Evolutionary Medicine and the Human Microbiome: A Symbiotic Relationship

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Abstract

Darwinian medicine, also Known as evolutionary medicine, integrates ecological and evolutionary ideas to guide, indicate, and inevitably improve research into medicine, public safety, and healthcare. Evolutionary medicine has been becoming more prevalent in the medical field in the last few years. The community of organisms that live in and communicate with the human body is termed the human microbiota. A shockingly high number of illnesses among humans have been related to different capabilities of the microbiome and specific microbiome-focused medications have proven extraordinary efficiency in treating specific ailments, such as repeated Clostridium difficile infection. This study aims to review the literature on the relationship between natural goods, conventional medication, and modern medication. Focusing on the evolutionary causes of human illnesses and how they evolve all through time, evolutionary healthcare (EM) is a rapidly expanding subject. The bacteria that make up the gut starts to form from birth and is typically done in three years in healthy people, however environmental influences, mainly the quantity and composition of the cuisine and antibiotic treatment, can affect the formation process. Researchers in evolutionary medicine refer to certain outcomes as evolutionary mismatches. Mismatch issues occur when organisms live in habitats in which they cannot be sufficiently adjusted, mainly as a result of dramatic shifts in the environment. The gut microbiome is now known to affect practically every other organ, including the brain and reproductive systems. The history and current understanding of gut-brain axis bidirectional communication in countless mental health disorders, with a focal point on anxiety and depression, whose prevalence has increased by more than 50% in the last three decades, with the COVID-19 pandemic being the most significant risk factor in recent years.

Keywords: Medicine, Human Microbiome, Gut-Brain Axis, Antibiotics, Mental Health

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Introduction

Darwinian medicine, also known as evolutionary medicine, combines ecological and evolutionary concepts to direct, elucidate, and eventually improve clinical studies, public safety, and medicine. The influential 1991 inspection by *Williams and Nesses* in The Annual Evaluation of Biology (William & Nesse, 1991) shows how historical, practical, and sociological perspectives are still relevant to the healthcare profession by interpreting sensitivity to disease as the result of evolutionary processes (Nesse & Williams, 2012; Stearns, 2012). Preliminary theories in evolutionary medicine demand extensive and diverse supporting evidence. For instance, Welford and Bossak (2010) suggest that bacteria-carrying insects may have played a role in the Black Death pandemic that transformed 14th-century Britain. This highlights the complexity of tracing historical disease patterns, making it particularly challenging to uncover evolutionary insights into conditions like autism. Together with the millions of microorganisms that inhabit our own cells, humans evolved into soft and graceful flexible organisms that respond differently to their host's constantly changing physiology. A breakdown in the microbiome has been related to several disorders, including inflammatory bowel disorder, MS, diabetes, allergies, and autism, and cancer (Peterson & Round, 2014; Garrett, 2015). Many possible elements common to healthy biological communities are being considered, including inherited organisms or genetic routes Shafquat et al. (2014) and additionally standards that relate to particular ecological assets, such as richness or stabilization (Faith et al., 2013).

The microbiota, or bacteria that remain within and around individuals; is estimated to be approximately ten times more frequent than human reproductive and somatic cells alike. The microbiome, which serves as a generic name for the genomics of these microbial living things, supplies capabilities that humans were able to create on their own (Gill et al., 2006). The community of organisms that live in and communicate with the human body are termed as the human microbiota (Grice & Segre, 2011).

Ten years ago, little was understood about the bacteria that live in various regions of the human organism, how they build societies with various levels of intricacy, and how they interact with other species' microbial communities. These questions are now approachable for the initially time because of the most recent developments of technology for gathering and assessing sequencing of DNA data. A high number of illnesses among humans have been related to different capabilities of the microbiome and specific microbiome-focused medications have proven extraordinary efficiency in treating specific ailments, such as repeated *Clostridium difficile* infection (Baken et al., 2011; Knight et al., 2017). This chapter aims to explore the intertwined evolution of human health and microbiomes, highlighting the role of evolutionary medicine in understanding modern diseases. It emphasizes the impact of environmental, dietary, and cultural shifts on the gut microbiota and its influence on immunity, mental health, and overall well-being.

History of Medicine

Due to limited direct evidence, ancient human disease must be inferred from indirect methods. For instance, research on our closest relatives, monkeys and great apes, indicates that being in a state of natural health does not equate to being free of disease. Numerous conditions affect wild monkeys, such as impacted teeth, parasitic worms, hernias, arthritis, and malaria. Early humans likely died from conditions still seen in wild primates. Ancient civilizations adapted to harsh environments through innovation. Humans eventually altered their surroundings in previously unheard-of ways through cultural development, even as they adjusted to its necessities. Humans also created new disease patterns through the socialization of animals, the development of intensely crowded communities, and the mastering of farming techniques. (Manger & Kim, 2017).

Generation of Medicine

Ancient Period

Religion significantly influenced the development of traditional medicine (Hinohara, 2001). The ancient Greeks laid the groundwork for contemporary medicine. Two forms of medicine were developed in ancient Greece. First, a priestly-religious one, incorporating the temple and goddess Asclepios; second, a scientific one, created by Hippocrates (Marketos & Poulakou, 1995).

Intermediate Period

From roughly 1700 to 1550 BCE, the second middle ages ended with a battle that influenced nearly every element of existence. Knowledge of this conflict is not limited to antiquated bureaucratic sources. Examining medical writings written during and after conflicts offers a unique perspective on political and armed forces ideologies. Because of the differences in who is receiving therapy, why, what, and how, as well as when the treatment is taking place, many sources can provide very useful information about shifting viewpoints. The answers to these issues also reveal an organization's current objectives. This category includes two medical papyri from the end of the Late Transitional Period and the beginning of the New Kingdom of Egypt. About 1600 BCE is when the Papyrus of Edwin Smith was created. It demonstrated the resurgence of surgical procedures for catastrophic injuries as a means of winning battles. On the other hand, the papyrus named Ebers, which was composed in 1550 BCE, captures the tranquility and stability of the early New Kingdom (Heffernan, 2023).

Modern Period

Theocratic or pyramidal medicine was converted into logical healthcare by the Hippocrates who also popularized the concept of "physis." When everything is taken into account, the Asclepieion on Kos clearly shows that he and his school followed a comprehensive worldview, combining scientific concepts with dietary and medical regimens and mental and physical activity while simultaneously pleading with God for assistance. Hippocrates also established the first moral guidelines and principles that continue to be relevant in the medical field today. Graeco-Roman medicine was brought to the West by Arab scholars, but over the ages, its face has changed due to renaissance, urbanization, and industrialization. With the advent of economics and molecular technology, contemporary medicine now runs the risk of industrializing itself. Maintaining the caliber of the medical profession in the future should take into account the appropriate use of new scientific information, tailored administration using a Hippocratic holistic approach, and sympathetic understanding for the patient who is suffering. (Falagas et al., 2006).

Natural products and conventional procedures are essential. Traditional Chinese medicine, Ayurveda, Kampo, traditional Korean medicine, and Unani have all been practiced and evolved into structured, controlled healthcare systems in various areas of the world. The aim of this study is to review the literature on the relationships among natural goods, conventional medications, and modern medicine. Additionally, it examines possible concepts and methods across these domains to enhance drug discovery. This study summarizes eight different types of traditional medical systems' distinctive features in terms of theory, application, present position or status, and contemporary research. Despite the fact that since 1805, Modern medicine has already greatly benefited from natural products and traditional remedies, Only a small fraction of medicinal plants have been scientifically studied. When used to develop novel pharmaceuticals, herbal remedies and conventional medicines offer unmatched advantages, such as a multitude of therapeutic knowledge and a unique range of chemical structures and biological activity (Yaun et al., 2016).

Evolutionary Medicine and Relation with Modern Disease

Focusing on the evolutionary causes of human illnesses and how they evolve all through time, evolutionary healthcare is a rapidly expanding subject. This section explores empirical studies on microevolutionary changes in human biology and disease. the generational variations in human morphology that have happened historically and continue to occur in populations today due to the processes of evolution offering insights into current health issues and implications for future generations. Understanding the coevolution of pathogens and human genes also involves analyzing ancient remains (Rühli & Henneberg, 2013). Anthropology also contributes to this field by examining how diet, reproduction, and lifestyle changes in modern societies differ from evolutionary norms, often leading to chronic diseases. EM encourages a broader view of health that incorporates biological, social, and cultural contexts (Trevanthan, 2007).

Origin of Human Microbiome

Microbial life has dominated Earth since the emergence of cells billions of years ago, shaping all subsequent life forms (Pace et al., 2012). Every kind of life on our planet evolved from microbes. Since they were the first to live there, they have shaped most subsequent existences and continue to do so (Appanna, 2018). The human gut microbiome contains over 100 times more genes than the human genome. These microbial symbionts' genomes, generally referred to as the microbes, give abilities that humans did not need to establish independently. (Turnbough et al., 2006). The genome of the 10^{13}–10^{14} bacteria which make up the human intestinal microbiota, or "microbiome," has approximately 100 times as many genes as the one we share (Gill et al., 2006).

The Human Genome Project is progressively advanced theoretically and operationally by the HMP. The HMP consists of multiple plans. It is a multidisciplinary initiative with several projects, particular in Europe, Asia, and In the USA (which was one of the upcoming phase of the national Vision for the Future of Medicine programme of the National Institutes of Science) (Washington Dc, 2007). There are a startlingly large number of Sbacteria within all the microbes that occupy the human body. We have known since the late 1970s that there are at least an order of magnitude of bacteria cells ($\sim 10^{14}$) in and on the human body than cells of humans ($\sim 10^{13}$) (fvPeterson et al., 2009, Bianconi et al., 2013).

Numerous human disorders have been linked to the diversity of the microbes in a particular bodily atmosphere, which is defined as the presence and distribution of multiple types of organisms: Low gut flora is related to bowel inflammation and being overweight (e.g., Tumbough et al., 2009; Qin et al., 2010) for instance, and a large diversity of infections caused by bacteria in the vagina (Fredricks et al., 2005). According to some projections, the total number of microorganisms in our bodies is 100 trillion cells, which is ten times the total amount of human cells. It is additionally believed that these microbes encode 100 times as many different genetic codes as our genome (Ley et al., 2006).

Recent studies have linked microbiome composition to conditions like cancer and autoimmune diseases. Both resident and migratory microbial cells, as well as their outcomes, such as deleterious metabolites, are constantly present in our organs (Rajagopals et al., 2017). To support the argument that recent modifications in the human microbiome have boosted the risk of AD, we use an evolutionary medicine methodology. Applying concepts of evolutionary biology to the study of human health and illness, evolutionary medicine is a broad academic field (Stearns et al., 2010). The proposed approach underlines how humans coevolved with symbiotic bacteria and how agriculture and the industrial revolution, two recent changes in the human environment and lifestyle, have modified the genetic composition of the symbiotic microbiota (Cho & Blaser, 2012).

Impact of Environment and Diet at Microbiome

Bacteria that settle the human large intestinal tract mostly gain their energy from nondigestible carbohydrates, which are those carbohydrates taken in from the diet that are not entirely absorbed in the upper gut. It is widely recognized that the amount of insoluble carbohydrates consumed during the diet increases the quantity of bacteria in the gut overall and the fermentation process by bacteria. The quantity and kind of indigestible sugars (such as resilient starch, sugar-free polymers, and prebiotics) also affect the species composition of the intestinal microbiota, as demonstrated by emerging molecular ecology data (Flint, 2012). However, environmental influences, mainly the quantity and composition of the cuisine and antibiotic treatment, can affect the formation process (Subramanian et al., 2014). Since the microbiome evolves in the beginning, it has had considerable effects on adult development and health. Nutrition practices, conceiving, taking antibiotics, habits, and their conception type can all have a direct effect on the microbiome's the structure and function in the very first days of life (Stiemsma & Michels, 2018).

Comparison between Ancient and Modern Population Microbiome

Humans live across diverse environments with highly varied diets, influencing their gut microbiota Humans gut microbiota composition is closer to that of omnivorous New World monkeys than it is to that of our closest evolutionary relatives, the big apes (Ley et al., 2008). An important factor influencing the variety of the gut microbiota is diet. Particularly in human populations, there are strong correlations between food choices and a number of microbial taxa. Both modern (Gomez et al., 2016; Obregon-Tito et al., 2015; Yatsunenko et al., 2012) and ancient (Tito et al., 2012; Tito et al., 2008) numerous species, including *Prevotella, Catenibacterium, Succinivibrio,* and *Treponema,* are more common in people that practice traditional persistent lifestyles, such as gathering and hunting or farming for survival. Higher intakes of fiber-rich foods and other complex carbohydrates are common characteristics of the diets of these populations. The specific loss of these bacterial species with the transition from rural-traditional to urban-industrial settings is the primary trend seen in global biogeographic testing of the human gut microbiome (Obregon-Tito et al., 2015). Particularly in developed nations, the modern diet tends to be lower in fiber and higher in processed foods, sweets, and fats. Different microbial species have increased as a result, including those that feed on simple sugars and fats (like *Firmicutes* and *Proteobacteria*), but beneficial microbes that depend on fiber (like *Bifidobacterium* and *Prevotella*) may be less common. Despite preservation challenges, archaeological coprolite samples offer valuable insight into microbiome evolution. Western populations lack several microbial taxa common in traditional societies, suggesting recent loss likely due to industrialization rather than evolutionary shifts (Gomez et al., 2016; Obregon-Tito et al., 2015). Comparing pre-industrial samples may clarify whether this microbial decline is global and irreversible.

Impact of Antibodies and Increased Sanitization on Microbiome

The microbiome serves as our link to understanding the deep evolutionary relationships between human health and ancient ecologies (Tito et al., 2012; Warinner et al., 2014; Maixner et al., 2016) because it is important in immune system development and regulation, pathogen protection, and environmental interface (Kumar et al., 2015; Zaura et al., 2014). By eliminating ecological niches and inhibiting pro-inflammatory or expanding signals, our unique microbiome can reduce infections and pathogenicity (Hooper et al., 2012; Brestoff & Artis, 2013). By sharing genetic elements like antibiotic resistance genes (ARGs) or via biochemical cross-feeding, our microbiome works as a cohesive unit to affect community structure and prevent ecological collapse. Our modern practices, which are embedded in the now-famous "hygiene hypothesis," have altered the selective environment and transmission of our microbiome through sanitization and a lack of exposure to environmental or infectious agents, as we are more aware (Bendiks & Kopp, 2013; Strachan, 1989). This theory has been revised to emphasize symbiotic agent exposure rather than infectious agent exposure (Haahtela et al., 2013) based on findings that autoimmune illness is linked to decreased microbial biodiversity (Knights et al., 2014; Kostic et al., 2015). Increased sanitation has also eliminated single and multicellular eukaryotic parasites in addition to bacteria, although less is known about their ecological significance in the larger microbiome, largely due to the higher difficulty of investigating them using molecular approaches. By changing the microbial ecology, these eukaryotic parasites can have a direct or indirect effect on the host. Though it is still difficult to separate these patterns from confounding factors like host habitation and food habits, it was recently suggested that eukaryotic parasites might have beneficial relationships with specific bacterial taxa in the gut (Morton et al., 2015).

Evolutionary Mismatch

The state in which a creature and its natural environment are out of rhythm is known as evolutionary mismatch. This can only be resolved by behavioural. adaptation, further evolution, or a change in the environment (LIoyd et al., 2011). The concept of evolutionary mismatch claims that cognitive and biochemical adaptations exist under conditions that are significantly distinct from the environments in which they first came up (Tooby & Cosmides, 1990; Nesse & Wilson, 2012).

A population's evolution has been mainly influenced by selection forces in the natural setting towards which it is primarily adapted, or the EEA. According to mismatch theorists, Homo sapiens had an EEA around 50,000 years ago and earlier, which is commonly defined as the African savannah (Lindberg, 2010).

The body and intelligence of people have evolved to live and flourish in an ancestral environment that has persisted for 99 percent of human history. An evolutionary mismatch has arisen because the ancestral environment in which the human brain grew differs drastically from the one that exists today (Li et al., 2018). In the literature, two separate mismatch hypotheses have been presented out, one of that deals with developmental disparities during a person's lifetime (Barker, 2004; Bateson et al., 2004; Gluckman et al., 2008; Schmidt, 2011) and one that deals with errors on an evolutionary timeline (Gluckman & Hanson, 2004).

Microbiome Role in Mental Health, Gut-Brain Axis

Evolutionary Prospective

Around 10^{13}–10^{14} viral and microbial cells that interact symbiotically with the host make up the gut microbiome. Human metabolic health depends on the activities of gut bacteria, and dysbacteriosis can be a factor in the pathophysiology of a wide range of illnesses. Due to new findings that link gut bacteria to mental and emotional processes, changes in the relationship between the gut microbiota and host have drawn some attention in the field of mental health. Importantly, gastrointestinal conditions like inflammatory bowel disease, which have been pathologically linked to microbiome function, are disproportionately associated with severe depressive disorder. In addition to being connected to the disease, the microbiome may also affect the effectiveness or adverse effects of pharmaceutical medications used to treat different illnesses (Flowers & Ellingrod, 2015).

The impact of gut microbiome, metabolites, omics, hormones, and stress on overall and mental health is becoming more well acknowledged. Ancient cultures understood the significance of nutrition and intestinal health to an individual's overall health. Western science and current scientific approaches are emerging to uncover the foundations and mechanisms underlying some ancient beliefs and behaviors. The gut microbiome is now known to affect practically every other organ, including the brain and reproductive systems. The history and current understanding of gut-brain axis bidirectional communication in countless mental health disorders, with a focal point on anxiety and depression, whose prevalence has increased by more than 50% in the last three decades, with the COVID-19 pandemic being the most significant risk factor in recent years (Hooper & Gordon, 2001).

Although other channels—the bulk of which are poorly understood, also contribute to this two-way communication, the vagal nerve is a crucial part of it. Because neither Lactobacillus nor Bifidobacterium species can permanently colonize the gut, it is difficult to maintain consistent amounts of these probiotics, which have the greatest impact on mental health symptoms. Numerous mental illnesses, including depression, have also been linked to ancient endogenous retroviral DNA in the human genome. These findings highlight the complicated and nuanced relationship between gut health and mental health issues (Verma et al., 2024). Mood and anxiety disorders are the typical mental health problems worldwide, with a more than 50% increase in prevalence over the previous 30 years. (Monroe & Harkness, 2022).

Gut microbiota is a complex community that helps to maintain dynamic metabolic ecological balance (Alander et al., 1999). The intestinal microbiota involves a wide diversity of microbial species and can be considered a postnatal acquired organ that executes different functions for the host. Intestinal microbes have developed a mutualistic relationship with their host and play a crucial role in the development of innate and adaptive immune responses (Hooper & Macpherson, 2010; Bäckhed et al., 2005), influence physiological systems throughout life by modulating gut motility, intestinal barrier homeostasis (Husbey et al., 2001; Verdu & Collins, 2004), absorption of nutrients and the distribution of somatic and visceral fat (Dumas et al., 2006).

Conclusion

For millions of years, bacteria and humans have coevolved, developing a partnership that is essential to our well-being. The microbiota has long been a silent ally in human survival, from aiding in food digestion to educating our immune systems. However, we've broken this age-old link with contemporary innovations like processed foods, antibiotics, and excessively clean surroundings. Evolutionary medicine demonstrates that by working with nature rather than against it, we can discover better ways to prevent and treat today's diseases by understanding our ancestry with germs.

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