


Native microbiomes in danger: Could One Health help to cope with this threat to global health?

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Abstract

Planetary health faces an emergency associated with global change. Climate change, the increase in world population and urban concentration, the hyperintensification of productive systems, and the associated changes in land use, among other factors, are generating a risky substrate for global health deterioration. The emergence of the coronavirus disease 2019 pandemic is an example of the problems that this situation can provoke. Several researchers and health professionals have addressed the role of microorganisms, particularly bacteria, in promoting global health, mainly in the past decades. However, global change has contributed to the extinction of a wide array of bacterial species and the disruption of microbial communities that support the homeostasis of humans, animals, and the environment. The need to protect the diversity and richness of native microbiomes in biotic and abiotic environments is crucial but has been frequently underestimated. The “One Health” approach, based on integrating traditionally unconnected fields such as human, animal, and environmental health, could provide a helpful framework to face this challenge. Anyway, drastic political decisions will be needed to tackle this global health crisis, in which the preservation of native microbial resources plays a critical role, even in preventing the risk of a new pandemic. This review aims to explain the importance of native microbiomes in biotic and abiotic ecosystems and the need to consider bacterial extinction as a crucial problem that could be addressed under a One Health approach.

Keywords: bacteria, global change, health, microbiome, One Health.

Introduction

The origin of planet Earth dates back about 4.6 billion years. In turn, fossil evidence of microbial life dating back about 3.7 billion years has been found in Precambrian rocks and stromatolites [1]. Recently published studies have reported the discovery of fossilized microorganisms 4.28 billion years old in ferrous sedimentary rocks [2].

Bacteria constitute the first forms of life on Earth, having a critical role in generating conditions for later life forms, mainly through the development of photosynthesis and the generation of oxygen in the atmosphere. However, human life on the planet (according to estimates of the appearance of the *Homo* genus) dates back to about 2.5 Ma ago, while *Homo sapiens* divergence from *Homo neanderthalensis* occurred before 315 ka and not earlier than 781 ka [3].

Bacteria are the major components of the communities of microorganisms present in a concrete environment, biotic or abiotic, known as microbiota. The microbiome is a concept commonly used in broader terms than microbiota and refers to the environment of these communities, including microorganisms,

their genomes, and products of their metabolism. Strictly, the microbiome can be defined as the set of genes in all the cells that make up the microbiota. The number of non-redundant genes in all these microorganisms, for example, in the human gut, is more than 100 times greater than the genes that make up the human genome [4].

The human microbiota is a set of interacting commensal microorganisms that inhabit the human body in coexistence with surfaces in all its cavities and the skin. This microbiota include bacteria (its most abundant component), archaea, fungi, viruses, and protozoa [5].

Recently, several critical functions in maintaining the body's homeostasis have been assigned to the microbiome, appearing to be responsible for maintaining the host's health in its broadest sense. These roles include digestion, prevention of chronic diseases such as obesity, diabetes, metabolic cardio and hepatic disorders, training of immune and endocrine systems, and promotion of mental health, among others [6, 7].

Although it is challenging to characterize a “normal” microbiota, the richness and diversity of these communities are considered indicators of healthy microbiota since they contribute to the wellness of the host. Characterizing these microbial communities is problematic since only a small proportion can be recovered by culturing. Culturable bacterial counts in soil, river, and ocean samples are <1% of that observed by direct microscopy [8]. Furthermore, a limited proportion of human and animal gut microbiota bacteria have been cultured in artificial media. However,

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in these cases, the percentages of bacterial recovery are still under debate [9]. A study performed by our group concluded that about 10% of ruminal bacteria could be cultured in artificial media [10]. Therefore, culture-independent techniques like high-throughput DNA sequencing are needed to study entire microbial communities.

Conventionally, it had been thought that there are sterile environments in the body under physiological conditions. Today, this paradigm is being questioned. Native microbiota has been described in diverse environments, such as the bladder [11], the lungs [12], and the mammary gland [13]. In these cases, microbiota plays a beneficial role in contributing to these organs' normal development and function. It has even been proposed that the intestine of the fetus harbors a regular bacterial community provided by maternal transfer through the placenta to the amniotic fluid during pregnancy and then swallowed [14].

Together, the host and its microbes form a holobiont, a concept first introduced by Lynn Margulis to describe a biological unity composed of a host and its microbiota [15, 16]. It is now known that both the host and microbiota establish a dynamic relationship that supports the holobiont homeostasis due to long-standing coevolution.

The term hologenome was proposed by Zilber-Rosenberg and Rosenberg [17] to describe the sum of the host genome and associated microbial genomes, the total genome of a holobiont, which has been increasingly used in association with the hologenome concept [18, 19].

A measure that reflects the significance of the microbial compartment on Earth has been provided by Bar-On *et al.* [20]. They have reported that the biomass of bacteria and archaea sums about 77 gigatons of carbon (GtC), while, in contrast, the total biomass of animals (including humans) is just 2 GtC.

Soil microbes sustain the ecosystem's health [21]. Bacteria play a relevant role in plant growth promotion through symbiotic interactions (with consequences on vegetal biodiversity and crop production) [22] and in the biogeochemical cycles. Biogeochemical cycles are pathways that allow the circulation of chemical elements through the different components of ecosystems. Bacteria are crucial to these recycling functions. Therefore, human activities can critically affect biogeochemical cycles when the diversity and function of bacterial communities are impacted in the context of global change [23].

Among the aquatic biota, microorganisms comprise the majority of aquatic biomass. They show great functional diversity and are responsible for most aquatic systems' productivity and biogeochemical cycles. Although often forgotten, aquatic microorganisms must be preserved since they play vital functions in the planet's life balance, feeding the plankton at the basic levels of the food web, and producing about half of the Earth atmospheric oxygen [24]. They are

remarkably sensitive and strongly affected by environmental disturbances of different origins. Through a broad spectrum of functions, they maintain the homeostasis and stability of aquatic ecosystems and significantly influence water quality [25]. Aquatic microorganisms have rapid growth rates and respond to low levels of contaminants and other physical, chemical, and biotic environmental changes [26].

Bacteria are Facing Extinction

Compelling evidence has shown that human activity contributes to bacterial disappearance, for example, through the extinction of plants and animals that lead to the extinction of microbial taxa specialized in the extinct host. From a holobiont perspective, given the close relationship between its members, one of the partners' disappearances inevitably leads to the loss of the holobiont organism [27].

Concerning the human gut microbiome, different authors have claimed that in the late 19th century, this microbial community began to change, particularly in industrialized developed societies. Certain indicator bacteria have significantly declined in the past decades, such as *Helicobacter pylori* and *Oxalobacter formigenes*, in this case, inducing an increase in the incidence of urinary stones [28, 29]. According to different authors, taxa such as *Desulfovibrio*, *Bacteroides*, *Prevotella*, and *Lactobacillus* and lineages in the families *Succinivibrionaceae*, *Paraprevotellaceae*, and *Spirochaetaceae* are significantly declining in the gut microbiota along with industrialization [30].

Several authors have shown that industrialization is correlated with a reduction in the human gut microbiota richness and diversity, finding that South American Amerindians' fecal bacterial diversity is about 2-fold that of healthy people in the United States [30]. This trend could be attributed, for example, to the higher consumption of processed food with high contents of fat and sugar and artificially supplemented with sweeteners, emulsifiers or preservatives, environmental chemical pollutants, sanitized water (e.g., chlorination), formula feeding replacing maternal lactation, an increase of C-section instead of natural birth, and the massive intake and misuse of medicines, particularly antibiotics [6, 31].

Additional pressures on the microbiome are associated with the Western lifestyle, like the increasing use of drugs. Studies of our group, among other findings, strongly suggest that exposure to volatilized cocaine leads to significant changes in the gut microbiota, including a significant decrease in the richness and diversity of the gut microbiota [32].

In this context, the significant shifts in the composition and functions of the gut microbiota have led to a substantial increase in the prevalence of chronic diseases such as diabetes, obesity, asthma and other respiratory diseases, allergies, inflammatory bowel diseases, and other conditions like autism spectrum disorder [33, 34].

The world population shows a growth rate of 1.1% per year, and the most significant weight of its growth (approximately 90%) occurs in developing countries. More than half of the human population today lives in large cities; by 2050, that proportion is expected to exceed 70%. However, nearly 1 billion people live in critical peri-urban settings in large cities in developing countries, where the fastest-growing human populations are expected to occur [35]. Several studies have proposed that the urban lifestyle contributes to the increasing prevalence of asthma, allergies, and other chronic diseases. A significant factor that explains this difference is the disruption of the protective exposure to microbes and their metabolites, particularly in children [36, 37].

Over the past decades, autochthonous soil bacteria have constantly been lost [38]. The loss of soil bacterial richness and biodiversity puts the biogeochemical cycle function, plant growth promotion, and control of soil-borne pathogens at risk [39, 40].

Strong evidence has demonstrated that chemical fertilizers (e.g., nitrogenous) and pesticides, associated with the explosive intensification of productive systems that started with the “green revolution” in the sixties, exert a deleterious impact on the abundance and diversity of bacteria in soil and other environments [41, 42].

In a recent study of our group [43], we found that glyphosate significantly alters the relative abundance of amplicon sequence variants classified as core members of the honeybee gut microbiota, increasing the abundance of *Gilliamella apicola* and *Lactobacillus kimbladii* (*Lactobacillus* Firm-5) and decreasing the abundance of the beneficial symbiont *Snodgrassella alvi*, compared with syrup-treated controls. It also increased the abundance of other species, including potentially pathogenic bacteria like *Staphylococcus* spp. Moreover, it has been shown that the ubiquitous presence of this herbicide in different ecosystems, such as rivers, induces a significant decrease in bacterial richness and diversity [44]. A significant impact on bacterial species loss by glyphosate has even been found in the earthworm microbiome [45].

The aquatic organisms are very susceptible to the impact of a wide array of chemicals that reach the ecosystem through sewage. Triclosan and triclocarban are antiseptics commonly included in antiseptic and cosmetic products for long-term daily use, particularly in those claiming extreme bactericidal action. It has been proved that triclosan and triclocarban have detrimental effects on aquatic organisms, including bacteria [46, 47]. Moreover, several authors have reported that triclosan and triclocarban exert a significant disrupting effect on the gut microbiota, inducing obesity, among other metabolic diseases [48, 49].

Human activity during the past century has generated an unequivocal effect on the global climate, causing warming. The main contributor to global

warming is CO₂ produced by anthropogenic activities [50]. By 2020, its atmospheric concentration had risen almost 50% above its pre-industrial level. The increase in temperature will accelerate the hydrological cycle (rain evaporation) and will increase the frequency and intensity of extreme weather events [51]. This phenomenon contributes to the extinction of bacteria from the environment. For example, unexpected episodes of abundant rain in 2015 and 2017 in the Atacama Desert, the driest desert on Earth, practically extinguished the autochthonous microbiota that was finely adapted to the extremely dry environments, where they had evolved for millions of years [52]. This study showed that extreme arid regions’ already low microbial biodiversity drastically decreases when water is supplied quickly and in great volumes, in this case, associated with climate change. This is also the case of Cuatro Ciénagas (México), where the wetland overexploitation provoked the loss of *Pseudomonas otitidis* metabolic flexibility and the extinction of the endemic auxotrophic specialist *Bacillus coahuilensis*. Human-driven influence on these particular environments having a high proportion of endemic species, which play a significant role in ecosystem functioning, is a severe extinction threat [53].

As mentioned above, a factor that has strongly contributed to microbiota dysbiosis and bacterial extinction is the massive and often unnecessary use of antimicrobials. This behavior induces the increase of resistant bacteria and metabolic and chronic diseases such as obesity or diabetes because of the deleterious impact on the gut microbiota [54, 55].

In the middle of the past century, humanity lived a “golden age” of antibiotics, as one-half of the drugs commonly used today were discovered in that period. A good part of the medical community even predicted the global end of bacterial infectious diseases, but the reality was more complicated. According to a report prepared by a team led by the economist O’Neill [56] at the request of the British government, in 2050, deaths attributable to antimicrobial resistance will exceed those caused by cancer (about 10 million people).

This problem is an example of a typical One Health issue. More than 70% (weight) of the antibiotics defined as medically important by the FDA are destined for animals [56]. Furthermore, antimicrobials used in human and animal medicine belong to the same families, including last-line antibiotics for human medicine, like colistin [57].

Antimicrobials have been massively used for decades as “growth promoters” in animal production, being administrated in subtherapeutic oral doses as non-specific enhancers of weight gain and feed conversion.

In the USA, the volume of antimicrobials used as growth promoters increased 50 times between 1951 and 1978 (from 110 to 5580 tons); in that period, the use of antibiotics for the treatment of infections in

humans and animals increased 10 times. In the UK, for example, the prevalence of tetracycline-resistant *Escherichia coli* in poultry increased from 3.5% to 63.2% in 4 years (1957–1960) after introducing the referred antibiotic [58].

This problem also has a deleterious environmental influence. Several authors have reported the spread and circulation of resistant strains among humans, animals, and the environment, and the effects of antimicrobials on native bacteria of different ecosystems, mainly aquatic environments [56, 59]. Between 40% and 90% of antibiotics (depending on the molecule) prescribed to humans and animals are excreted in feces and urine in their active forms, reaching the environment [59].

Preservation of Native Bacteria must become a One Health Challenge

The One Health concept resides in an interdisciplinary approach to managing human, animal, and environmental health and ecological interactions among these compartments. Therefore, this approach offers an ideal framework to address the circulation and transfer of bacteria among humans, animals, and ecosystems, whether pathogenic or non-pathogenic. The recent and fast development of omics technologies has broadened this perspective, allowing the study of whole bacterial communities.

One Health deals with a systemic and horizontal strategy to design and implement practices, programs, policies, legislation, and research to achieve better global public health results [60].

At the international level, it has been agreed to name “One Health” to this new way of facing the challenges currently posed by health promotion at a global level from a systemic and multidisciplinary perspective. From an operational viewpoint, One Health could be conceived as a strategy, setting goals and assessing achievements and results in public health performance [61].

The challenges to be addressed from “One Health” perspective are diverse and of significant magnitude. The spread of zoonoses, the resistance of bacteria to antimicrobials, and the fair availability and safety of food and water, among many others, can be mentioned.

In 2010, Food and Agriculture Organization (FAO), World Animal Health Organization (OIE), and World Health Organization (WHO) formalized their collaboration to prevent and control health risks at the human-animal-environment interface (Hanoi, Vietnam, April 19–21, 2010). The Tripartite Concept Note, in which WHO, FAO, and OIE formalized the commitment to perform “Complementary work to develop regulations, standards, and field programs to achieve the goal of One Health,” was catalyzed by the global upheaval generated from the risks posed by a possible epidemic of Highly Pathogenic Avian Influenza (HPAI, H5N1) in the early 2000s [62].

At present, the nature of the One Health global movement is discussed. Different authors characterize One Health as a framework, an agenda, a scientific approach, or an institutional agreement, among other definitions. However, it is generally agreed that it arose as a response to an institutional global health crisis that was dramatically exposed by the coronavirus disease 2019 (COVID-19) pandemic [63].

Different global health challenges in the 90s pressured health institutions and revealed the organizational and scientific limitations of the actors responsible for managing questions of world health. Particularly, the H5N1 avian influenza virus catalyzed the formalization of One Health as a strategy to face new threats through its systemic collaborative and holistic approach [64].

The COVID-19 pandemic uncovered the limitations of the international health system and cast doubts about the effectiveness of the instruments dedicated to managing global public health.

One of the most important dimensions incorporated in the One Health approach is the pivotal role of the environment in the strategies for global health promotion. Numerous historical antecedents document the need to assume an integrative perspective of health. Hippocrates (460–370 BC) had already proposed an interdependence between unusual conditions of the environment, climate, health, and the prevalence of infectious diseases [65, 66].

Some issues frequently appear as typical health challenges that must be faced following a One Health approach, such as the control of zoonotic, foodborne, and waterborne diseases, antimicrobial resistance, or the need for fair access to healthy food and fresh water worldwide. However, the importance of microbial preservation has been underestimated. Understanding the relationships of the microbiome between the environment, humans, and animals should lay the groundwork for developing systemic and innovative strategies for diagnosis, treatment, and intervention. Among these possible interventions, restoration of human and animal microbiomes and disturbed environments could be considered as alternatives to face the emergency we are currently experiencing [19, 24–54].

Different researchers are expressing the need to generate microbial repositories to preserve the diversity of ancestral microbes from humans, especially those less exposed to the industrialized Western lifestyle [30, 67]. Additionally, banks of fecal material are being proposed to improve fecal transplant, already used to treat resistant *Clostridioides difficile* infections, but with a promising potential for treating inflammatory bowel disease, obesity, diabetes, or autism, among other pathologies [68, 69]. Different authors have proposed the restoration of microbial biodiversity and associated metabolic activity through environmental microbiome rewilding, although research is needed to elucidate the mechanisms for these possible interventions [70].

The fast development of “omics” (e.g., genomics, proteomics, metabolomics, metagenomics, or transcriptomics) has facilitated the characterization of the structure and function of whole microbial communities of different origins, obtaining large amounts of data. The strengthening of analysis capacities of the increasing volume of these data has become a bottleneck for generating interdisciplinary scientific knowledge to design specific evidence-based policies [71].

Conclusion

Researchers, health professionals (particularly medical doctors), and transnational institutions (e.g., WHO, OIE, and FAO) must face the preservation of autochthonous microbiomes as a crucial global health challenge. Furthermore, pathogenic and non-pathogenic microbial transfer mechanisms and routes among humans, animals, and the environment need to be elucidated. The health crisis that the world is facing, including an alarming prevalence of chronic diseases, needs to be addressed by promoting changes in the industrialized lifestyle, particularly on the basis of its hyperintensive production systems. COVID-19 (an emerging zoonosis) has shown how the environmental disruption ended with a dramatic pandemic, involving a complex network of interactions among wild and domestic animals, humans, microbes, and the environment. Although the COVID-19 pandemic’s devastating results are already being suffered, the world is treating its symptoms but not its causes. Therefore, the occurrence of new pandemics, even more severe than COVID-19, cannot be ruled out [72].

The achievement of relevant improvements under the One Health framework will depend on political decisions that lead to effective actions, following an integrated and systemic approach based on scientific evidence. Particular attention to the health of vulnerable communities and systems under risk must align with the declared intentions of multinational organizations and governments worldwide.

Author’s Contributions

PZ: Conceived the idea, collected and analyzed the literature, and wrote and approved the final manuscript.

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Competing Interests

The author declares that he has no competing interests.

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