Review

MOLECULAR METABOLISM

The changing microbial landscape of Western society: Diet, dwellings and discordance

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ABSTRACT

Background: The last 50–100 years has been marked by a sharp rise in so-called "Western-diseases" in those countries that have experienced major industrial advances and shifts towards urbanized living. These diseases include obesity, type 2 diabetes, inflammatory bowel diseases, and food allergies in which chronic dysregulation of metabolic and/or immune processes appear to be involved, and are likely a byproduct of new environmental influences on our ancient genome. What we now appreciate is that this genome consists of both human and co-evolved microbial genes of the trillions of microbes residing in our body. Together, host–microbe interactions may be determined by the changing diets and behaviors of the Western lifestyle, influencing the etiopathogenesis of "new-age" diseases.

Scope of review: This review takes an anthropological approach to the potential interplay of the host and its gut microbiome in the post-industrialization rise in chronic inflammatory and metabolic diseases. The discussion highlights both the changes in diet and the physical environment that have co-occurred with these diseases and the latest evidence demonstrating the role of host–microbe interactions in understanding biological responses to the changing environment.

Major conclusions: Technological advances that have led to changes in agriculture and engineering have altered our eating and living behaviors in ways never before possible in human history. These changes also have altered the bacterial communities within the human body in ways that are seemingly linked with the rise of many intestinal and systemic metabolic and inflammatory diseases. Insights into the mechanisms of this reciprocal exchange between the environment and the human gut microbiome may offer potential to attenuate the chronic health conditions that derail quality of life. This article is part of a special issue on microbiota.

Keywords Microbiome; Circadian; Inflammation; Western diet; Short-chain fatty acids

1. INTRODUCTION

The early 19th century marked the beginning of the Industrial Revolution in the United States, resulting in both cultural and economic shifts. Manufacturing and industry have changed how humans interact with and behave in the physical environment. Eating behavior and preferences have shifted toward convenience, packaging, and taste. Sleep can now be manipulated by artificial lighting, and labor and habitation have become primarily indoor activities. While industrialization and modern medicine have nearly eliminated deaths from acute infectious diseases and increased average lifespan, they have also created a new era of disease marked by sub-acute, chronic dysregulation of metabolic and immunological processes. Diabetes, obesity, food allergies, and inflammatory bowel diseases are among the negative health consequences whose increase in prevalence during industrialization has been linked to modern diets and our sterile, manufactured habitats [1,2].

Multiple factors are involved in the rise of these diseases. However, there is a growing appreciation for the contribution of an individual's native bacterial milieu to the complexity of these disorders. The bacteria in the human body and the genes they possess, the collective microbiome, play important developmental roles in educating the intestinal immune system [3]. Specific species of bacteria are required for immune development, and, in the early stages of life, these bacteria are maternally and environmentally acquired [4]. It is therefore important to consider whether alterations in our physical environment in recent history have led to a shift in bacterial communities. The relative role of our microbiome in human health and disease and its adaptive evolution to "Westernization" will likely hold important, identifiable clues to the etiopathogenesis of modern diseases.

2. EVOLUTION OF THE WESTERN DIET AND MICROBIAL SELECTION

2.1. Western dietary trends

Evolution represents an ongoing interaction between an individual's genome and environment over the course of multiple generations. When the environment remains relatively constant, genetic traits that represent optimal survival for the population as a whole are maintained. As environmental conditions shift, directional selection moves the average population genome toward a new norm. Individuals possessing

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the previously optimal genome experience evolutionary discordance between genome and environment, which manifests phenotypically as increased morbidity and mortality, and reduced reproductive fitness [5]. There is evidence that the significant dietary changes that occurred with the introduction of agriculture and animal husbandry occurred too recently on an evolutionary time scale for the human genome to successfully adapt [6]. The result of this discordance between our ancient, genetically determined biology and the dietary patterns of today's Western populations is the myriad of so-called "new age" diseases characterized by chronic states of metabolic derangement and misguided immune responses [7–9].

Before the development of agriculture and animal husbandry, early ancestral, humans' dietary choices were limited to minimally processed, wild plant and animal foods. However, with the initial domestication of plants and animals, the original nutrient characteristics of these formerly wild foods changed, subtly at first, but more rapidly with advancing technology after the Industrial Revolution [10]. Furthermore, the advent of agriculture introduced novel foods as staples for which the human genome had little evolutionary experience. Dairy foods, cereals, refined sugars, refined vegetable oils, alcohol, salt, and fatty domesticated meats were not present in the pre-agricultural diet. They now make up the primary constituents of the post-agricultural, typical Western diet and are consumed in caloric excess. The amounts of the three major macronutrients, carbohydrates, fats, and proteins, became skewed in the Western diet, and their composition has dramatically changed [11].

In the United States for example, the per capita consumption of all refined sugars in 2000 was 69 kg, whereas in 1970 it was 56 kg [12]. This 30-year trend for increased sugar consumption is representative of a much larger worldwide trend. The per capita refined sucrose consumption in England, for example, rose steadily from 6.8 kg in 1815 to 54.5 kg in 1970 [13]. Similar trends have been reported during the Industrial Era for other nations of northern Europe [14]. These changes in sugar consumption are not only reflected in quantity, but also in the increasingly processed nature of the sugars consumed. With the advent of chromatographic fructose enrichment technology in the late 1970s, it became economically feasible to manufacture high-fructose corn syrup (HFCS) in mass quantity [15]. In 1970 of the 56 kg sugar consumed per capita, 46.2% came from sucrose and 0.2% came from HFCS, while in the year 2000 of the 69.1 kg per capita, 29.8% came from sucrose and 28.9% came from HFCS [12]. With industrialization came not only the processing and refinement of sugars, but also of fats, and is most evidenced by the use of refined vegetable oils.

During the period from 1909 to 1999, a striking increase in the use of vegetable oils occurred. Per capita consumption of salad and cooking oils, shortening, and margarine increased 130%, 136%, and 410%, respectively [11]. These trends were made possible by the industrialization and mechanization of the oil-seed industry. The advent of mechanically driven steel expellers and hexane extraction processes allowed for greater world-wide vegetable oil productivity, whereas new purification procedures allowed for the use of nontraditionally consumed oils, such as cottonseed [16]. New manufacturing procedures allowed vegetable oils to take on atypical structural characteristics [17]. As a consequence, the large-scale addition of refined vegetable oils to the world's food supply after the Industrial Revolution profoundly altered many aspects of fat intake.

2.2. Gut microbiome responses to Western vs. non-Western diets

These technological advances of the food industry were likely unparalleled in any other point of our biological history, and, therefore, it is likely not a coincidence that metabolic and inflammatory diseases of Western populations have rapidly increased. If discordance between genes and environment occurs in the host, the same is likely true of the microbiota in the gut environment. Indeed, evidence for discordance in the gut microbiome is supported by multiple studies exploring microbiomes from native populations on multiple continents with indigenous dietary practices. Yatsunenko et al. demonstrated that the gut microbiota of individuals in the United States is far less diverse than the microbiota of native Amazonian and Malawian populations. Increased bacterial diversity in the gut is generally accepted as a marker of health. Not only is there less microbial diversity in the American gut, the composition of bacteria is different as well [18]. Strikingly, the microbial differences in richness and diversity emerge post-weaning upon adaptation to the native diet [18].

Similarly, a recent study compared the microbiomes of the BaAka pygmies of Central Africa, a native hunter–gatherer population, to their neighboring agriculturist Bantu community representing a "transitionary" dietary pattern that is a combination of an ancient hunter–gatherer diet and the modern day diets of industrialized nations. While a relatively small study cohort of 29 individuals from each group, sequencing data revealed that the gut microbiota composition of the BaAka pygmies is more similar to the known composition of wild primates, whereas the Bantu composition is more similar to Western microbiomes [19]. The authors suggest that these populations may elucidate changes that occurred in the human gut microbiome in response to evolving agricultural and dietary practices and the resulting modern day Western diet.

One possible mechanistic underpinning for these potentially deleterious microbial changes may be decreased consumption of microbially accessible carbohydrates (MACs) in the form of fiber-rich foods. Sonnenburg et al. demonstrated that in rodents, decreased consumption of MACs over successive generations could result in complete loss of entire genera or species of microbiota, highlighting that "unhealthy" microbiomes can be permanently inherited if diets continue to lose their fiber component. Even more striking was the finding that the re-introduction of MACs into the diet was unable to recover the lost species to a greater and greater degree with each subsequent generation, suggesting extinction from the gut microbiota [20,21]. The long-term consequences of specific species extinction are not known, but a meaningful implication would be a decrease in bacterially-produced short-chain fatty acids (SCFA's) over time.

It has been well-described that the microbiota which can metabolize MAC's produce SCFAs of which acetate, butyrate, and propionate are the dominant forms [22]. To the microbiota, these are a necessary waste product to balance the redox equivalent product in the gut anaerobic environment [23], but to the intestinal colonocytes, SCFAs are the primary source of energy, comprising 60–70% of their energy supply [24]. In germ-free mice, colonocytes exhibit a deficiency in mitochondrial respiration and undergo autophagy. However, in a study monocolonizing germ-free mice with *Butyrivibrio fibrisolvens*, a butyrate-produced bacteria, the colonocytes were rescued from both the mitochondrial deficiency and autophagy [25]. Therefore the gradual loss of SCFA's over generations could result in serious defects in gut health. The clinical importance of these SCFAs to intestinal health and homeostasis has been demonstrated in several studies in which administration of SCFA's orally or via direct irrigation to patients with ulcerative colitis, Crohn's disease, and antibiotic-resistant diarrhea has shown amelioration of symptoms [26–28]. While more studies are needed, collectively, these data suggest that the shift away from the higher MAC diets of our ancestors may result in the loss of critical gut functions conferred by SCFA-producing bacteria.

Beyond the gut, SCFA's play a role in systemic metabolism, potentially as signaling molecules. Rodent studies have demonstrated increased

