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The Influence of Microorganisms on Human Health

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The Influence of Microorganisms on Human Health

By

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Abstract

The purpose of this thesis is to explore the interplay between the environment, lifestyle, and composition of human microbiomes across different communities, with a specific focus on immune and digestive health. This literature review investigates three distinct types of communities: isolated/traditional, transitional, and urban/industrialized communities, each characterized by unique environments, societal structures, and interactions. These factors contribute to the distinct microbial populations and compositions within each community. It is impossible to avoid contact with microorganisms as they are present in every aspect of our lives, from the air we breathe, the water we drink, the soil we walk on, the food we consume, even our workspaces, schools, and medications. Microbial communities exist everywhere, and at the center of this microbial society are humans themselves. The interactions between humans and microorganisms impact disease and the functioning of various physiological systems of the human body. By exploring these factors, this review highlights the relationship between humans and the microorganisms that inhabit our world.

Introduction

Humans and Microorganisms

Microorganisms have evolved to form relationships with different organisms and biological systems. These systems have all grown to rely on microorganisms, small single-celled organisms such as Bacteria, viruses, or fungi, influencing the development and evolution of these systems (Hooper et al., 2012). Humans have also evolved complex relationships with microorganisms, affecting the growth and development of human health via the development and function of the immune and digestive systems (Hooper et al., 2012). These microorganisms are important because they can influence how the human body processes food (Silbergeld et al., 2008), performs metabolic functions (Zupancic et al., 2012), reacts to pathogens (Stetzenbach, 2009), responds to allergens (Stein et al., 2016), and much more. Microorganisms are exchanged by interactions with physical touch and body fluids or commonly through food, such as consuming fresh fruits and vegetables from the garden (Silbergeld et al., 2008). Through these microbial interactions, humans ultimately evolved with microorganisms in their system, forming dependent relationships that can be generationally traced in human cells and genetics (Davenport et al., 2017).

Among the various methods through which humans interact with microorganisms, food is one of the most common routes of microbial inoculation. Food acts as a vehicle to introduce microbial diversity into the human gut and is essential to human evolution and survival. Humans have incorporated microorganisms into their diets in numerous ways, including oral supplements, fresh fruits and vegetables, pickled foods, yogurt, and probiotic juices, are a short list of how people have introduced and incorporated microorganisms into their diet to help care

for their physical and immune health (Silbergeld et al., 2008). While food is a prominent method to introduce microorganisms into the human gut, it is important to recognize that countless other interactions contribute to the complex relationship between humans and their microbiomes. These interactions collectively shape and influence the dynamics of the human-microorganisms ecosystem.

Early Life Interactions

Humans begin their relationship with microorganisms as soon as they are born (Nuriel-Ohayon et al., 2016). Birthing practices, i.e., cesarean, vaginal, contact from the placenta, or skin-to-skin with parents, can influence the microorganisms introduced to the newborn (Nuriel-Ohayon et al., 2016). This event can determine how a baby fights off pathogens in their first year. Other aspects of health and development affected by the introduction of microorganisms can include metabolic processes, hormone production and responses, immune development, and immune adaptation (Nuriel-Ohayon et al., 2016). Therefore, from the very start of life, microbial interactions play a large role in human growth and development, exemplifying humans' dependency on microbial support in their systems. Another common method that introduces microorganisms to infants is breast milk. Breast milk contains microorganisms commonly used to help start a newborn's immune development (Nuriel-Ohayon et al., 2016). The microbiome of breast milk allows newborns to slowly adapt to the change in their environment through their mothers, who have already produced the antibodies necessary to protect them from their surroundings (Nuriel-Ohayon et al., 2016). Thus, not only do humans rely on microorganisms to guide immune system development, but they also aid in our bodies acclimating to new environments.

Exposure to Microorganisms in the Environment

Microorganisms are everywhere in the environment (Gilbert et al., 2018). Some main environmental microbial communities that humans heavily interact with include the water, air, and our homes. Water is an essential source of life on planet Earth; without water, many living organisms would not survive. Microorganisms also rely on water and live abundantly in water at high species diversity (Callewaert, 2020). So many microorganisms occupy water that there are hundreds, if not thousands, of unknown microorganisms (Callewaert, 2020). Researchers worldwide have taken water samples and tested them for these tiny occupants. For example, a water sample from Yellowstone presented nearly 1 trillion different microbial species (Hugenholtz et al., 1998). Samples from spring water from France have also demonstrated similar outcomes, with over 600 bacterial species found within the water sample (Callewaert, 2020). Hence, interactions with water, such as drinking, swimming, or washing, allow humans to obtain minerals that help with homeostasis within the body and build more diverse microbiomes. Water filtration due to urbanization has decreased the number of microbial species humans interact with, primarily pathogens, reducing the risk and spread of disease and infections.

Pathogenic vessels like water are a few ways microorganisms can travel into the human body. The air can also act in the same way. Diseases such as smallpox, tuberculosis (TB), influenza (flu), fungal spores, or water vapor could travel in the air (Stetzenbach, 2009). Airborne microorganisms typically interact with the respiratory system of living organisms and, through the gas exchange system, could enter the bloodstream and travel through a different part of the body (Stetzenbach, 2009). Therefore, air quality and the people one interacts with can be a health concern. Particles that travel through the air can come from people talking, dogs barking, pollutants, and more; these impact the development of the immune system and the microbiome.

An environment that humans consistently interact with more than any other is their homes. Microbial diversity has evolved for humans and microorganisms due to urbanization; the obsession with cleanliness and sterility has affected the microbiome of humans living in urban or rural homes (Gibbons, 2016). Researchers have discovered that built environments such as homes, schools, or workplace offices comprise twenty to thirty percent of human-associated microorganisms (Gibbons, 2016). They described these environments as "wastelands for microbial accumulation" (Gibbons, 2016). These wastelands contain dead skin cells, hair, and saliva particles, all containing microorganisms (Gibbons, 2016). Continually interacting with built environments can lead to communities with similar microbiomes using common spaces. A similar microbiome can be beneficial as it can protect populations from diseases to those who are immunocompromised, newborn, or unvaccinated.

Microorganisms in Human Systems

Human relations with microorganisms through food, birth, vehicles such as water and air, and built environments allow microbes to be incorporated into body systems (Callewaert, 2020). Microorganisms play a role in dermatological health and lie on the surface, within, or below the skin (Callewaert, 2020). They come from exchanges with water, hygiene, and clothes, playing a role in diversifying our skin microbiome (Callewaert, 2020). Bacteria such as *Staphylococcus* on the skin's surface are usually harmless to humans. However, once it enters the body or goes beneath the skin, it can cause bloodstream infections or cellulitis respectively (Cogan et al., 2008). Microorganisms also play a crucial role in gut health, developing a microbiome system that aids digestion, metabolism, and nutrient absorption. A study in India examined the gut microbiome diversity in urban and rural communities at sea level and high altitudes (Das et al., 2018). Researchers found that rural communities had greater microbial diversity, with the

bacteria class, *Firmicutes* mainly dominating the gut ecosystem (Das et al., 2018). *Firmicutes* can dominate approximately 90% of the gut microbiome, contributing to efficiently extracting energy from food and absorption of nutrients and calories into the body (Magne et al., 2020).

Whether positive or negative, microorganisms play an essential part in human functions.

Pathogenic exposure induces the body to build the immune system to manufacture antibodies to protect from future infections. Meanwhile, support in gut health aids the body in processing foods that contain high contents of fiber and protein that usually require much energy to break down alone.

Impacts on Human Health

Naturally, microorganisms affecting bodily systems led to them influencing human health. This is particularly true of the gut microbiome, which affects metabolism and nutrient acquisition during digestion (Napolitano & Covasa, 2020). The changes in microbial metabolism contribute to diseases such as obesity, undernutrition, or malnourishment (Napolitano & Covasa, 2020). Microorganisms can slow down human metabolism, absorb the nutrients meant for the body, or quicken the rate of metabolism respectively (Napolitano & Covasa, 2020). Clinical trials of fecal microbiota transplants show that the effect of the microorganisms on human health can be transferred between individuals (Napolitano & Covasa, 2020). Fecal microbiota transplant is a procedure where health providers transfer the microbiome from a healthy gut to an unhealthy gut (Napolitano & Covasa, 2020). Fecal microbiota transplant treatments have helped save lives from infections such as *Clostridium difficile* (*C. diff*), a condition that causes diarrhea and colitis (Napolitano & Covasa, 2020). Continuing with its success, physicians have attempted to treat obesity through this method to positively impact weight loss, body composition, and metabolic processes (Napolitano & Covasa, 2020). Therefore, the microorganisms within the gut heavily

control how the body processes and consumes food (Kau et al., 2011). The gut microbiome even impacts the immune system. Nutrient intake and absorption are essential to endocrine signaling for hormones like Leptin derived from adipose tissue; it regulates appetite, maintains thymic output, and promotes T-cell proliferation and regulation (Kau et al., 2011). Thus, decreases in Leptin due to lack of nutrition from poor digestion and metabolism could compromise cellular immunity and protection. Microorganisms play a vital role in the function of body systems when interacting with the human body. However, they also contribute to a larger ecosystem of the body, connecting and maintaining body systems and functions.

Microbial Relationships with Human Diseases

Now that the human microbiome is recognized to play a central role in the human system, researchers are focused on applying this knowledge to advance medicine. *Biological diversity* is a concern for all ecological and biological systems. Each system component contributes to maintaining balance and supporting one another (Turnbaugh et al., 2007). Researchers have taken samples from humans worldwide to understand better the type of microbiome present in people and their relationship with humans. A large project called *The Human Microbiome Project*, started by the National Institute of Health (NIH) in 2007, compared samples from the gut, skin, stool, and more; to learn more about pathogenic relationships, bacterial lineage and overall expand on genomics and genetic knowledge (Proctor et al., 2019). Another area of interest for many researchers is pharmaceutical-microbial interactions. Microorganisms can inhibit the effect of drugs, and drugs could equally inhibit microbial growth and alter their habitat (Barron, 2023). For instance, the rise of antibiotic resistance leaves a threat to effective treatment for pathogens, leaving scientists searching to cultivate more vital medication (Barron, 2023). Therefore, understanding how drugs and microorganisms influence each other is essential

to treating illnesses and diseases and understanding metabolism and nutrient intake (Barron, 2023).

A lack of microorganisms or insufficient of a particular type of microbe could also lead to adverse reactions. Studies have shown that children who live in traditional agricultural environments have lower sensitization to allergies, such as a lower prevalence of atopic dermatitis, asthma, or hay fever, compared to children who live in more rural settings (Holbreich et al., 2012). Compared to urban environments, studies examining children from rural environments showed a lesser prevalence of illness and disease among young children who live in rural environments (Stein et al., 2016). This demonstrates how microorganisms play an essential role in the human immune system and that the environment that humans interact with affects responses to pathogens and the environment.

However, the human environment is constantly changing. Urbanization is quickly changing the cityscape, forcing alterations to lifestyles, equally contributing; climate change is changing the quantity and accessibility to resources. Microorganisms can help reduce the rate at which climate change is happening (Cavicchioli et al., 2019). These rapid changes have already forced microorganisms to adapt and change. For instance, ocean acidification causes microorganisms to focus on maintaining structure rather than function or reproduction (Cavicchioli et al., 2019). If they are incapable of doing either, bacteria colonies will die out. Microorganisms heavily support the ecosystem of corals, and changes to the ocean that affect microbes can largely contribute to coral bleaching, devastating the ecosystems surrounding a coral reef, destroying shelter, sources of food, and biodiversity of the ecosystem that once took place (Cavicchioli et al., 2019).

This thesis aims to explore **how the living mode of human populations affects health and immune development through interactions with microorganisms**. To address this question, a literature review of different human societies worldwide will be conducted. The focus will be on isolated/traditional, transitional, and urban communities, as each group exhibits different lifestyles that influence their relationship with microorganisms. Studies by Schnorr et al., Smits et al., and Walker et al. will be examined to understand how limited interaction with modern medicine and urbanized societies affects microbial diversity, the immune system, and gut microbiome development in isolated communities. Studying isolated societies has shown that they possess greater microbial diversity, bringing insight into paleolithic microbial and human relationships that are typically absent from other communities. Transitional communities maintain traditional practices while interacting with urbanized societies. Works by Stein et al. and Zupancic et al. provide insights into the unique microbial and human relationships found in these communities, particularly allergy prevalence among young children, offering researchers information on the impact of allergens and microorganisms on immune responses. The immune and gut microbial interactions in urban and industrial communities are analyzed through the works of Sonnenburg et al., Tasmin et al., and Okada et al. Unlike the other groups, urban communities struggle to maintain microbial diversity within the human microbiome, providing insight into the consequences of increased sanitation, sterility, and interaction with modern technology and medicine.

Literature Review

Microorganisms play a large role in developing the human microbiome. Influences from early life and the environment can affect different body systems and how one reacts toward

external stimuli and pathogens. Therefore, learning the importance of microbial interactions can give insight into the benefits and negatives of microbial interactions and how it impacts human health and development. By looking at different communities, it can demonstrate the vast possibilities in microbial relationships with humans and how these interactions are maintained.

Isolated/Traditional Community Microbial Interactions

A *traditional community* is a homogeneous, endogamous social group that shares a common ancestry, language, cultural heritage, customs, and traditions and resides in a common area. They are isolated from industrialized societies and rarely interact with modern technology and medicinal practices. Their isolation has cultivated a unique microbiome different from any other group worldwide. This section will focus on isolated communities without interaction or minimal contact with modern civilizations. Today, traditional communities are a tiny fraction of the human population. The ones that exist today survived due to their physical isolation from society and/or resistance to colonization attempts (Walker et al., 2015).

Traditional communities have many interesting features with respect to the human microbiome. Due to their limited contact with industrialized cities and modern civilizations, people from these communities eat different foods, such as consuming more rare meats and vegetables. Their microbiome helps protect them from pathogens and digestion compared to industrialized communities, where cooking food is often required to help assist in the digestion process. They also interact with an environment with more bacteria due to less sanitation and less interaction with sterile environments; microorganisms consistently interact with the bodily systems of this community, leading to a more diverse and oftentimes stable microbiome (“The Hadza People.”, 2021). Gaining insight from groups like these helps learn more about human immune and gut development and allows scientists to understand better how microorganisms

interact with humans. Since isolated groups do not face many lifestyle changes within their societies, it also allows researchers to take a glimpse of ancient microbiomes and human relationships (“The Hadza People.”, 2021). Therefore, a traditional group category was used for the comparison for this paper.

The Hadza tribe is a traditional hunter-and-gatherer community from Northern Tanzania that has received much attention because they have little access to antibiotics, modern medicinal practices, modern sanitation, or agricultural products (“The Hadza People.”, 2021). The studies in this paper show the Hadza people's microbiome in a new light to look at what many refer to as a glimpse into what a paleolithic microbiome could have looked like in humans (“The Hadza People.”, 2021). Researchers have found that their community's food-foraging methods have led the Hadza people to have a vibrant diversity of gut microbiome (Schnorr et al., 2014). Researchers believe that the composition of the Hadza microbiome is due to the fibrous plants that the community consumes.

One important question from these findings is how individuals vary within these communities in their gut microbiome. Significant differences in their gut microbiome, especially between gender, can be seen. Gut and fecal sample studies have indicated that assigned roles within the community could have led to these microbiome differences (Schnorr et al., 2014). These assigned roles could include the responsibilities of each community member; the men of the Hadza tribe are usually tasked with leaving the compounds of their residence to go hunting and foraging; meanwhile, women of the community are usually foraging nearby their homes and prioritizing more domestic needs for the family and community (Smits et al., 2017). For example, males often leave the proximity of the tribe to hunt; meanwhile, females usually stay back to take care of their families and contribute to food sources by picking berries and

harvesting foliage (Schnorr et al., 2014). Although the people of this community are constantly around each other, their community roles allow them to interact with different microorganisms.

Gut Microbiome in Isolation

The influence microorganisms have on the immune system can come from the gut. Food and orifices on the body are some ways microorganisms enter the body. A study by Smits et al. examined 350 stool samples and 18 different Hadza tribe populations, dissecting the microbiome taxa present in the gut. This study found that the gut microbiome of the Hadza people changes based on the season, forming a cyclic pattern of microbiome reconfiguration (Smits et al., 2017). During the dry season, more meat is consumed compared to the wet season, where more plants, berries, and foliage become a main part of the diet (Smits et al., 2018). Diet is a large contributing factor to the gut microbiome, changing as much as 62% - 76% between seasons (Smits et al., 2017). This influences changes in digestive enzymes like CAZymes, related to digesting animal carbohydrates, and immune system responses, like a lower appearance of transmittable diseases (Smits et al., 2017). Researchers believe the constant change and adaptability could explain the microbiome of the Hadza people, who can support pathogenic bacteria not commonly seen in healthy individuals from an urban community. Bacteria such as Spirochaetaceae, Succinivibrionaceae, Prevotellaceae, and Treponema, are just a few that, on average, seen approximately 15% - 20% more within the Hadza people, whereas in urban communities, 0.006% - 0.8% on average (Smits et al., 2017). This exemplifies the diversity and complexity of the Hadza microbiome that could explain how this community can eat foods such as raw meats and foods high in fiber without becoming ill (Smits et al., 2017).

The relationship between microorganisms and humans is a product of evolution, resulting in a codependent relationship where humans rely on microorganisms to help maintain body

systems and functions, meanwhile microorganisms rely on humans as hosts and for survival. The microbiome composition found in human systems has been linked to influence by the lifestyle in which one pertains. A paper by Schnorr et al. also discussed the gut microbiota of the Hadza tribes, investigating how bacteria co-evolved with humans, their diversity, and their role in metabolism. In this study, researchers discovered gender to be a dominating factor in microbiome differences within this community. The sexual division of labor divides roles amongst the community and exposure to different environments. Men of the tribe hunt for game meat and honey, traveling far distances to complete foraging tasks; meanwhile, women of the community stay within camp borders, gathering berries and plant foods (Schnorr et al., 2013). Although food is shared among everyone, most of what is foraged tends to be eaten by the hunter (Schnorr et al., 2013). Therefore, the diet, community roles, and environment contribute to the gut microbiome of a community.

Bacteria such as *Spirochaetaceae*, *Succinivibrionaceae*, *Prevotellaceae*, and *Treponema* are also mentioned in this study and are described as opportunistic pathogens (Schnorr et al., 2013). These pathogens initiate their place quickly after infecting a host; however, in the Hadza gut, they have been seen to be a stabilizing factor, contributing to low rates of infectious diseases, metabolic diseases, and nutritional discrepancies that are usually seen in more urban and industrialized groups (Schnorr et al., 2013). A bacteria, the *Bifidobacteria*, is absent in the adult Hadza gut but common in the adult urban gut. On average, *Bifidobacteria* makes up approximately 10% of the gut microbiome but is completely absent in the Hadza gut. Researchers hypothesize that continual consumption of dairy into adulthood in urban communities contributes to the presence of *Bifidobacteria*; meanwhile, the Hadza people stop consuming dairy a year after they are born, only consuming breast milk from their mothers

(Schnorr et al., 2013). Although these findings have helped scientists learn more about the microbiome of early hominins, gradual modernization within the Hadza tribes has demonstrated the effects of urbanization on the gut microbiome of traditional communities (Smits et al., 2017).

The Immune System in Isolation

As mentioned, the microbiome of the Hadza people is vastly diverse. Smits et al. discussed the seasonal gut cycles that noticed antibiotic-resistance genes linked to the increased diversity of microbiome composition (Smits et al., 2017). The study explains that antibiotic treatments can cause the gut microbiome environment to become unstable and only capable of supporting a limited number of bacterial communities (Smits et al., 2017). The implications of these findings demonstrate that the Hadza microbiome's microbial diversity is not only due to the environment and diet of the community but the differences in genetics as well (Smits et al., 2018). Antibiotic resistance was likely incorporated into their systems over time to prevent the elimination of a bacterial or microbial group. The immune system was developing a method to protect the microbiome.

Movement of Microorganisms into Transitional Communities

Transitional communities serve as a bridge between isolated and industrialized communities, providing insight to groups that keep traditional practices while engaging with modern society. Traditional communities are characterized as groups residing outside towns and cities that have low population densities and small settlements supporting agricultural lifestyles (Barker, 2012). This section focuses on the Amish Mennonite community, who are originally from Switzerland, Germany, Russia, Alsace, and Holland but have immigrated to the US in the 19th and 20th centuries, where they currently reside in Pennsylvania, Ohio, and Indiana. This

community is known for separating themselves from modern living and inventions, relying on traditional living and agricultural techniques. What makes this group different from the Hadza people is that they still interact with people who live in the modern world. For instance, during Rumspringa, which typically spans two years during adolescence, usually between 16-20 years old, Amish young adults are introduced to the modern world, where they are permitted to play sports, play video games, meet people, and more. The purpose of Rumspringa is to allow young adults to choose whether they would like to stay within the community and to become baptized by the church. Approximately 85-90% of young adults return to the community after their time out (Barker, 2012). Thus, this makes the Amish people an interesting group to study for their microbiomes. Although they lived in an environment vast with microbial diversity, how does this affect the public health of the people they interact with and outside the community?

Traditional Digestive Systems

Studies show that the gut microbiome is an important foundation for health. Researchers have found that the composition of one's gut can contribute a lot to diseases such as obesity or, on the opposite end, malnutrition. An article by Zupancic et al. discussed the relation of gut microbiota with metabolic syndrome, investigating how the microbiome influences gut and digestion health within the Amish community. Gut microbiota influences energy homeostasis, host signaling, insulin resistance, gut permeability, inflammation, and immune responses (Zupancic et al., 2012). The Amish community is relatively homogenous in terms of their lifestyle and population compared to the urban populations. This allows researchers to examine these factors without great variation.

The study demonstrated that particular taxa of bacterial species, such as Bacteroidetes, Firmicutes, and Actinobacteria, are some that play a role in obesity and metabolic regulation;

therefore, their presence in the gut microbiome also influences metabolic syndrome (Zupancic et al., 2012). Since these bacterial classes influence metabolism, they also impact nutrition breakdown and absorption, influencing what fatty acids or ions are absorbed or excreted through the body (Zupancic et al., 2012). Bacteroidetes, Firmicutes, and Actinobacteria are also seen in the gut of urban communities; however, the Amish's farm lifestyle and consistent contact with the outdoors and livestock, allow their gut microbiota to have greater diversity and abundance (Zupancic et al., 2012). The significance of this study is that microorganisms can influence the development of diseases. The presence of certain microorganisms in the gut can cause someone to become predisposed to developing metabolic syndrome or the ability to regulate metabolism and nutrition absorption.

Immune System and Effects

The way the Amish interact with both rural and urban environments allows for a stronger immune system due to their wide range of exposure. Studies have shown that children raised in this environment show less prevalence of developing asthma and allergies, believed to be the result of their microbiome (Stein et al., 2016). A study by Sterin et al. believed that the method of farming and lifestyle could significantly contribute to immune system development.

Communities such as the Hutterite people show at least 4 to 6 times greater prevalence of allergies and asthma, although they have a similar lifestyle to the Amish people. This community incorporates industrial farming practices and techniques believed to change their environment and therefore change their microbiome (Stein et al., 2016). The study found that differences in the microbial composition of the environment and homes contributed mainly to the development of asthma and allergies as well (Stein et al., 2016); interestingly, the Amish household had greater exposure to common allergens and significantly higher endotoxin levels in airborne dust

within their homes compared to the Hutterite homes, suggesting that cleanliness could be a contributing factor to immune development as well.

Stein et al. also took blood samples from young children to analyze the composition of their white blood cells and changes in their immune systems over time. Amish children were found to have more immature neutrophils and monocytes with reduced HLA-DR expression, indicating a more significant anti-inflammatory function response (Stein et al., 2016).

Researchers initially suspected that the environment the children are exposed to is causing the immune system to develop in this way; however, gene sequencing found that gene *TNFAIP3* which encodes a ubiquitin-editing enzyme controls the activity of inflammatory pathways (Stein et al., 2016). This gene is highly expressed in Amish children and is believed responsible for the protective effects against allergens and asthma (Stein et al., 2016).

This study did not specifically name any microorganisms or bacteria contributing to these effects. Researchers were not able to identify the microbial composition of the samples taken. However, an emphasis on microbial exposure, diversity, and co-evolution heavily implied that the relation between immune development to asthma and allergen reactions relied on genetics and the microbiome of the environment and the individual (Stein et al., 2016).

Urban and City Microbiology Community Relationships

Urban and industrial societies stand out the most among the groups examined so far due to their separation from traditional practices and lifestyles that help them to be more connected to other parts of the world. These communities engage in extensive interactions, leading to more prevalent contact and disease transmission. Urban/industrialized communities are defined as an urban agglomeration with a high human population and infrastructure of built environments, they are an urban morphology of cities, towns, conurbations, or suburbs. Microbiome studies from

dense populations have brought vast understandings of cleanliness, public health, individual health, health maintenance, disease spread, and much more. In these communities, technology such as modern medicine, antibiotics, recreational drugs, sanitation, and processed foods is more easily accessible. This creates a less stable microbiome that is also susceptible to consistent changes. One factor significantly different from the traditional and transitional community is that people who live in urban and industrial environments are not exposed to the outdoors as much as their counterparts. This leads to less bacterial exposure and variety, allowing for more susceptibility and development of allergies, auto-immune diseases, immunocompromised diseases, artificial sensitivity development such as to water or the sun due to being enclosed indoors for long periods, high exposure to pollution, mental and physical strain from societal and work expectation. These factors separate industrialized communities from each other and heavily impact the growth and development of city dwellers' microbiomes. In this section, high-density cities in the U.S. will be the focus.

Digestive System in the City

The gut of urban individuals have a unique but less diverse microbiome than the gut systems of other communities. The article by Sonnenburg et al. describes changes in gut microbiota as a decrease in the “VANISH” taxa or “microorganisms volatile and/or associated negatively with industrialized societies of humans” (Sonnenburg et al., 2019). VANISH microorganisms are important because they play a role in digesting complex plant polysaccharides and fibers that would otherwise be excreted through the body as waste in industrialized populations (Sonnenburg et al., 2019). They also support CAZYmes, which are essential in digesting many complex carbohydrates; hence, many isolated communities can digest rare meat and fibrous foods. Developments such as chemically altered, ultra-processed

foods with preservatives and additives have impacted the gut microbiome (Sonnenburg et al., 2019). The decrease in microbial diversity does not only appear in humans; soil micro-diversity also decreases. Installations of city parks and green spaces have been demonstrated to be beneficial for community health; however, these isolated mini ecosystems in cities primarily interact with humans and their urban environments (Tasnim et al., 2017). Even though exposure brought by green spaces and cleanliness practices can change the distribution of microorganisms across hosts. For instance, fecal samples from industrialized individuals demonstrated that there is a larger Bacteroidetes and Firmicutes population in human guts; meanwhile, soil samples showed a greater of Proteobacteria and Verrucomicrobia (Tasnim et al., 2017). This shows that there was less overlap between microbial communities with humans and the environment, contributing to less biodiversity in the human microbiome.

Urban Impacts on the Immune System

The effects of reduced microbial diversity in the gut are not limited to the gut system but also extends to the immune system as well. An article by Sonnenburg et al. discusses microbiota vulnerability in industrialized environments and its impacts on the human immune system. Antibiotics and sterilized medical practices have been used to save countless lives. However, these advancements have also contributed to changes in the microbiome of industrialized populations. These changes have led to many chronic and non-communicable diseases (Sonnenburg et al., 2019). The constant exposure of these microorganisms to sanitation, antibiotics, and modern medical practices has evolved into “new” industrialized microorganisms (Sonnenburg et al., 2019). The result of industrialized microbiomes can cause complications when finding treatment for bacterial infections, leading to increased antibiotic resistance in industrialized communities (Sonnenburg et al., 2019). The lack of pathogenic exposure due to

sanitation and increased cleanliness, although it stops the spread of infectious diseases, can negatively affect the immune system development and decrease the immune response to pathogens over time (Sonnenburg et al., 2019).

An increasing pattern in immune disorders and allergic diseases but decreases in infectious diseases in industrialized populations has also emerged (Okada et al. 2010). Statistics demonstrate that one in five children will develop asthma in these communities, and the risk of atopic dermatitis has tripled for children in these communities (Okada et al. 2010). The significance of these occurrences demonstrates that the microbiome significantly differs from previously examined communities. Okada et al. explored the hygiene hypothesis in this paper, looking at epidemiological data from migration studies. They discover that development in the immune system does not end as one reaches adulthood. The immune system is constantly changing and developing throughout one's lifetime. Studies examining Pakistan immigrants moving to the United Kingdom and Asian immigrants moving to the United States found an increase in immune diseases the longer they resided in their new environment and a continual decrease in infectious diseases with each generation (Okada et al. 2010). Although sanitation could not be linked to these findings in this study, they found that the industrialized environment where interactions with the Earth have decreased can play a large role in microbial community changes.

Future Developments of Microbial Research

The study of microbial influence between communities has demonstrated the factors that play into immune health and gut development in human health. Environment, food, genetics, access to medicine, cleanliness, and direct human interaction play a part in influencing one's

microbiome. As represented in Figure 1, all microbial interactions are connected, and microorganisms are everywhere.

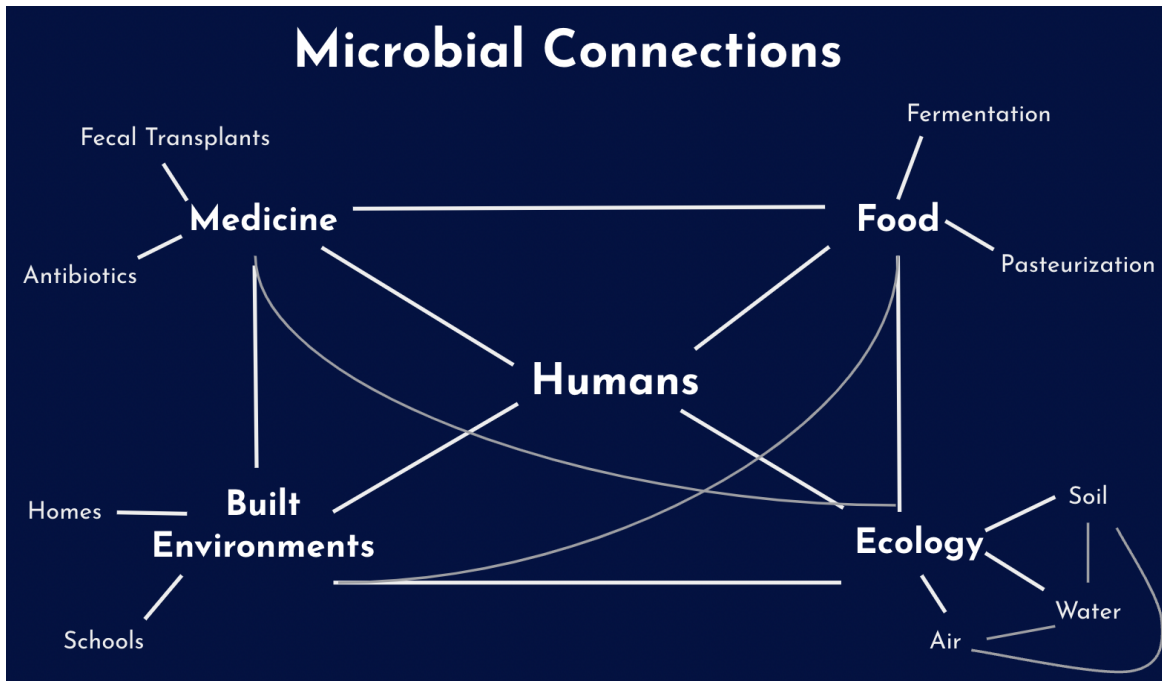


FIGURE 1. Web diagram demonstrating microbial interactions with humans and everything surrounding them.

Understanding that microorganisms are everywhere, researchers can use this information by studying microbial interactions and implementing it into technological and scientific advancements. An article by Vitorino and Bessa explored microbial advancements in food, agriculture, chemical and fuel, environmental, medical, and material. One notable section from their article was the medical technology microbiology section. They discuss solutions for the biocontrol of diseases, the production of vaccines, the production of antibiotics, the production of biotherapeutics, and many more. For instance, mosquitos are a known culprit of spreading diseases such as dengue, yellow fever, chikungunya, and the Zika virus (Vitorino & Bessa, 2017). Researchers introduce the bacteria *Wolbachia* to the mosquitos, and this approach has resulted in a 50% decrease in the survival of these mosquitos. Female mosquitos are primarily targeted as this bacteria can transmit vertically from the female to the offspring (Vitorino &

Bessa, 2017). After transmission to offspring, Wolbachia can manipulate its host to cause feminization, death of males, parthenogenesis, cytoplasmic incompatibility, and in some cases, lead to embryonic mortality (Vitorino & Bessa, 2017). This is one of many examples and developments that have demonstrated the use of microorganisms.

Conclusion

This thesis explored the contributions of microorganisms to the development and changes of the human immune system and gut microbiota. Early and late-life microbial interactions, food, environment, and lifestyle, were examined to analyze microbial interrelationships on humans and one's lifestyle. This led to a study examining the gut and immune systems of three different communities that live three different lifestyles to show significant differences between the communities and their role in the microbiome and health of these communities. Isolated, transitional, and industrialized communities vary in technological advancements and interactions; with these limited interactions, researchers could study their different microbiomes to give insight into microbial impacts on human health and human body systems.

The comparison of these communities demonstrated two large factors that played a role in human health. The first finding is interactions with the environment. The type of environment one is surrounded by contributes significantly to the microbial diversity within a human population. The Hadza community had the greatest microbial diversity meanwhile, the industrialized showed the least diversity. Microbial diversity was inversely related to the prevalence of immune diseases and allergies, exemplified by the gut system. The greater the microbial diversity, the more likely food could be digested and absorbed into the body. Overall,

this demonstrates the significance of preserving microbial diversity to support better health and digestion, and absorption of nutrients.

Along with the environment, understanding the presence or lack of microorganisms in different communities has shown relationships between different diseases. For instance, industrialized communities have a greater prevalence of autoimmune diseases and allergies; Amish communities have a greater risk of metabolic syndrome. Understanding microbial relationships not only helps improve the health of communities but also improves the health outcomes for the global community. For years, epidemics have been a concern for many communities worldwide; however, recently, pandemics have been a main topic of conversation and worry for the whole world. Examples such as COVID-19 and the impacts of global warming changing the environment have led to new perspectives on how to approach human health. This would include bringing new perspectives on microbial interactions with humans.

In conclusion, microbial interactions are important for overall human health, and finding ways to preserve beneficial human-associated microbial communities is one of many methods that can help treat and learn about diseases. The Human Microbiome Project has collected samples from individuals and communities worldwide, creating a database of microorganisms in the human body. Findings from these studies can be used to help discover new medications or bio-technology to help improve the environment or improve agricultural practices. Microorganisms are a vast part of this world but also a vast part of human health.

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