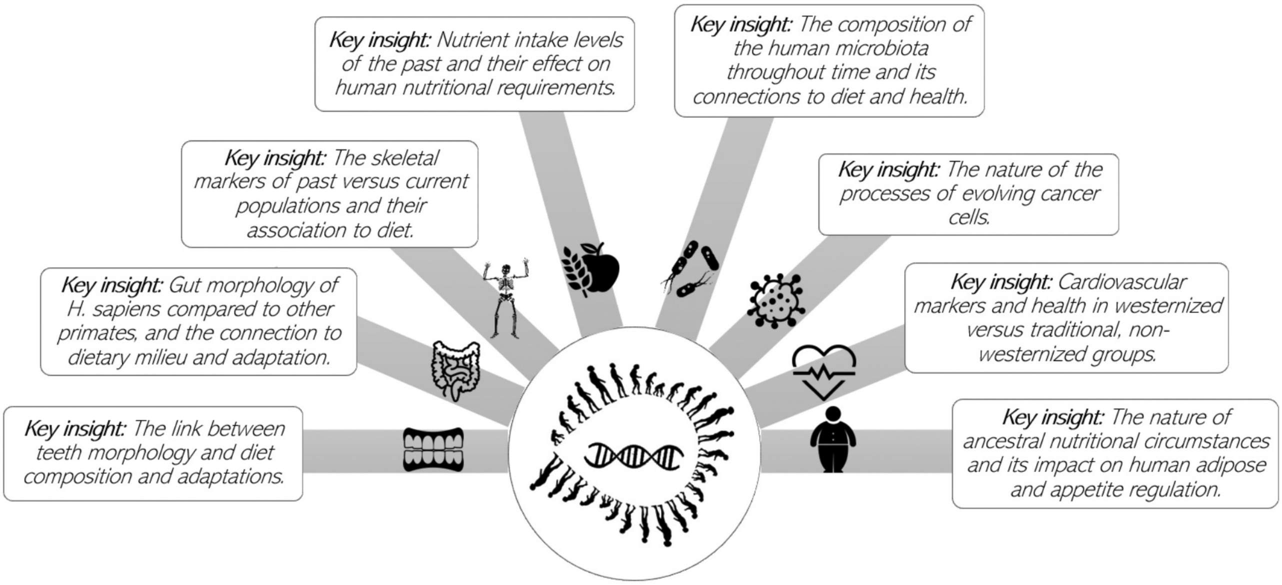

FIGURE 2 Evolution as connective tissue in nutrition. A selection of core subjects that find support and nurture in fundamental insights.

of plant fibers is achieved would be promising as therapeutic products.

IBS is a prevalent disorder, estimated to be affecting about 1 in 10 people globally (99), and complaints covered by this umbrella, including food intolerance and sensitivity, bloating, flatulence, and irregular bowel habits, are among the most frequently encountered issues by dietitians. This signifies that rigorous and thorough science and education are of great importance in this area. An evolutionary perspective lends valuable insight by spotlighting the dietary and microbial elements and inputs that have informed our biological development, the nature of evolution and adaptation within both our human and microbial selves, and areas in which discussion and research are required and warranted.

A set of evolutionary inquiries that can facilitate a deeper understanding of inflammatory diseases, nutrition transition, and food (in)tolerance is shown in **Table 1**.

Concluding Remarks

The year 2019 marked the 160th anniversary of the publication of Darwin's groundbreaking work *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life* (100). In that time, his fundamental insights have become embedded into the very core of natural science. In biology, evolution, and in particular, the mechanism of natural selection, is the great unifier and explainer, as epitomized by the famous quote by evolutionary biologist Theodosius Dobzhansky: "Nothing in biology makes sense except in the light of evolution" (101). In dealing with living organisms, nutrition and health sciences are undeniable intrinsically linked with biology. Yet, teachings on the subject have largely been dissociated from it. As a result, many within the field possess at best a rudimentary understanding of the fundamental laws and principles that govern life on Earth. A greater incorporation of evolutionary biology into nutritional curricula is required to correct this deficiency.

In this paper, 3 examples of educational utility have been discussed. The experiences of the author are that the described evolutionary facets do not demand a complete curricular reorganization but rather may be implemented into existing course material and education, with the purpose of facilitating deeper and more coherent thinking and learning. However, students should ideally have a basic understanding of evolution, and in particular, selection and adaptation, when entering the themes. An introductory course or classes in evolutionary biology may serve the students very well, considering the universality of evolutionary principles to life processes and characteristics. Looking beyond the 3 examples provided in this text, evolutionary inquiry and thinking may be fruitfully employed in a range of subjects, from skeletal health to cancer development to gastrointestinal physiology (**Figure 2**). A list of scientific resources that can be utilized for educational purposes is provided as a **Supplemental Appendix**.

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Data Availability

No new data were collected for this article.

References

1. Basile AJ, Schwartz DB, Rigdon J, Stapell H. Status of evolutionary medicine within the field of nutrition and dietetics: a survey of

professionals and students. Evol Med Public Health 2018;2018(1):201–10. doi: 10.1093/emph/eoy022.
2. Cordain L, Eaton SB, Sebastian A, Mann N, Lindeberg S, Watkins BA, et al. Origins and evolution of the Western diet: health implications for the 21st century. Am J Clin Nutr 2005;81(2):341–54.
3. Konner M, Eaton SB. Paleolithic nutrition: twenty-five years later. Nutr Clin Pract 2010;25(6):594–602. doi: 10.1177/0884533610385702.
4. Brunham RC. The genome, microbiome and evolutionary medicine. Can Med Assoc J 2018;190(6):E162–E6. doi: 10.1503/cmaj.170846.
5. Trevathan WR, Smith EO, McKenna J. Evolutionary medicine and health: new perspectives. 1st ed. Oxford (UK): Oxford University Press; 2007.
6. Román-Franco AA. Medicine in the 21st century: towards a Darwinian medical epistemology. P R Health Sci J 2009;28(4):345–51.
7. Eaton SB, Strassman BI, Nesse RM, Neel JV, Ewald PW, Williams GC, et al. Evolutionary health promotion. Prev Med 2002;34(2):109–18. doi: 10.1006/pmed.2001.0876.
8. Gardner C, Cole DC, Ryan L. Public health for the hunter-gatherer in us all. Can J Public Health 2020;111(5):701–4. doi: 10.17269/s41997-020-00341-2.
9. Ruiz-Núñez B, Pruimboom L, Dijck-Brouwer DA, Muskiet FA. Lifestyle and nutritional imbalances associated with Western diseases: causes and consequences of chronic systemic low-grade inflammation in an evolutionary context. J Nutr Biochem 2013;24(7):1183–201. doi: 10.1016/j.jnutbio.2013.02.009.
10. González Olmo BM, Butler MJ, Barrientos RM. Evolution of the human diet and its impact on gut microbiota, immune responses, and brain health. Nutrients 2021;13(1):196. doi: 10.3390/nu13010196.
11. Carrera-Bastos P, Fontes-Villalba M, O'Keefe JH, Lindeberg S, Cordain L. The western diet and lifestyle and diseases of civilization. Res Rep Clin Cardiol 2011;2:15. doi: 10.2147/RRCC.S16919.
12. Kuipers RS, Joordens JC, Muskiet FA. A multidisciplinary reconstruction of Palaeolithic nutrition that holds promise for the prevention and treatment of diseases of civilisation. Nutr Res Rev 2012;25(1):96–129. doi: 10.1017/s0954422412000017.
13. Andrews P, Johnson RJ. Evolutionary basis for the human diet: consequences for human health. J Intern Med 2020;287(3):226–37. doi: 10.1111/joim.13011.
14. Rook GA. 99th Dahlem conference on infection, inflammation and chronic inflammatory disorders: Darwinian medicine and the 'hygiene' or 'old friends' hypothesis. Clin Exp Immunol 2010;160(1):70–9. doi: 10.1111/j.1365-2249.2010.04133.x.
15. Swain Ewald HA, Ewald PW. Natural selection, the microbiome, and public health. Yale J Biol Med 2018;91(4):445–55.
16. Eaton SB, Konner M, Shostak M. Stone agers in the fast lane: chronic degenerative diseases in evolutionary perspective. Am J Med 1988;84(4):739–49. doi: 10.1016/0002-9343(88)90113-1.
17. Kuzawa CW, Thayer ZM. Timescales of human adaptation: the role of epigenetic processes. Epigenomics 2011;3(2):221–34. doi: 10.2217/epi.11.11.
18. Furman D, Campisi J, Verdin E, Carrera-Bastos P, Targ S, Franceschi C, et al. Chronic inflammation in the etiology of disease across the life span. Nat Med 2019;25(12):1822–32. doi: 10.1038/s41591-019-0675-0.
19. Kinney JW, Bemiller SM, Murtishaw AS, Leisgang AM, Salazar AM, Lamb BT. Inflammation as a central mechanism in Alzheimer's disease. Alzheimers Dement (N Y) 2018;4:1, 575–90. doi: 10.1016/j.trci.2018.06.014.
20. Berk M, Williams LJ, Jacka FN, O'Neil A, Pasco JA, Moylan S, et al. So depression is an inflammatory disease, but where does the inflammation come from? BMC Med 2013;11(1):200. doi: 10.1186/1741-7015-11-200.
21. Shah PK, Lecis D. Inflammation in atherosclerotic cardiovascular disease. F1000Research 2019;8:F1000 Faculty Rev–1402. doi: 10.12688/f1000research.18901.1.
22. Miller AH, Raison CL. The role of inflammation in depression: from evolutionary imperative to modern treatment target. Nat Rev Immunol 2016;16(1):22–34. doi: 10.1038/nri.2015.5.
23. Myles IA. Fast food fever: reviewing the impacts of the Western diet on immunity. Nutr J 2014;13(1):61. doi: 10.1186/1475-2891-13-61.
24. Wiertsema SP, van Bergenhenegouwen J, Garssen J, Knippels LMJ. The interplay between the gut microbiome and the immune system in the context of infectious diseases throughout life and the role of nutrition in optimizing treatment strategies. Nutrients 2021;13(3):886. doi: 10.3390/nu13030886.
25. Lacourt TE, Vichaya EG, Chiu GS, Dantzer R, Heijnen CJ. The high costs of low-grade inflammation: persistent fatigue as a consequence of reduced cellular-energy availability and non-adaptive energy expenditure. Front Behav Neurosci 2018;12:78. doi: 10.3389/fnbeh.2018.00078.
26. Lee C-H, Giuliani F. The role of inflammation in depression and fatigue. Front Immunol 2019;10:1696. doi: 10.3389/fimmu.2019.01696.
27. Blaisdell AP, Lau YL, Telminova E, Lim HC, Fan B, Fast CD, et al. Food quality and motivation: a refined low-fat diet induces obesity and impairs performance on a progressive ratio schedule of instrumental lever pressing in rats. Physiol Behav 2014;128:220–5. doi: 10.1016/j.physbeh.2014.02.025.
28. Friend DM, Devarakonda K, O'Neal TJ, Skirzewski M, Papazoglou I, Kaplan AR, et al. Basal ganglia dysfunction contributes to physical inactivity in obesity. Cell Metab 2017;25(2):312–21. doi: 10.1016/j.cmet.2016.12.001.
29. Holloway RL. The evolution of the hominid brain. In: Henke W, Tattersall I, editors. Handbook of paleoanthropology. Berlin, Heidelberg (Germany): Springer Berlin Heidelberg; 2015. p. 1961–87.
30. Bradbury J. Docosahexaenoic acid (DHA): an ancient nutrient for the modern human brain. Nutrients 2011;3(5):529–54. doi: 10.3390/nu3050529.
31. Hardy K, Brand-Miller J, Brown KD, Thomas MG, Copeland L. The importance of dietary carbohydrate in human evolution. Q Rev Biol 2015;90(3):251–68. doi: 10.1086/682587.
32. Milton K. The critical role played by animal source foods in human (Homo) evolution. J Nutr 2003;133(11):3886S–92S.
33. Burini RC, Leonard WR. The evolutionary roles of nutrition selection and dietary quality in the human brain size and encephalization. Nutrire 2018;43(1):19. doi: 10.1186/s41110-018-0078-x.
34. Simopoulos AP. Evolutionary aspects of diet: the omega-6/omega-3 ratio and the brain. Mol Neurobiol 2011;44(2):203–215. doi:10.1007/s12035-010-8162-0.
35. Jensen IJ, Eilertsen KE, Otnæs CHA, Mæhre HK, Elvevoll EO. An update on the content of fatty acids, dioxins, PCBs and heavy metals in farmed, escaped and wild Atlantic salmon (*Salmo salar* L.) in Norway. Foods 2020;9(12):1901. doi: 10.3390/foods9121901.
36. Cordain L, Watkins BA, Florant GL, Kelher M, Rogers L, Li Y. Fatty acid analysis of wild ruminant tissues: evolutionary implications for reducing diet-related chronic disease. Eur J Clin Nutr 2002;56(3):181–91. doi: 10.1038/sj.ejcn.1601307.
37. Rule DC, Broughton KS, Shellito SM, Maiorano G. Comparison of muscle fatty acid profiles and cholesterol concentrations of bison, beef cattle, elk, and chicken. J Anim Sci 2002;80(5):1202–11. doi: 10.2527/2002.8051202x.
38. Crawford MA, Broadhurst CL. The role of docosahexaenoic and the marine food web as determinants of evolution and hominid brain development: the challenge for human sustainability. Nutr Health 2012;21(1):17–39. doi: 10.1177/0260106012437550.
39. Innis SM. Dietary omega 3 fatty acids and the developing brain. Brain Res 2008;1237:35–43. doi: 10.1016/j.brainres.2008.08.078.
40. Pottala JV, Yaffe K, Robinson JG, Espeland MA, Wallace R, Harris WS. Higher RBC EPA + DHA corresponds with larger total brain and hippocampal volumes: WHIMS-MRI study. Neurology 2014;82(5):435–42. doi: 10.1212/wnl.0000000000000080.
41. Morton SU, Vyas R, Gagoski B, Vu C, Litt J, Larsen RJ, et al. Maternal dietary intake of omega-3 fatty acids correlates positively with regional brain volumes in 1-month-old term infants. Cereb Cortex 2020;30(4):2057–69. doi: 10.1093/cercor/bhz222.

42. Batuman V. Salt and hypertension: why is there still a debate? Kidney Int Suppl 2013;3(4):316–20. doi: 10.1038/kisup.2013.66.
43. He FJ, Jenner KH, Macgregor GA. WASH—World Action on Salt and Health. Kidney Int 2010;78(8):745–53. doi: 10.1038/ki.2010.280.
44. He FJ, MacGregor GA. A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. J Hum Hypertens 2009;23(6):363–84. doi: 10.1038/jhh.2008.144.
45. DiNicolantonio JJ, Lucan SC. The wrong white crystals: not salt but sugar as aetiological in hypertension and cardiometabolic disease. Open Heart 2014;1(1):e000167. doi: 10.1136/openhrt-2014-000167.
46. Deschênes G. Sodium-not harmful? Pediatr Nephrol 2020;35(9):1771–6. doi: 10.1007/s00467-019-04356-x.
47. Alderman MH. Reducing dietary sodium: the case for caution. JAMA 2010;303(5):448–9. doi: 10.1001/jama.2010.69.
48. Graudal N. A radical sodium reduction policy is not supported by randomized controlled trials or observational studies: grading the evidence. Am J Hypertens 2016;29(5):543–8. doi: 10.1093/ajh/hpw006.
49. Oliver WJ, Cohen EL, Neel JV. Blood pressure, sodium intake, and sodium related hormones in the Yanomamo Indians, a "no-salt" culture. Circulation 1975;52(1):146–51. doi: 10.1161/01.cir.52.1.146.
50. Kurokawa K, Okuda T. Genetic and non-genetic basis of essential hypertension: maladaptation of human civilization to high salt intake. Hypertens Res 1998;21(2):67–71. doi: 10.1291/hypres.21.67.
51. Eaton SB, Konner M. Paleolithic nutrition. A consideration of its nature and current implications. N Engl J Med 1985;312(5):283–89. doi: 10.1056/nejm198501313120505.
52. Powles J, Fahimi S, Micha R, Khatibzadeh S, Shi P, Ezzati M, et al. Global, regional and national sodium intakes in 1990 and 2010: a systematic analysis of 24 h urinary sodium excretion and dietary surveys worldwide. BMJ Open 2013;3(12):e003733. doi: 10.1136/bmjopen-2013-003733.
53. Meneton P, Jeunemaitre X, de Wardener HE, MacGregor GA. Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. Physiol Rev 2005;85(2):679–715. doi: 10.1152/physrev.00056.2003.
54. Min B, Fairchild RL. Over-salting ruins the balance of the immune menu. J Clin Invest 2015;125(11):4002–4. doi: 10.1172/JCI84690.
55. Evans RDR, Antonelou M, Henderson S, Walsh SB, Salama AD. Emerging evidence of an effect of salt on innate and adaptive immunity. Nephrol Dial Transplant 2019;34(12):2007–14. doi: 10.1093/ndt/gfy362.
56. Liu Z, Li SK, Huang CK, Huang CF. A high-sodium diet modulates the immune response of food allergy in a murine model. Nutrients 2021;13(11). doi: 10.3390/nu13113684.
57. Charoenngam N, Holick MF. Immunologic effects of vitamin D on human health and disease. Nutrients 2020;12(7):2097. doi: 10.3390/nu12072097.
58. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357(3):266–81. doi: 10.1056/NEJMra070553.
59. Ze H, Hochberg I. Evolutionary perspective in rickets and vitamin D. Front Endocrinol 2019;10:306. doi: 10.3389/fendo.2019.00306.
60. Institute of Medicine. Dietary Reference Intakes for calcium and vitamin D. Washington (DC): The National Academies Press; 2011.
61. Lucas R, Neale R. What is the optimal level of vitamin D? Separating the evidence from the rhetoric. Aust Fam Physician 2014;43(3):119–22.
62. Vieth R. What is the optimal vitamin D status for health? Prog Biophys Mol Biol 2006;92(1):26–32. doi: 10.1016/j.pbiomolbio.2006.02.003.
63. Krzyścin JW, Guzikowski J, Rajewska-Więch B. Optimal vitamin D3 daily intake of 2000IU inferred from modeled solar exposure of ancestral humans in Northern Tanzania. J Photochem Photobiol B 2016;159:101–5. doi: 10.1016/j.jphotobiol.2016.03.029.
64. Vieth R. Why the optimal requirement for vitamin D3 is probably much higher than what is officially recommended for adults. J Steroid Biochem Mol Biol 2004;89-90(1-5):575–9. doi: 10.1016/j.jsbmb.2004.03.038.
65. Papadimitriou DT. The big vitamin D mistake. J Prev Med Public Health 2017;50(4):278–81. doi: 10.3961/jpmph.16.111.
66. Luxwolda MF, Kuipers RS, Kema IP, Dijck-Brouwer DA, Muskiet FA. Traditionally living populations in East Africa have a mean serum 25-hydroxyvitamin D concentration of 115 nmol/l. Br J Nutr 2012;108(9):1557–61. doi: 10.1017/s0007114511007161.
67. Oberg J, Jorde R, Almås B, Emaus N, Grimnes G. Vitamin D deficiency and lifestyle risk factors in a Norwegian adolescent population. Scand J Public Health 2014;42(7):593–602. doi: 10.1177/1403494814541593.
68. Schleicher RL, Sternberg MR, Lacher DA, Sempos CT, Looker AC, Durazo-Arvizu RA, et al. The vitamin D status of the US population from 1988 to 2010 using standardized serum concentrations of 25-hydroxyvitamin D shows recent modest increases. Am J Clin Nutr 2016;104(2):454–61.
69. Meyer HE, Falch JA, Søgaard AJ, Haug E. Vitamin D deficiency and secondary hyperparathyroidism and the association with bone mineral density in persons with Pakistani and Norwegian background living in Oslo, Norway, The Oslo Health Study. Bone 2004;35(2):412–17. doi: 10.1016/j.bone.2004.04.003.
70. Richard A, Rohrmann S, Quack Lötscher KC. Prevalence of vitamin D deficiency and its associations with skin color in pregnant women in the first trimester in a sample from Switzerland. Nutrients 2017;9(3):260. doi: 10.3390/nu9030260.
71. Åkeson PK, Lind T, Hernell O, Silfverdal SA, Öhlund I. Serum vitamin D depends less on latitude than on skin color and dietary intake during early winter in Northern Europe. J Pediatr Gastroenterol Nutr 2016;62(4):643–9. doi: 10.1097/mpg.0000000000001028.
72. Jablonski NG, Chaplin G. The colours of humanity: the evolution of pigmentation in the human lineage. Phil Trans R Soc B Biol Sci 2017;372(1724):20160349. doi: 10.1098/rstb.2016.0349.
73. Clemens TL, Adams JS, Henderson SL, Holick MF. Increased skin pigment reduces the capacity of skin to synthesise vitamin D3. Lancet North Am Ed 1982;319(8263):74–6. doi: 10.1016/s0140-6736(82)90214-8.
74. Farrar MD, Kift R, Felton SJ, Berry JL, Durkin MT, Allan D, et al. Recommended summer sunlight exposure amounts fail to produce sufficient vitamin D status in UK adults of South Asian origin. Am J Clin Nutr 2011;94(5):1219–24.
75. Libon F, Cavalier E, Nikkels AF. Skin color is relevant to vitamin D synthesis. Dermatology 2013;227(3):250–4. doi: 10.1159/000354750.
76. Jayson S, Ferguson A, Goetz M, Routh A, Tapley B, Harding L, et al. Comparison of the nutritional content of the captive and wild diets of the critically endangered mountain chicken frog (*Leptodactylus fallax*) to improve its captive husbandry. Zoo Biology 2018;37(5):332–46. doi: 10.1002/zoo.21442.
77. Sterling EJ, Dierenfeld ES, Ashbourne CJ, Feistner AT. Dietary intake, food composition and nutrient intake in wild and captive populations of *Daubentonia madagascariensis*. Folia Primatol (Basel) 1994;62(1-3):115–24. doi: 10.1159/000156768.
78. Gaengler H, Clum N. Investigating the impact of large carcass feeding on the behavior of captive Andean condors (*Vultur gryphus*) and its perception by zoo visitors. Zoo Biology 2015;34(2):118–29. doi: 10.1002/zoo.21202.
79. Less EH, Lukas KE, Bergl R, Ball R, Kuhar CW, Lavin SR, et al. Implementing a low-starch biscuit-free diet in zoo gorillas: the impact on health. Zoo Biology 2014;33(1):74–80. doi: 10.1002/zoo.21115.
80. Potter MA, Hendriks WH, Lentle RG, Thomas DV, Minson CJ, Pindur NB. An exploratory analysis of the suitability of diets fed to a flightless insectivore, the North Island brown kiwi (*Apteryx mantelli*), in New Zealand. Zoo Biology 2010;29(5):537–50. doi: 10.1002/zoo.20283.
81. Chan EKF, Timmermann A, Baldi BF, Moore AE, Lyons RJ, Lee S-S, et al. Human origins in a southern African palaeo-wetland and first migrations. Nature 2019;575(7781):185–9. doi: 10.1038/s41586-019-1714-1.
82. Eaton SB. The ancestral human diet: what was it and should it be a paradigm for contemporary nutrition? Proc Nutr Soc 2006;65(1):1–6. doi: 10.1079/pns2005471.
83. Molinaro L, Pagani L. Human evolutionary history of Eastern Africa. Curr Opin Genet Dev 2018;53:134–9. doi: 10.1016/j.gde.2018.10.002.

84. Spreadbury I. Comparison with ancestral diets suggests dense acellular carbohydrates promote an inflammatory microbiota, and may be the primary dietary cause of leptin resistance and obesity. Diabetes Metab Syndr Obesity Targets Therapy 2012;5:175–89. doi: 10.2147/DMSO.S33473.
85. Barabási A-L, Menichetti G, Loscalzo J. The unmapped chemical complexity of our diet. Nat Food 2020;1(1):33–37. doi: 10.1038/s43016-019-0005-1.
86. Gerbault P, Liebert A, Itan Y, Powell A, Currat M, Burger J, et al. Evolution of lactase persistence: an example of human niche construction. Phil Trans R Soc B Biol Sci 2011;366(1566):863–77. doi: 10.1098/rstb.2010.0268.
87. Arjamaa O, Vuorisalo T. Gene-culture coevolution and human diet. Am Sci 2010;98:2, 140–7. doi: 10.1511/2010.83.140.
88. Leturque A, Brot-Laroche E, Le Gall M. Carbohydrate intake. Prog Mol Biol Transl Sci 2012;108:113–27. doi:10.1016/B978-0-12-398397-8.00005-8.
89. Masoumi SJ, Mehrabani D, Saberifiroozi M, Fattahi MR, Moradi F, Najafi M. The effect of yogurt fortified with *Lactobacillus acidophilus* and *Bifidobacterium* sp. probiotic in patients with lactose intolerance. Food Sci Nutr 2021;9(3):1704–11. doi: 10.1002/fsn3.2145.
90. Hertzler SR, Clancy SM. Kefir improves lactose digestion and tolerance in adults with lactose maldigestion. J Am Diet Assoc 2003;103(5):582–7. doi: 10.1053/jada.2003.50111.
91. He T, Priebe MG, Zhong Y, Huang C, Harmsen HJ, Raangs GC, et al. Effects of yogurt and bifidobacteria supplementation on the colonic microbiota in lactose-intolerant subjects. J Appl Microbiol 2008;104(2):595–604. doi: 10.1111/j.1365-2672.2007.03579.x.
92. Hertzler SR, Savaiano DA. Colonic adaptation to daily lactose feeding in lactose maldigesters reduces lactose intolerance. Am J Clin Nutr 1996;64(2):232–6.
93. Forsgård RA. Lactose digestion in humans: intestinal lactase appears to be constitutive whereas the colonic microbiome is adaptable. Am J Clin Nutr 2019;110(2):273–9.
94. Hamaker BR, Tuncil YE. A perspective on the complexity of dietary fiber structures and their potential effect on the gut microbiota. J Mol Biol 2014;426(23):3838–50. doi: 10.1016/j.jmb.2014.07.028.
95. Rowland I, Gibson G, Heinken A, Scott K, Swann J, Thiele I, et al. Gut microbiota functions: metabolism of nutrients and other food components. Eur J Nutr 2018;57(1):1–24. doi: 10.1007/s00394-017-1445-8.
96. Leach JD. Evolutionary perspective on dietary intake of fibre and colorectal cancer. Eur J Clin Nutr 2007;61(1):140–42. doi: 10.1038/sj.ejcn.1602486.
97. Black CJ, Staudacher HM, Ford AC. Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis. Gut 2022;71(6):1117–26. doi: 10.1136/gutjnl-2021-325214.
98. Wang L, Alammar N, Singh R, Nanavati J, Song Y, Chaudhary R, et al. Gut microbial dysbiosis in the irritable bowel syndrome: a systematic review and meta-analysis of case-control studies. J Acad Nutr Diet 2020;120(4):565–86. doi: 10.1016/j.jand.2019.05.015.
99. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. Clin Gastroenterol Hepatol 2012;10(7):712–21, e4. doi: 10.1016/j.cgh.2012.02.029.
100. Darwin C. On the origin of species by means of natural selection, or preservation of favoured races in the struggle for life. 1st ed. London: John Murray; 1850.
101. Dobzhansky T. Nothing in biology makes sense except in the light of evolution. Am Biol Teacher 1973;35:3, 125–29.
102. Cave C, Hein N, Smith LM, Anderson-Berry A, Richter CK, Bisselou KS, et al. Omega-3 long-chain polyunsaturated fatty acids intake by ethnicity, income, and education level in the United States: NHANES 2003–2014. Nutrients 2020;12(7):2045. doi: 10.3390/nu12072045.
103. Eaton SB, Eaton SB, III, Sinclair AJ, Cordain L, Mann NJ. Dietary intake of long-chain polyunsaturated fatty acids during the paleolithic. World Rev Nutr Diet 1998;83:12–23. doi: 10.1159/000059672.