


The human microbiome

Life on Earth depends on microbes. If we modify their relationship with the environment or eliminate them, we endanger all life on the entire planet. Microbes are the oldest inhabitants of Earth, constituting an invisible world – complex, challenging and diverse. They represent an unknown microuniverse full of puzzle and beauty, which need to be explored from multiple perspectives.

We humans need the microbial world to strengthen our defences, to degrade and remove waste and to produce substances essential for life. We carry roughly as many bacteria on and in our bodies as human cells. The bacteria in us are as vital to us as our kidneys, hearts or brains, and can rightly be viewed as an organ like these – the Microbiome.

Equal
The amount of microbes in the human microbiome is roughly equal to the number of cells in the body.




1000 species
Though there is no accurate estimate of the total number of microbial species in the human microbiome tract over a 1000 species that are found in the gastrointestinal have been cultured and classified.

Other humans
Humans acquire most of their microbiome from other humans.



Covered
Bacteria and other microorganisms are found in and on many parts of the human body. This includes the gastrointestinal tract, vagina, skin and mouth – we are essentially covered by microorganisms.

0,2 kg
The total microbial biomass in an average adult is approximately 0,2 kg.



The Earth
Microbes include bacteria, algae, fungi, and protozoa and they are among the oldest living organisms on Earth. Bacteria, in particular, are found everywhere in water, soil, and even air.



The Basics

What are microbes?

Microorganisms or 'microbes' are small living organisms that we need a microscope to see. Microbes include bacteria, algae, fungi, and protozoa and they are among the oldest living organisms on Earth. Bacteria, in particular, are found everywhere in water, soil, and even air. They are capable of living in extreme conditions, such as boiling water, frozen ground, acid volcanoes, and at the bottom of the ocean. Some can reproduce by doubling every 20 minutes; others can survive for centuries in a resting stage.

What are the microbiome and microbiota?

Microbes permeate not just the entire planet but are also found in large quantities inside and on the human body¹. This ecosystem is collectively known as the human microbiome and its microbial inhabitants are called the microbiota. However, the term microbiome is used ambiguously to also mean the total pool of genes carried by the microbiota, also known as the metagenome.

How many microbes live in the human body?

The amount of microbes in the human microbiome is roughly equal to the number of cells in the body. The total microbial biomass in an average adult is approximately 0,2 kg².

There is no accurate estimate of the total number of microbial species in the human microbiome tract over a 1000 species³ that are found in the gastrointestinal have been cultured and classified. The composition of bac-

terial species in the human microbiome changes over time and when a person is sick or takes antibiotics, these changes may be substantial².

Where is the microbiome located?

Bacteria and other microorganisms are found in and on many parts of the human body. This includes the gastrointestinal tract, vagina, skin and mouth – we are essentially covered by microorganisms. However, the vast majority of bacteria reside in the human large bowel², and this is also the most studied part of the human microbiome.

How do we get a microbiome?

Humans acquire most of their microbiome from other humans. Babies probably encounter microbes already in their mother's womb, but the colonisation begins at birth with a flush of bacteria from their mothers when they are born vaginally. Their next sources are breast milk and family – especially siblings – and as they continue to grow and are exposed to different foods, other people, pets and other environmental microbes, their microbiome becomes more established⁴.

Children who are born via caesarean section do not receive the initial flush of bacteria (mainly lactobacilli) from their mothers, and are instead colonised by bacteria from the skin of the parents and staff. Thus their microbiome is very different during the first years of their life.

Effects of Antibiotics on the Microbiome

All antibiotics kill both pathogens at the site of infection and bacteria belonging to the normal microbiome. This may cause several unwanted side effects and diseases described below:

Decreased diversity

A cornerstone of any well-functioning ecosystem is high diversity. Exposure to antibiotics can lead to changes and/or destabilisation (dysbiosis) in the human microbiome. This can in turn lead to diseases not necessarily directly caused by a single pathogen but caused by disruption of the composition and diversity the microbiome¹⁷.

Selection of resistant bacteria

Whenever a population of bacteria is exposed to an antibiotic, any bacteria that are resistant to it, either by mutation or transferred resistance, gain an advantage. As many other bacteria die, the resistant ones are able to increase in number. Widespread use of antibiotics leads to selection of bacteria that in turn may spread and cause infections that are difficult to treat¹⁸.

Transmission of resistance

Many bacteria are capable of transferring genetic material to each other via three routes: conjugation, transduction or transformation. Due to these processes, when one bacterium carries a gene causing resistance to a given antibiotic, the resistance gene can be passed on to other bacteria¹⁹.

Antibiotic-associated diarrhoea

Clostridium difficile (C. diff) is an example of a bacterial pathogen that is also found in healthy individuals. However, use of antibiotics, especially broad-spectrum antibiotics, even at appropriate doses can cause dysbiosis allowing the pathogen to grow. This can result in severe diarrhoea and gastrointestinal infections²⁰.

Modifying the Microbiome

Probiotics

Probiotics are defined as live microbes that cause a health benefit to the host. Commonly used probiotics are species belonging to three genera: *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces*²¹. In some cases, probiotics have been shown to modulate the composition of the microbiome and help restore or maintain human health by preventing growth of pathogenic bacteria^{22,23}.

Prebiotics

Prebiotics are substances that are beneficial for microbial growth. All known prebiotics are carbohydrates that are indigestible by mammals but fermented by the microbiota. In contrast to the probiotics, where live bacteria are eaten, prebiotics help existing bacteria to grow. Examples of prebiotic foods are asparagus, onions and oats²³.

Microbial transplants

In children delivered via caesarean section, concerns are that the lack of early colonisation with lactobacilli and bifidobacteria from the mother may have adverse health effects. Trials have been made where the newborn has been swabbed with the mother's vaginal microbiota. The results show that the babies develop a normal microbiome more rapidly than without the procedure²⁴.

Faecal transplants have shown to alter the microbiome and be a successful treatment approach for intestinal disorders, especially in patients with *Clostridium difficile* infection²⁵. The theory is that a dysbiosis can be restored

to a healthy composition by inoculating it with a healthy microbiota.

Environmental Microbiomes

Apart from the human microbiome, researchers are also studying the microbiomes of other systems such as hospitals, animals, different habitats on Earth and even the Earth as a whole. The Earth Microbiome Project²⁶, founded in 2010, is a massively collaborative effort involving over 500 investigators, using crowd-sourced samples, to understand patterns in microbial ecology across the biomes and habitats of our planet.

The most influential bacteria for life on Earth are found in the soil, sediments and seas. The most well known functions of these are probably providing nutrients like nitrogen and phosphorus to plants as well as producing growth hormones. Also, by producing antibiotic compounds and by their sheer number the beneficial bacteria may keep pathogenic bacteria at bay²⁷. By decomposing dead organic matter, they contribute to soil structure. The different compositions in different soils can even affect which plants are able to grow in a certain place²⁸.

The more spectacular species of environmental microorganisms are capable of living in extreme conditions: salt lakes, hot springs or mud pots near volcanoes, some producing beautiful, vivid colours.

The most influential bacteria for life on Earth are found in the soil, sediments and seas.



Laguna Colorada in Peru. The water is colored red by microbes/microorganisms.

Antibiotics and the Environment

The myriads of different species of bacteria and fungi found in the soil cause competition for nutrients and living space among the microorganisms. Some species have conjured some competitive advantages by producing antibiotics. These substances are released into the nearest surroundings, inhibiting the growth of other bacteria²⁹.

Natural antibiotics

Some of these are known to man, and have been harnessed as antibiotics in medicinal use. Examples include penicillin, synthesised by the fungus *Penicillium chrysogenum*, tetracyclines synthesised by *Streptomyces* species, and polymyxins synthesised by *Bacillus polymyxa*. Some estimates claim that approximately 80% of the antibiotics used in human medicine are either originally from the soil microbiome, or modified derivatives of such²⁹.

The latest substance found from the soil microbiome is teixobactin. The discovery of teixobactin was announced in 2015. It is a substance produced by the previously uncultivable bacterium *Eleftheria terrae*³⁰.

Antibiotic resistance

The other side of the story of antibiotics is the story of resistance. For an ecosystem containing antibiotic producing bacteria to be in balance, there need to be bacteria

resistant to these antibiotics. And so there are. For every class of antibiotics in human use, there are resistant bacteria. Antibiotic resistance has even been found in caves secluded from human influence.

Selection of resistance

With the use of antibiotics in human medicine and food production comes selection of resistance in bacteria, not only in our human microbiome, but also in animals and the environment. When human activities release antibiotics to the environment – through wastewater, manure or release from aquaculture – resistant bacteria and resistance genes are enriched. These bacteria are then able to spread and share the resistance genes to other bacteria they encounter³¹.

Antibiotics affect environmental microbiomes

Release of antibiotics to the environment may also affect the composition of the soil microbiome³². Spread of antibiotic containing manure has, for example, been shown to inhibit nitrogen-fixing bacteria and cause a shift in the populations in favour of fungi. At high loads of antibiotics near the outlets of wastewater treatment plants, the microbiomes have changed even more, with high degrees of resistant bacteria³³.

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