Our microbiomes: what do they do for us?

Miss, why do I have bacteria in and on me and what do they do?

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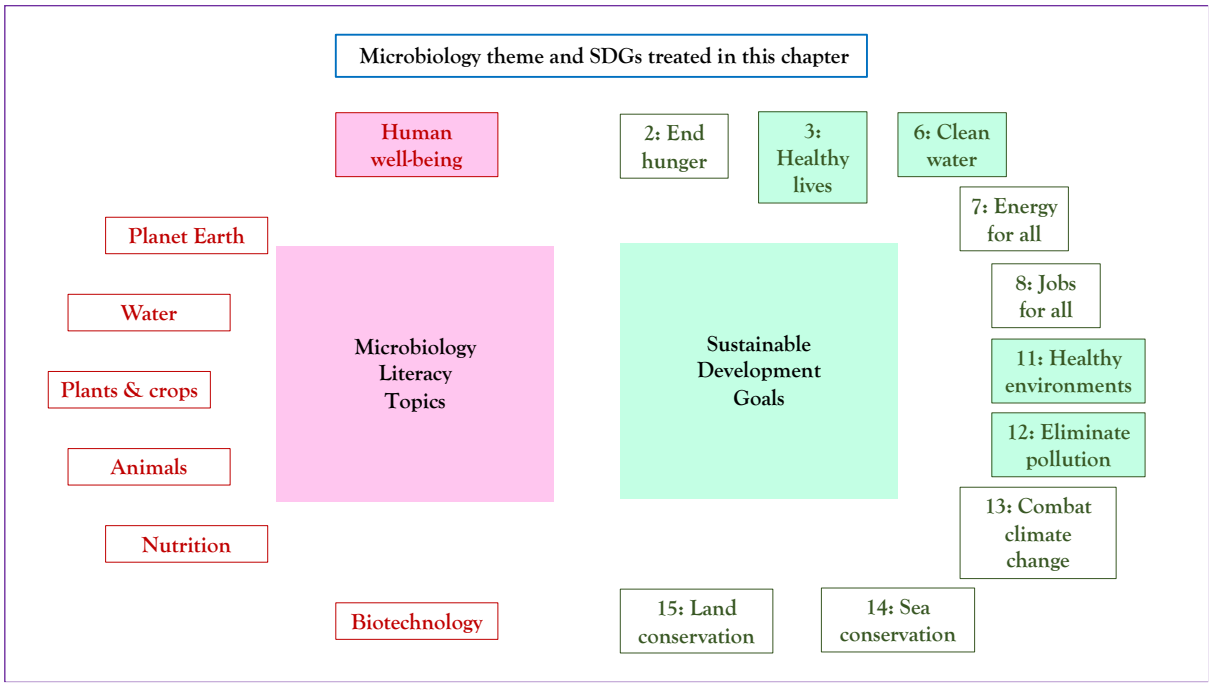
Storyline

From the time we're born, we share our bodies with trillions of microbes that call us home. This vast ecosystem of microorganisms including bacteria, fungi and viruses are collectively known as the human microbiome. These commensal organisms are found virtually everywhere – the surface of our skin and mucosal surfaces, inside our mouths, and even in our guts. Our bodies have developed a mutually beneficial relationship with these microbes, a concept known as symbiosis. In fact, we cannot live without them! While bacteria were once assumed to be dangerous and something to be eliminated, science now knows we actually depend on these microbes for several important functions: they aid in digestion, help to educate and stimulate our immune system, and produce important substances called metabolites that are essential for our overall health. It is becoming increasingly evident that supporting our microbiome can have a major impact on human health and disease.

The Microbiology and Societal Context

The microbiology: human well-being, microbiome enrichment and immune system development; communal relationships between bacteria and humans; nutrition and how to support beneficial bacteria, protection against pathogens, biotechnology (bacteria in healthcare). *Sustainability issues*: healthy lives, healthy environments, food and energy.



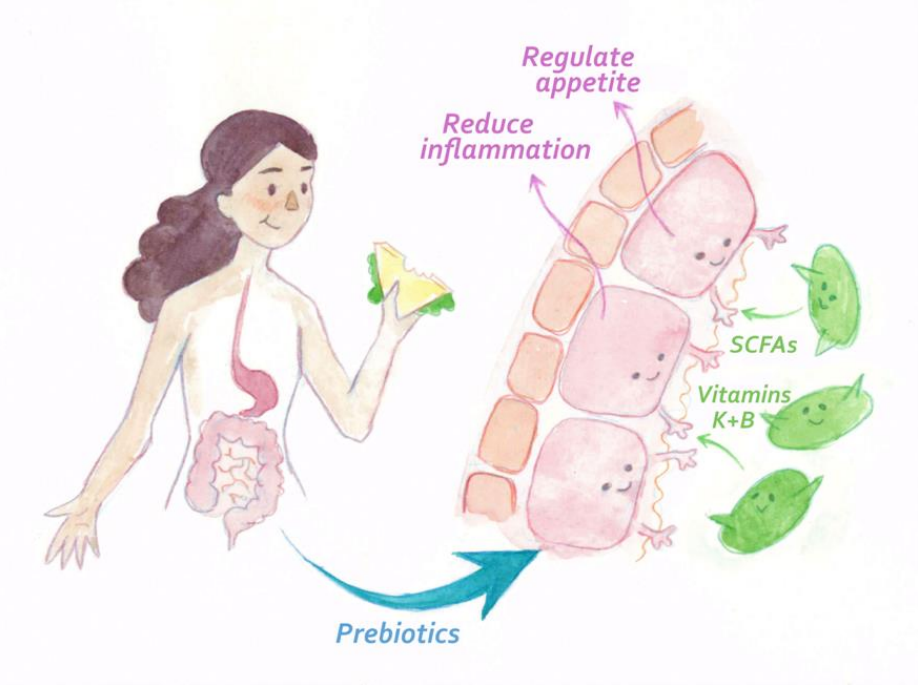
Our Microbiome: the Microbiology

1. ***The bacteria living in and on us contribute to the regulation of our immune system.*** The immune system is a network of cells and organs that our bodies have developed to protect us from disease and to respond to any foreign substances that might be a threat, including potentially dangerous microorganisms called pathogens. The bacteria residing in our gut can

produce beneficial substances, such as short chain fatty acids (SCFAs), that support the immune system by enhancing gut barrier function – the gate-keeping function of the cell sheet lining the intestine which regulates what passes through into our bodies and what is kept out and stays in the gut – promoting the development and recruitment of immune cells and preventing inflammation in the gut. We want our immune system to fight off potentially dangerous microbes, but also tolerate the harmless and beneficial microbes and the substances they produce in order to support these critical functions. This crosstalk between our gut microbiota and immune system helps keep us healthy.

2. ***The human microbiome acts as a living barrier to infections.*** Beneficial bacteria throughout the human body work with our immune system to induce protective responses when threatened by pathogens. For example, symbiotic microbes on our skin prevent the growth of more harmful organisms, and in our mouths, the oral microbiome helps protect against the invasion and colonisation of pathogens in the respiratory tract. Perhaps the most extensively studied is the gut microbiome, which includes both a physical barrier, i.e. the epithelial cells and mucus layer that line the intestines, as well as a chemical barrier of inflammatory molecules and other protective substances that the epithelial and immune cells produce. Our gut microbes represent the first line of defence of the gut barrier, and help keep it healthy by producing anti-inflammatory SCFAs, activating cell receptors to promote an immune response when needed, or by releasing antibacterial molecules called bacteriocins to inhibit the growth of potentially harmful microbes. Together, this close interaction between the gut bacteria and the intestinal barrier helps our body monitor for dangerous pathogens and protect us from infections.

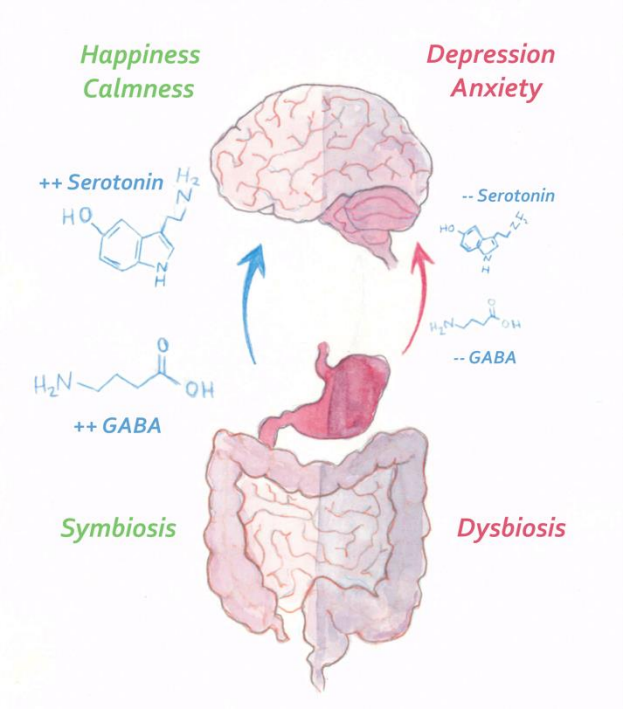
3. ***The gut microbiome supports our health through the synthesis of vitamins and other beneficial metabolites.*** We know how important it is to feed our bodies nutrient-rich foods, but it's also important to nourish our gut bacteria. The microbes living in our large intestine rely on prebiotics – foods that cannot be fully digested by humans – for energy and survival. Fermentation of carbohydrates produces generally beneficial metabolites, such as the short chain fatty acids acetate, propionate and butyrate, all of which perform important roles in the human body. These SCFAs serve as fuels – sources of energy – for gut epithelial cells, help reduce inflammation, and help regulate appetite and glucose levels. Gut bacteria can also produce vitamins such as vitamin K, biotin, cobalamin, folates, riboflavin and thiamine. While these vitamins are important for human health, they can also be used by other bacteria to support growth and survival.



4. ***The human gut microbiome plays a critical role in metabolism.*** Food sources that human cells can't break down, such as complex carbohydrates, are converted by gut bacteria into metabolites that the body can absorb. While a healthy microbial community can provide us with beneficial substances such as vitamins and SCFAs, scientists have found that an imbalance in the gut microbial community – known as dysbiosis – is closely linked to the development of obesity, diabetes and cardiovascular disease. This is because gut bacteria can influence specialised cells in the intestinal tract called enteroendocrine cells, which can produce hormones that regulate your appetite and metabolism. Bacteria and their metabolites can stimulate the release of these hormones, which can influence key metabolic processes such as hunger or satiety (fullness), insulin sensitivity, glucose tolerance and fat storage. In normal concentrations, this microbe-mediated hormone release helps maintain our energy levels, but too much or too little can contribute to the development of metabolic diseases.

5. ***Inflammation is a natural defence mechanism that recognises damaged cells or pathogens and begins the healing process, and this can be influenced by the microbiome.*** While it plays a necessary role in fighting infections, too much inflammation can be a cause for concern. Many diseases of the developed world have been linked to inflammation, including cardiovascular disease, obesity and inflammatory bowel disease (IBD), and scientists are now finding that an imbalanced microbiome plays an important role in this process. Luckily, a healthy microbiome can help prevent inflammation! Those undigested fibres (prebiotics) that reach the large intestine are fermented by bacteria to produce SCFAs that can exert many beneficial effects; they can activate receptors on intestinal epithelial cells and immune cells to promote anti-inflammatory cytokines, inhibit inflammatory responses by immune cells such as monocytes, and promote cellular repair in the colon. Through the production of these signalling molecules, the human microbiome plays a major role in maintaining a healthy balance of inflammation in the body.

6. ***Our microbiomes not only influence our physical health, but they also play a major role in our mental health.*** Signals can be exchanged between the central nervous system (the brain and spinal cord) and the gut, meaning that our gut bacteria can influence our mood and behaviour. Much of the research has focused on a chemical messenger called serotonin, which helps to regulate mood, happiness and anxiety; reduced levels of serotonin have been linked to depression. It is estimated that over 90% of our body's serotonin is produced and stored in the gut, and this is stimulated by SCFAs. Another mood-boosting bacterial metabolite is called Gamma-Aminobutyric Acid (GABA), which is produced by certain bacteria in the gut and has a calming effect to help reduce anxiety, stress and fear. Exactly how the gut microbiota signal to the brain is still not clear, but there is evidence to suggest gut-derived signals travel through the vagus nerve that connects the digestive system to the brain to exert their mood-altering effects.



7. ***Microbiomes that are diverse and balanced exert numerous health benefits; however an imbalanced microbial composition can have a negative impact on health.*** The key to a healthy microbiome is having high microbial diversity, meaning there are many different species that are evenly spread out. Different kinds of bacteria serve different functions, so having a more diverse microbiome means there are more species that can perform the critical duties that help keep you healthy. A reduction in diversity or imbalance of gut microbial populations – dysbiosis – has now been linked to numerous diseases. During a state of dysbiosis, there is a negative shift between beneficial microbes and pathogens, and this can decrease intestinal barrier protection and potentially benefit infectious pathogens. One way this can occur is through the overuse of antibiotics, which kill off the bacteria causing infections but also kill off our beneficial bacteria. This leaves room for potentially harmful (opportunistic) bacteria to grow and take over while beneficial bacteria decline. In addition to antibiotics, other lifestyle factors can also contribute to microbial dysbiosis. Remember that we have multiple microbiomes (including the gut, skin, mouth, and vagina) and that dysbiosis can affect many areas of our health, sometimes resulting in brain fog, depression, anxiety, skin issues, fatigue, autoimmunity and allergies.

8. ***Microbiota transplants: unlocking the powers of a healthy microbiome.*** Dysbiosis has been linked to many diseases including inflammatory bowel disease, obesity, type 2 diabetes and cardiovascular disease. While microbiome research is still in its infancy, researchers are taking what they've learned about the importance of the microbiome in these conditions to develop new treatment options for patients. Put simply, a faecal microbiota transplant (FMT) replaces the dysbiotic microbiome of sick patients with the gut microbiome from a healthy donor. FMT is currently used for the treatment of *Clostridioides difficile* (*C. diff* for short) infection, a serious infection caused by a pathogenic bacterium that some people can get in hospital settings and

after the use of antibiotics. The success rates of treating recurrent (repeated) *C. diff* infection with FMT are as high as 92%, leading researchers to explore FMT for the treatment of other diseases such as inflammatory bowel disease and metabolic conditions. While this is an exciting area of research, FMT does not come without risks. What exactly a 'healthy microbiome' looks like is still not clear, and it is critical to screen healthy donors to prevent the transmission of potentially harmful pathogens such as viruses, parasites, or drug-resistant strains of bacteria. Although FMT is promising for the treatment of some medical conditions, it should only be performed by specialised health care practitioners because of the associated risks and how much we still don't know about the microbiome.

9. ***The good news is, there are several things we can do every day to help support a healthy microbiome to get the most health benefits from our microbes***. Studies show that a more diverse microbiome is more resilient to disruption, meaning it can quickly adapt to disruptions and help prevent dysbiosis-associated diseases. A more diverse microbiome means a greater diversity and abundance of enzymes capable of performing different functions that contribute to our overall health. We can increase our microbiome diversity by eating a diverse range of high-fibre foods, spending time outdoors and with animals, and avoiding the unnecessary use of antibiotics and disinfectants that harm good bacteria along with the bad.

Relevance for Sustainable Development Goals (SDGs) and Grand Challenges

The human microbiome relates to several SDGs, including

- **Goal 3: Promote healthy lives at all ages through early education of microbiome importance**. The microorganisms living in and on us have a profound impact on our overall health. These microbial communities are dynamic and can be influenced by a variety of environmental and lifestyle factors, so it is important to educate from a young age to encourage informed choices to optimise both physical and mental wellbeing. This can be done through encouraging a healthy, diverse diet, discussing the negative impact of things such as smoking and drugs on the microbiome, as well as the consequences of hyper-sanitisation and antibiotic overuse. Exercise can also have a beneficial effect on the microbiome and could be encouraged as part of a healthy lifestyle. The transmission of pathogens in the microbiome (gut, oral, or vaginal) can negatively impact the health of others if proper hygiene is not maintained and exposure to others when sick is not minimised. This is especially important for high-risk populations such as those with weakened immune systems.
- **Goal 6 Access to clean food impacts our microbiomes**: When pathogenic microorganisms get past the barrier of our protective microbiomes, there can be serious health consequences. Foodborne pathogens, for example, affect millions of people every year. The most common types of foodborne illnesses are caused by bacterial species such as *Salmonella* and *Campylobacter*, which can be found in raw and undercooked meat and cause gastrointestinal symptoms like diarrhoea. Education on safe food storage and preparation can help avoid contamination and resulting illness.
- **Goal 11: Maintaining healthy environments while embracing our coexistence with microbes**. The modern compulsion to keep our hands and homes obsessively clean with constant hand sanitiser and bleach (hyper-sanitisation) may be doing more harm than good. Microorganisms are crucial for our wellbeing and people who grow up with these levels of sanitation and lack of exposure to microbes can actually have impaired immune system

development. This idea has been termed the hygiene hypothesis. At the same time, appropriate sanitation such as washing your hands after using the toilet and sanitising things that have had contact with known contaminants is important in preventing transmission of disease.

- **Goal 12: Promote sustainable consumption patterns to help eliminate waste**. The Westernised diet is generally characterised by high intakes of processed and pre-packaged foods. This is not only detrimental to the human microbiome, as processed foods generally lack the important prebiotics that feed our beneficial bacteria, but also requires the use of energy and resources for processing (e.g. heating, cooling, or electricity) and results in substantial generation of waste such as plastic or aluminium packaging. Additionally, a high demand for meat production has raised major concerns for its contribution to global warming because cows and other farm animals produce methane, a potent greenhouse gas. Eating a largely unprocessed, plant-based diet consisting of whole grains, fruits and vegetables that require little packaging would not only improve human health but could help reduce waste and pollution from processing plants.

Potential Implications for Decisions

1. ***Individual***
   a. How individual lifestyle choices (diverse and high-quality diet, appropriate hygiene, exercise, smoking, unnecessary medications) may affect individual health?
   b. Financially, is buying and preparing fresh, high-quality foods possible as opposed to inexpensive processed and packaged foods?
   c. How can personal health choices affect the health of others?

2. ***Community policies***
   a. School food policies: are clean, healthy foods to support a healthy microbiome available and affordable?
   b. Is education on the effects of lifestyle choices on our microbiomes and health a part of the curriculum?
   c. Are businesses such as restaurants and retail shops practising appropriate sanitation to avoid transmission of microbial infection?

3. ***National policies***
   a. National Dietary Guidelines: do they reflect what we know about nutrition required to support a healthy microbiome?
   b. Overuse of antibiotics – Hospital guidelines and requirements for prescribing antibiotics, do the benefits outweigh the long-term negative effects?
   c. Healthcare economics of dysbiosis-linked diseases, including mental health.

Pupil participation

1. ***Class discussion on importance of a healthy immune system***
   a. Explain how microbes protects us.
   b. How can we improve the health of our microbiomes?

2. ***Exercises***
   a. List five things that could negatively affect your microbes (smoking, no hand washing, no exercise, picky eating)

b. List three ways to support your microbes (diverse food, pets

The evidence base, further reading and teaching aids

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Glossary

Commensal: A relationship in which one organism obtains food or other benefits from another organism without helping or hurting it. Many commensal bacteria have a place to live and source of nutrients in and on the human body without positively or negatively impacting us.
Symbiosis: A mutually beneficial relationship between different organisms. Many bacteria in the gut live in symbiosis with their host, gaining access to shelter and nutrients while producing substances that are beneficial for host health.
Metabolites: End products and intermediates of cellular metabolism. Examples of bacterial metabolites include lactic acid, ethanol, and certain amino acids.
Short chain fatty acids: Fatty acids with fewer than 6 carbon atoms. They are produced when bacteria in the gut ferment indigestable carbohydrates and have been shown to have many beneficial effects. Major bacterial-derived short chain fatty acids include acetate, proprionate and butyrate.
Pathogens: any disease-causing organism, for example certain viruses, bacteria, protozoa, fungi, algae, worms, etc.
Enteroendocrine cells: specialised hormone-producing cells found within the gastrointestinal tract that play a role in food digestion and absorption, insulin secretion and appetite.
Serotonin: A type of chemical that relays signals between nerve cells (also known as a neurotransmitter). It is found primarily in the digestive system and helps regulate mood, emotions, sleep, appetite and digestion.
Dysbiosis: An imbalance in the microbial communities that live in and on the body, especially in the gut. This can mean a reduction in beneficial bacteria and increase in potentially harmful bacteria.
Opportunistic: This usually refers to microorganisms (such as bacteria, viruses, fungi, etc.) that do not normally cause harm, but can become pathogenic following a disruption to their host (such as a weakened immune system, dysbiosis, prior infection, wound or medication, etc.)