The gut microbiome – balancing the body

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Introduction

Did you know that there are an estimated 37 trillion human cells in the adult body? In fact, there are only an estimated 100-400 billion stars in the Milky Way, so there are more cells in the human body than there are stars in the Galaxy!

In addition to human cells, there are also another 30-100 trillion non-human cells, such as bacteria, archaea and fungi, and non-living organisms such as viruses, that live on or in the human body. These microscopic organisms (microorganisms) and their interactions with a specific environment, such as the gut or skin, are known as the **microbiota**. You may be more familiar with the terms ‘friendly bacteria, commensal bacteria, or flora’. The organisms of the microbiota, their genetics and the substances they release interact with each other and their environment to form the **microbiome**. Humans have several microbiomes, including in the gastrointestinal tract (gut), urogenital tract (urinary and genital systems) and on the skin.

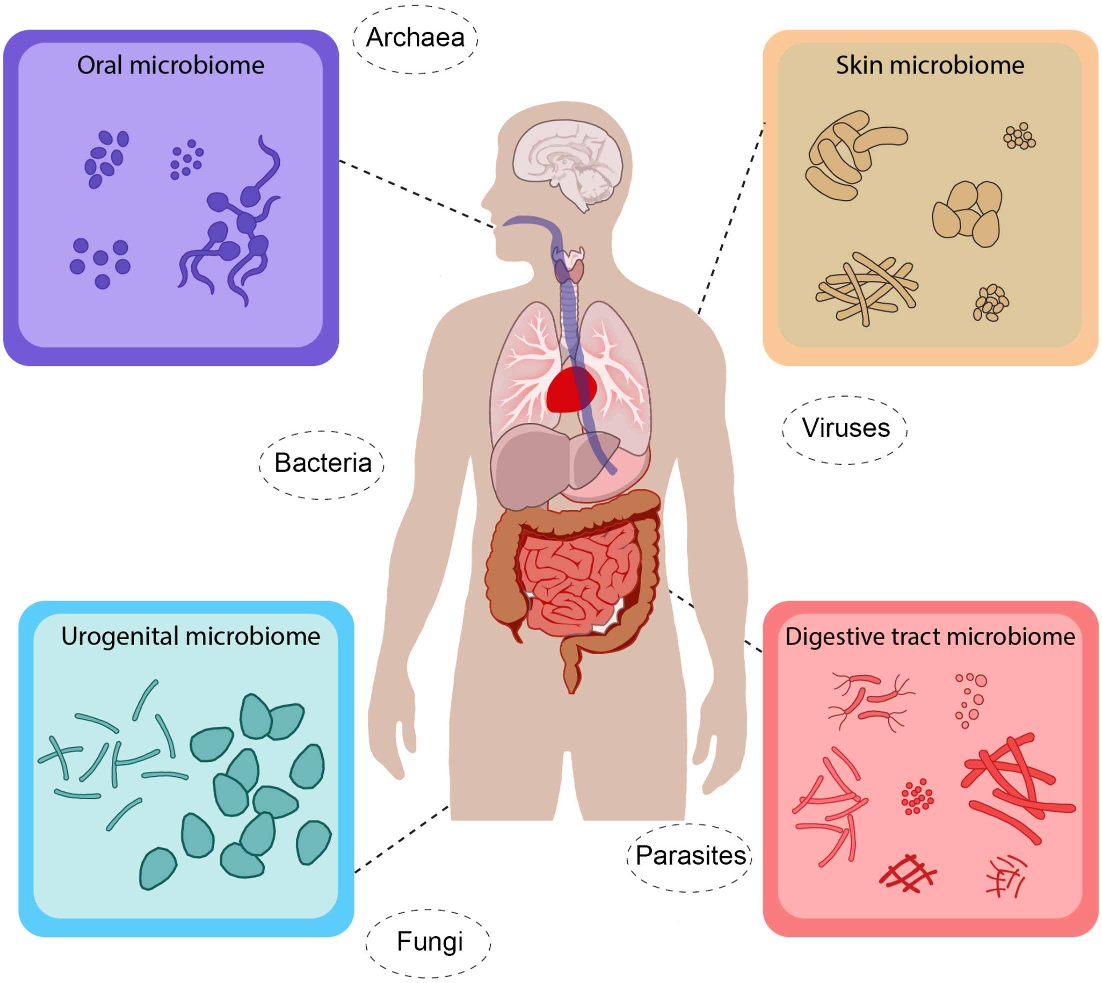

Figure 1 Microbiomes around the body

Scientific research is increasingly showing the importance of these microbiomes for the correct functioning of the human body and for maintaining health. In fact, disruption to these microbiomes can lead to a number of long-term health conditions, such as cardiovascular and respiratory diseases, some cancers and some mental health disorders.

The gut microbiome is the largest and most diverse of the microbiomes and is particularly important in maintaining optimal health. However, there are numerous factors which can affect the balance of the microorganisms in the gut microbiome, such as genetics, age, menopause, pollutants, and diet. The microorganisms of the gut microbiome are located throughout almost the entire length of the gastrointestinal tract (gut). The main anatomical components of the GI tract can be seen in Figure 2.

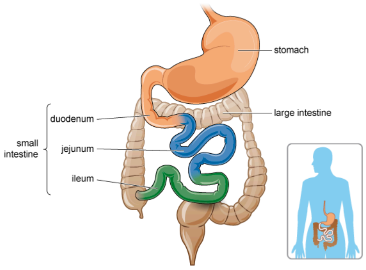

Figure 2 Simplified representation of some components of the gastrointestinal tract (gut)

During this free course, *The gut microbiome – balancing the body*, you will initially explore the gut microbiome in more detail. You will learn about the typical components of the gut microbiome, and how every human's microbiome is unique, before moving on to consider the various functions of the gut microbiome. You will then look at factors that can affect the microorganisms of the gut microbiome, and how this can contribute to the development of a number of common health conditions. The course will conclude by briefly looking at some of the ways in which we can improve the health of our gut microbiomes.

After studying this course, you should be able to:

- demonstrate and understand what the gut microbiome is and outline how it functions within the human body
- describe some of the ways the gut microbiome can be altered by factors including genetics and age, as well as lifestyle factors, such as diet and exercise
- explain the importance of the gut microbiome for human health
- recognise the impact of dysbiosis on the development of various health conditions
- outline strategies to improve the health of the gut microbiome.

This OpenLearn course is an adapted extract from the Open University course SK190 *Human biology: a body in balance*.

1 What are microbiomes?

Humans live in a variety of environments, such as cities, deserts, river deltas and mountain tops. Humans also live alongside a wide variety of animals and plants, eat a large variety of foods, and travel to diverse environments. Microorganisms, also known as microbes, can be found in all these environments alongside humans. Microorganisms are usually single-celled (for example, bacteria) or multi-celled (such as some fungi) that can only be seen through a microscope.

The warm core temperature of the human body and resource-rich internal environment makes the human body optimal for the growth and maintenance of the body's own cells. However, it also means that this is an ideal environment for the growth and survival of some microorganisms.

The vast majority of microorganisms that humans encounter on a daily basis are harmless. However, some microorganisms can invade the body and use resources at a cost to the human host, or excrete damaging waste products and toxins, all of which can cause disease or even death. These microorganisms are called **pathogens** and are potentially disease-causing microorganisms. Pathogen is a broad term that encompasses different types of microorganisms, including bacteria, viruses, fungi, protozoa and parasites. Some molecules are disease-causing too, such as toxins and prions. However, some microorganisms can actually be beneficial to humans, and these are known as **symbionts**, and this includes the microorganisms of the microbiome.

Often, the terms microorganisms, microbiota and microbiome are used interchangeably, which can be confusing. However, they have all have slightly different meanings and this is shown in Figure 3.

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Figure 3 The difference between microorganisms, microbiota and microbiome

The key difference is that the microbiota refers purely to the collective group of organisms living within a specific environment, such as the gut. So, the gut microbiota is all of the bacteria, fungi, viruses, etc, that are found within the gut.

Fun fact: tricky terminology

Scientific terminology can sometimes be challenging! The words often seem very long and complicated. To help understand them, it can be useful to break the words down into smaller parts. For example, microbiome can be broken down as follows:

micro- derived from the Greek words for 'small' or 'tiny'

-biota also has Greek origins, relating to 'life'

-biome translates as 'the root of life' and also meaning 'community, area or environment'.

So, microbiota refers to the small living microorganisms in their specific environment. The microbiome refers to the environment *and* the microbiota *and* their genetic make-up *and* all the substances they produce to interact to form a community.

Question 1

Thinking about a specific type of microorganism mentioned earlier, can you use the information above to deduce what the word ‘viriome’ means?

- This word can be broken down into ‘viri’ which relates to viruses, and ‘ome’ which, as you learnt above, means ‘community or environment’. So a viriome of an environment is the total virus content within it.

The microbiome includes the microbiota but also includes other elements, such as structural components, the metabolites (substances produced by the microbiota) and the environmental conditions themselves, such as the wall of the gut and substances it produces.

The gut microbiome is highly dynamic, with constant interaction between the human cells, the microorganisms of the gut microbiota, and the substances they produce. The microorganisms of the gut microbiota even interact and influence the behaviour of each other! You’ll learn more about this shortly.

1.1 Overview of the gut microbiome

The gut microbiome is composed of trillions of bacteria, viruses, archaea and fungi. In fact, it is estimated that there are 10^{14} bacteria in the gut – that’s 100,000,000,000,000 individual bacteria living in our guts! However, the microbiome is dynamic and many of these bacteria will be dying or lost on a daily basis, while it is thought that 10^{11} new bacteria enter the gut every day, travelling from the pharynx (back of the throat) to the rest of the gastrointestinal (GI) tract.

Fun fact: Dealing with very large or very small numbers

You may have noticed that the paragraph above used two ways of writing the same number. One approach involved writing out lots of zeros, while the other approach used the number 10, raised to the power of 14 – an approach known as scientific notation.

Using scientific notation removes the difficulty of having to keep an eye on all those zeros and reduces the potential to accidentally miss one out or include an extra one! Scientific notation can be used to write very large numbers and also for writing very small numbers.

For example:

(a) A population of 100,000,000 microorganisms could be written as 1×10^8

(b) The diameter of a particular bacterium might be written as 0.000006 m, or 6×10^{-6} m

- **Question 2**

  In example (a) above, how many zeros are there in the number written in full, and what is the power of 10 used when the number is written in scientific notation?

- There are 8 zeros in the number written in full, and the power of 10 used in the scientific notation is 8. Essentially, you have moved the decimal point 8 spaces.

Question 3

In example (b) above, how many zeros are there in the number written in full, and what is the power of 10 used when the number is written in scientific notation?

- There are 6 zeros in the number written in full, and the power of 10 used in the scientific notation is -6. Essentially, you have moved the decimal point 6 spaces.

This may help you to convert from a number in full, to a number of scientific notation. When converting a very large number into scientific notation, the power of 10 will be a positive value (as in example a), and when converting a very small number into scientific notation, the power of 10 will be a negative value (as in example b). To work out what the power should be, you simply count how many times you moved the decimal point.

The composition of the gut microbiome changes throughout our lives. During the first 3 years of life our gut microbiome is formed and affected by various factors, such as breastfeeding, weaning and bacteria found in the local environment. As we age, two groups of bacterial species become predominant, called Firmicutes and Bacteroidetes, which form about 90% of the gut microbiota (Arumugam, 2011).

Figure 4 shows the distribution of the most common bacterial groups found in microbiomes around the body. You may notice that the different parts of the GI tract contain different proportions of the bacteria.

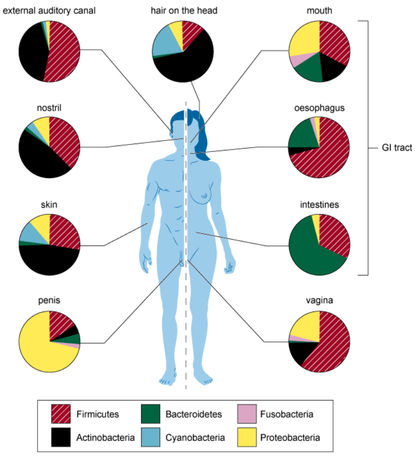

Figure 4 Distribution of bacteria found on or in different parts of an average healthy body

Question 4

What is the most common bacterial group in the oesophagus and in the intestines?

- Firmicutes is the most common group of bacteria in the oesophagus, while Bacteriodetes is the most common bacterial group in the small and large intestines.

The six most common bacterial groups found in the microbiota are Firmicutes, Bacteroidetes, Fusobacteria, Actinobacteria, Cyanobacteria and Proteobacteria. The distribution of bacterial groups or species in an individual forms their **enterotype**, and this is named after the predominant bacterial type present in that individual. For example, an individual with the highest proportion of Bacteroidetes in their gut microbiome would be referred to as having a Bacteroidetes enterotype. The identification of these enterotypes may have important consequences for health (you'll learn more about the importance of bacterial diversity and balance later).

The bacteria of the gut microbiome interact with the local gut environment and with each other to play several important roles in the human body. These fall into five main functional categories:

- metabolic
- structural
- protective
- communication
- immune.

You will explore the many functions of the gut microbiome in detail later in the course.

1.2 Balancing the gut microbiome

The balance between the different bacterial groups within an individual's enterotype is important in maintaining health, as is the balance between pathogenic and symbiotic bacteria of the microbiome. In fact, some microorganisms within the microbiota actually help to maintain this balance between pathogens and beneficial/harmless microbiota (working alongside the immune system) to avoid the development of disease.

In Figure 4, you saw that there is a different distribution of bacteria contained within the different microbiomes around the body. While this figure shows the typical distribution of bacteria, every human actually has a unique combination of microorganisms that form their microbiota. This can be seen in Figure 5, which shows the bacterial groups of the gut microbiota from five individuals.

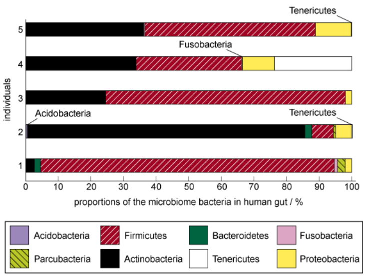

Figure 5 Bar chart (presented horizontally) showing the proportions of the different bacterial groups making up the microbiota within the gut of five individuals

■ **Question 5**

Based on the information in Figure 5, which individual has greater diversity in their gut microbiota, individual 1 or individual 3?

■ Individual 1 has 6 bacterial groups present in their gut microbiota. In contrast, individual 3 has three bacterial groups present in their gut microbiota. Based on the information in the figure, individual 1 has a more diverse gut microbiota.

Fun fact: gaseous by-products!

The unique microbiota profiles of each individual produce a unique combination of gases that are made as a by-product from the food that is consumed. As a result, each individual has a unique gas profile that can be measured. It is even thought that these gases may have important functions within the body, contribute to the development of diseases and might even be useful for the treatment of some conditions in the future! (Kalantar-Zadeh, 2019)

There are many factors which contribute to the microbiota profile of an individual. These include:

- genetic make-up
- exposure to microorganisms during pregnancy and early postnatal development
- geographical exposure to different environments
- diet
- exercise
- antibiotics, antimicrobials and other medications
- infection and disease
- age, including menopause.

Some factors, such as medications, menopause and disease, reduce the diversity of the organisms in the gut microbiota. Certain foods can also disrupt the normal balance of the bacterial species within the microbiota, while some other foods, pre/probiotics and exercise can improve the health of the microbiota, by promoting the growth of beneficial bacteria. All of these factors can have an impact on the health of the individual, and in the next section you are going to start to learn more about an unbalanced microbiome.

1.3 Loss of balance – dysbiosis

The importance of a healthy microbiome for human health is becoming increasingly clear. A healthy microbiome needs a good diversity of microorganisms within the microbiota and a balanced ratio of the two main bacterial groups: Firmicutes and Bacteroidetes. This is shown in Figure 6, where the Firmicutes and Bacteroidetes are shown to be in balance (the actual amounts and ratio will vary between individuals).

Fun fact: What are ratios?

Ratios are a simple way of comparing two or more quantities. In the example discussed here, the ratio would be the number of Firmicutes compared to the number of Bacteroidetes. Ratios are typically expressed as numbers separated by a colon. As a simple example, if you had 3 apples and 6 pears in a fruit bowl, the ratio of apples to pears would be 3 to 6 (3:6) or simplified to 1:2.

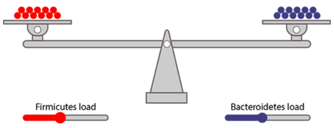

Figure 6 There is a healthy (but not necessarily equal) ratio of Firmicutes and Bacteroidetes in healthy individuals

Loss of diversity of the microorganisms within the microbiota is known as **dysbiosis**, and can contribute to a number of conditions affecting the gut, including irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), as well as affecting other parts of the body.

Question 6

There are three mechanisms through which dysbiosis might occur. For example, there is a loss of overall bacterial diversity. Thinking back to what you have read earlier, select the correct word from the drop-down menu to complete the other two mechanisms.

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If there is a loss of bacterial diversity, the ratio between the bacterial groups Firmicutes and Bacteroidetes can change. But why is this important? As mentioned earlier, the microorganisms that compose the microbiome not only affect the cells of the human host, but also influence each other. That is, they have a symbiotic relationship with each other. Some of the microorganisms are known to secrete molecules that are beneficial for other microorganisms, and with dysbiosis these symbiotic relationships are disrupted.

Diet and pathogenic bacteria are both important causes of dysbiosis. Ultra-processed foods (UPFs), alcohol and foods rich in sugar or food additives can lead to dysbiosis. Bolte et al. (2022) found that processed or animal-based foods were associated with increased numbers of opportunistic pathogenic bacteria which reduced microbiota diversity. Conversely, plant-based foods, fish and fermented foods increased the number of healthy bacteria which helped to reduce the number of pathogenic bacteria.

Some of the common signs and symptoms of dysbiosis include:

- bad breath (halitosis)
- nausea
- bloating
- constipation and/or diarrhoea
- abdominal pain
- rash or redness
- fatigue and brain fog.

You will learn more about the role of dysbiosis in various health conditions in Section 4. First, you are going to learn more about some of the functions of the gut microbiome.

2 Functions of the gut microbiome

As you have learnt previously, the gut microbiome has important roles in the normal functioning of the human body.

- **Question 7**

  Can you remember the five main functions of the gut microbiome?
- The five main functions are:
  - metabolic
  - structural
  - protective
  - communication
  - immune.

You will learn about each of these functions in more detail in the following sections.

2.1 Metabolic – digestion of food

The microorganisms of the gut microbiome play an important role in several metabolic processes – that is, the chemical processes that take place in an organism to produce energy or resources necessary for life.

The breaking down, or digestion, of the food we eat is an important metabolic process, as it enables us to gain energy and nutrients from food. The energy obtained from food is used as fuel by the cells throughout the body, while the nutrients are used as building blocks to manufacture important molecules.

Food is digested within the human gut via several mechanical and chemical processes, and involves many specialised molecules, called enzymes. Once broken down into smaller components, the nutrient molecules cross the gut wall and enter the bloodstream to travel around the body to where they are needed. However, certain substances cannot be digested by the human host.

While most of the digestion by the human host takes place in the stomach and small intestines, a small proportion of the food will not have been fully digested by the time it reaches the large intestine. Here, the microbiota of the microbiome produce their own enzymes which digest some of the remaining food products, particularly complex carbohydrates and dietary fibre, but also some protein and fats. The nutrients from these substances are then absorbed across the gut wall of the human host or used by the bacteria of the microbiome as a food source.

The digestion of dietary fibre by the microbiome is particularly important, as a group of important molecules are produced as a by-product. These molecules are known as **short-chain fatty acids (SCFAs)** and are absorbed into the human body (Figure 7) where they have several important functions.

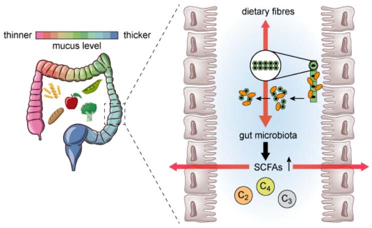

Figure 7 Role of the colon (part of the large intestine) in the digestion of dietary fibre with the production and absorption of SCFAs into the body. The long dietary fibre molecules (shown in green) are broken down into smaller molecules by the orange microorganisms of the microbiota. Some of these smaller molecules are absorbed across the gut wall, while others are used as fuel stores by the microbiota. The microbiota then produce SCFAs (shown by the circles C2, C3 and C4), which are also absorbed across the gut wall.

Fun fact: amazing molecules!

You will learn more later in this course, but in brief, SCFAs can provide energy for the body, regulate appetite, reduce obesity and insulin resistance in diabetes, destroy colorectal cancer cells, provide energy for other microbiota, and prevent gut dysbiosis. SCFAs are also involved in several communication pathways within the body, and recent evidence suggests that they can interact directly with the brain (Silva, Bernardi and Frozza, 2020) and may have a long-lasting impact on neurological and behavioural processes.

As well as producing molecules of use to the human host, some of the bacteria in the microbiome will use the fibre from the diet as their own food source. A lack of fibre can result in some bacterial groups dying out due to a lack of nutrients, leading to an imbalance in the diversity of the microbiota. This is one of the reasons having a diet high in fibre is important for maintaining good health. One type of Firmicutes bacteria, called *Lactobacillus*, is particularly important for digesting dietary fibre to produce SCFAs (and vitamins). *Lactobacillus* bacteria are found in high proportions in fermented food, such as kimchi, sauerkraut, yoghurt, and kefir, and in many probiotics (you will learn about probiotics at the end of this course).

2.2 Metabolic – production of nutrients

In addition to digesting the food we eat to provide the human host with nutrients, the gut microbiome also manufactures important micronutrients, such as vitamins and minerals, which are essential to the survival of the human host and other microbiota. For example, the B vitamins are all synthesised by the microbiome. In addition, the microbiota increases absorption of other dietary vitamins and minerals in different parts of the GI tract.

Figure 8 shows some of the dietary micronutrients and SCFAs produced by the microbiome and absorbed across the host gut wall.

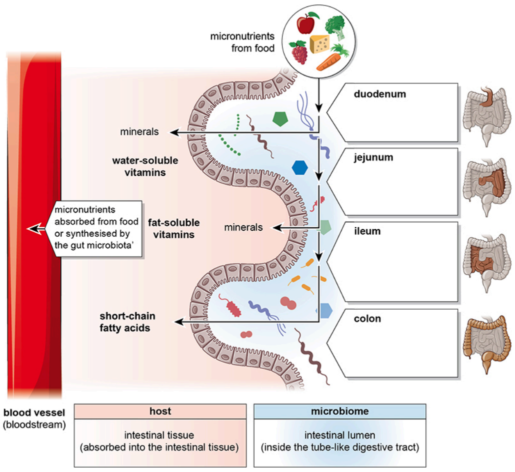

Figure 8 Micronutrients present within the intestinal gut microbiome from the dietary sources and synthesis by the gut microbiome are transported into the intestinal tissue and then into the bloodstream for the host to use

Fun fact: why is it called the 'small' intestine?

The length of the tube that forms the small intestine is around 6 metres in an adult, compared to the length of the tube forming the large intestine, which is only around 1.5 m in length. So, you might wonder why the small intestine is called 'small'. The name refers to the diameter of tube, rather than length. The diameter of the small intestine is much smaller than that of the large intestine.

The B vitamins synthesised by the gut microbiome are important in the generation of energy in the cells. Some bacterial groups in the gut microbiome, such as Firmicutes and Bacteroides, synthesise:

- fat-soluble vitamins such as vitamin A, D, E, and K (around half the daily requirement of vitamin K is provided by gut bacteria)
- water-soluble vitamins – B vitamins such as folate, thiamine, biotin, riboflavin and pantothenic acid, and vitamin C.

The gut microbiome is an important additional source of the water-soluble vitamins, as levels of these vitamins in food are often inadequate and they cannot be stored in the body.

2.3 Metabolism of drugs and xenobiotic chemicals

Another important function of the gut microbiome is the metabolism of some chemicals which are foreign to the human body. Such substances are known as xenobiotics.

Question 8

Every human is exposed to some xenobiotic chemicals during their lifetime. From your general knowledge, think of some categories of xenobiotics you may have come across before.

- Some of the categories of xenobiotic chemicals you may have thought of include food additives, such as flavourings and colourings, pesticides, cosmetics, and fragrances. You might also have considered drugs (both medicinal and recreational), industrial chemicals and environmental pollutants.

As well as producing enzymes that are important for digesting components of the food eaten by the human host, the gut microbiome also manufactures enzymes which can break down some xenobiotic chemicals (Zhoa, 2023).

Figure 9 Medications and chemicals ingested from the environment can be modified by the gut microbiome

It has long been known that the human host genetics, age, sex assigned at birth, lifestyle, metabolism, disease status, other medications and environmental factors can all affect how different individuals respond to medications. This is termed **individual variability in drug response (IVDR)**. However, recent research has shown that the gut microbiome of the individual also plays an important role in the IVDR. This new area of research has been called pharmacomicrobiomics.

As you will learn shortly, the gut microbiome can be modified (both beneficially and detrimentally) in many ways. This can potentially alter the way an individual will respond to a medication, for example, changing drug efficacy and therapeutic effects. So, this modification of the microbiome is potentially an important new way that drugs can be made more effective in an individual, or have fewer side effects and interactions with other medications.

The Human Microbiome Project (HMP) in collaboration with the National Institutes of Health (NIH) are investigating the diversity and function of the human gut microbiome (much like the Human Genome Project), to identify its impact on health human and IVDR (HMPDACC, n.d.).

2.4 Structural integrity of the gut wall

The human gut wall is made up of several layers of different tissue types, including muscle, nerves and blood vessels and an innermost mucosal layer. The cells of the mucosal layer of the small intestine secrete important enzymes for digestion of food and allow nutrients to pass through them into the bloodstream. They also secrete mucus to lubricate the contents in the gut tube. The inner layers of the gut wall are highly folded into finger-like projections known as **villi**, which increase the surface area of the gut (Figure 10).

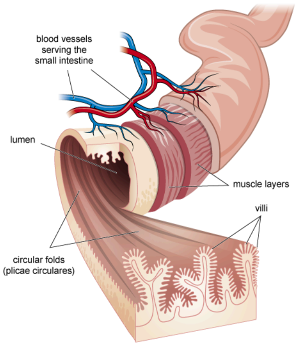

Figure 10 Schematic of the small intestine, showing the individual layers and highly folded surface of the internal layers of the gut. Blood vessels supply oxygen to the gut wall and transports nutrients to the rest of the body.

- **Question 9**

  Why do you think a large surface area would be useful in the gut?

- The large surface area created by the presence of villi and folds in the gut wall of the small intestine maximises the absorptive capacity of the gut (i.e. more of the nutrients obtained from the digestion of food substances, can be absorbed from the gut lumen).

The mucosal cells of the innermost layer are tightly bound to one another, to prevent pathogens in the food from crossing over into the tissue of the gut or into the bloodstream. These cells are held together by protein complexes known as tight junctions (Figure 11).

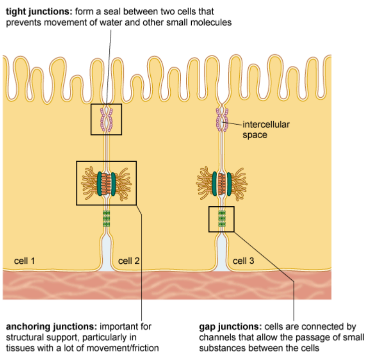

Figure 11 Cells are connected to each other by three main types of junctions: tight junctions, anchoring junctions, and gap junctions

A healthy gut microbiome helps to maintain the structural integrity of the gut wall in several ways. Firstly, it helps to regulate the proteins that are made by the human gut cells which are needed to secure the cells to each other via tight junctions. This helps to maintain the structural integrity of the gut wall and prevent it from becoming permeable to damaging substances. Additionally, the SCFAs produced by the microbiome modify the production of mucus by the gut wall, and affect how the immune cells located in the gut respond to pathogenic invaders (Sanders, 2021). These all have an important role in the health of the gut wall, and consequently the human host.

Dysbiosis is associated with increased permeability of the gut. That is, the tight junctions between the cells of the gut wall become weakened and substances that normally would not be able to cross the gut wall can enter the local tissue or bloodstream. The presence of such substances triggers an immune response, leading to significant inflammation of the gut. Several health conditions are associated with this increased permeability and inflammation, as you'll learn later in this course.

2.5 Protection against pathogens

Another important function of the gut microbiome for human health is protection against invading pathogens (Figure 12). Pathogens can be harmful to the human host in two ways. Firstly, by penetrating through the gut wall and causing an infection and/or inflammation, and secondly by replacing some of the resident symbiotic microorganisms within the microbiome through colonisation, which then causes dysbiosis and alters the normal functioning of the microbiome.

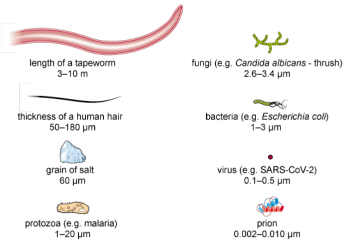

Figure 12 The six groups of pathogens illustrated with their size compared to other cells and objects

Until recently, it was unclear how the microbiome prevented colonisation by pathogens. However, recent research from the University of Oxford has identified that the beneficial bacteria of the microbiome consume the nutrients that pathogenic bacteria need to grow and replicate, so the pathogenic bacteria cannot thrive and instead die out (Spragge et al., 2023).

The researchers tried to identify if there were particular species or groups of microbiota bacteria that are important for protection against the pathogenic bacteria. While they identified that certain bacterial species were better for consuming the nutrients that the pathogens needed to survive, individual bacterial species were very poor at preventing pathogenic colonisation. Instead, the bacterial species needed to be in communities of at least 50 different types of bacterial species to fully prevent the pathogens from multiplying. This again highlights the ways in which the different bacterial species within the microbiome interact and function collectively, and the importance of a balanced microbiome.

2.6 Communication within the body

In the previous sections, you have learnt that the gut microbiome affects digestion of nutrients, structural integrity of the gut wall, prevents pathogens from entering the body and can contribute additional micronutrients to the body. However, the effects of the gut microbiome extend beyond the GI tract, and it can affect many processes throughout the body. For example, the gut microbiome can affect appetite, energy levels, metabolism, and body temperature. The gut microbiome also communicates with the brain to affect cognition (the way we think), behaviour, mood, and mental health (Bastiaanssen et al., 2020).

The gut microbiome communicates with the rest of the body and brain via:

- the nervous system (neural pathway)

- circulating hormones (endocrine pathway)
- immune cells and molecules (immune pathway).

2.6.1 Neural pathway – the microbiota-gut-brain axis

The nerve cells located in the wall of the GI tract form the **enteric nervous system (ENS)**, which supplies the entire length of the gut. The long projections of these nerve cells extend out of the gut wall and merge to form the **vagus nerve**, which travels all the way up to the brain (Figure 13).

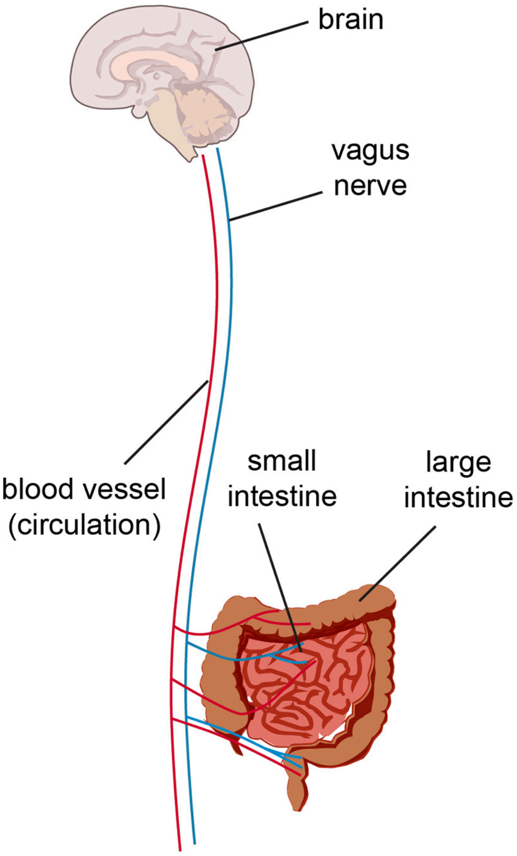

Figure 13 Simplified representation of the vagus nerve communicating between the GI tract and brain

Fun fact: another brain?

The ENS is often referred to as 'the second brain' or 'the brain in your gut' because of the extensive number of nerve cells located in the gut wall. The ENS contains more than 100 million nerve cells!

The ENS can function independently, but it can also function in coordination with the brain, and this is often referred to as the **gut-brain axis**. The gut-brain axis is vital for regulating appetite, metabolism, and gastrointestinal function (e.g. gut motility).

As you learnt earlier, the gut microbiome produces metabolites, such as SCFAs, which pass into the cells of the gut wall. These metabolites then stimulate the vagus nerve, to send signals to the brain, such as hunger signals. However, this communication with the vagus nerve is bidirectional, and the brain can send signals back to gut to modify gut motility and other functions. This is termed the microbiota-gut-brain axis, and is shown in Figure 14.

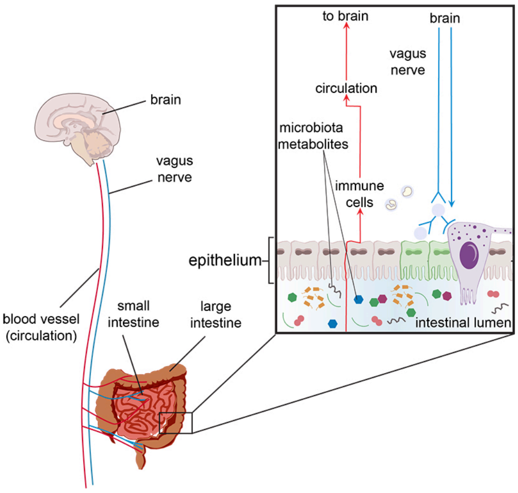

Figure 14 Microbiota gut-brain axis. Communication between the gut and brain is bidirectional. Metabolites produced by the microbiome are sensed by the intestinal cells, and this relays a signal via the vagus nerve to the brain. The metabolites can also be detected by immune cells which can directly stimulate the brain or stimulate the vagus nerve.

- **Question 10**

  Earlier you learnt a way that the microbiome can directly relay information to the brain. What were the metabolites involved in this direct mechanism called?

- Short chain fatty acids (SCFA)s. The SCFAs produced by the microbiome can cross the gut wall to enter the bloodstream and travel to the brain. These SCFAs can modulate brain and behaviour to alter brain function, such as cognition (Chen, Xu and Chen, 2021).

In the next section, you'll learn about other ways the gut microbiome can influence the brain.

2.6.2 Gut microbiome and hormone signalling

In addition to the mucosal cells lining the inner surface of the gut wall, there are specialised hormone-producing cells interspersed between them. These are known as **enteroendocrine cells (EECs)** where entero = gut and endocrine = hormone.

EECs are scattered all along the length of the GI tract and produce a wide range of hormones. Some of the hormones produced by the EECs act locally to affect the functioning of the gut, such as modifying gut motility. Other hormones enter the bloodstream and travel to the brain. The metabolites made by the microbiome can stimulate the enteroendocrine cells (Figure 15), to trigger the same signalling pathways resulting in messages in the brain modifying satiety, hunger, and mood.

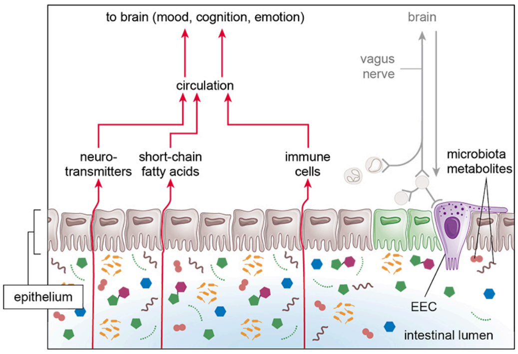

Figure 15 The location of enteroendocrine cells in the gut wall and signalling to the brain

The EECs in the gut are also the largest producer of serotonin – a hormone which is important in the regulation of mood in the brain. However, some species of microbiota bacteria also directly produce and secrete serotonin and together they make approximately 95% of the body's serotonin. Serotonin is associated with feelings of happiness, calmness, and focus, as well as the initiation of sleep. Reduced concentrations of serotonin have been linked to depression, anxiety, mood disorders and not being able to enjoy things. Recent evidence has indicated that changes in the gut microbiome can alter the amount of serotonin produced, which may provide a previously unknown mechanism for how diet and the gut microbiome can affect mood and mental health (Stasi, Sadalla and Milani, 2019).

As you can see, there are several mechanisms by which the gut microbiome could potentially help to regulate mood, cognition, emotion, and even pain.

2.7 Gut microbiome and the immune response

- **Question 11**

  From your everyday knowledge, what, in simple terms, is the function of the immune system?

- The immune system protects the body from invading pathogens or toxins – microorganisms or substances which can cause disease or even death.

The immune system consists of several different types of immune cells, tissues and organs located throughout the body. This includes the **lymphatic system**, composed of lymphatic vessels that travel throughout the body and lymphatic tissue, such as lymph nodes. Lymph nodes can become enlarged during infection, when they are often referred to as swollen glands.

There are large numbers of lymph nodes in the abdomen surrounding the GI tract. In addition, the majority of immune cells in the body are located in specialised areas of **gut-associated lymphatic tissue (GALT)** mainly located in the wall of the small intestine (Figure 16). The tonsils, adenoids and appendix are all GALT.

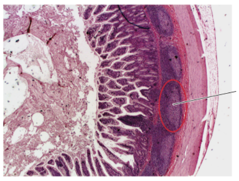

Figure 16 A cross-section of the small intestine with GALT circled in red known as a Peyer's patch

There is a close interaction between the gut microbiota and the GALT cells, and imbalance of the gut microbiota can alter the way in which the immune system is regulated. As you learnt earlier, the gut microbiome is important for maintaining the structural integrity of the gut wall. If this is compromised during dysbiosis, the gut wall can become more permeable to pathogens and toxins consumed in the food. This can trigger an inflammatory immune response by the GALT tissue and other immune cells located throughout the GI tract and has been linked to the development of some autoimmune conditions.

The metabolites from the microbiome can also communicate with the immune cells directly, to trigger a widespread immune response or send signals to the brain via the vagus nerve. Conversely, the immune system and stress can affect the health and diversity of the gut microbiome.

2.8 Gut microbiome and stress

Stress is the body's physiological response to a potential internal or external threat that can involve and/or impact several of the body systems and functions. Intense, short-term threats lasting for minutes to hours are categorised as acute stress, while longer periods of stress lasting for weeks to months are categorised as chronic stress. The acute stress response results in immediate changes in the functioning of the body that are beneficial to the survival of the organism, such as increased heart and respiratory rate.

During stress, cortisol is secreted from the adrenal glands. For response to an immediate stressful event, such as threat to life or other danger, raised cortisol is important for preparing the body to respond to the threat, such as increasing energy levels and awareness. Part of the response to cortisol is to redirect blood away from the gut to organs vital for survival, such as muscles for running and heart for delivering oxygen to the muscles. Video 1 contains a brief summary of some of the effects of the acute stress response on the body.

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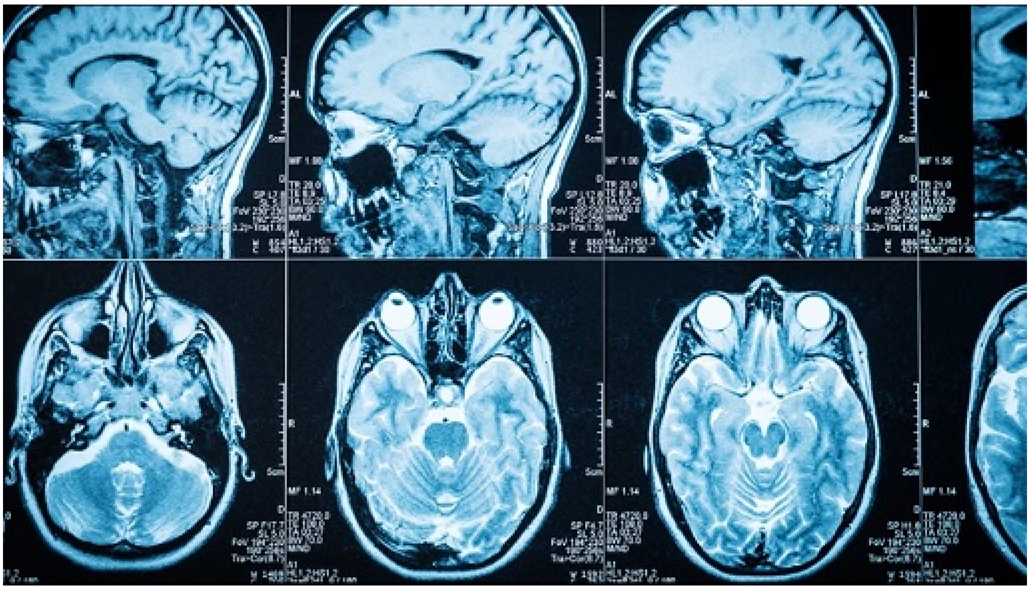
Video 1 Overview of body systems affected by the acute stress response



With prolonged or chronic stress, cortisol levels stay high for prolonged periods of time. As a result, the reduced blood flow to the GI tract can have an impact on the health and diversity of the microorganisms in the microbiome. Typically, there is a reduction in the bacteria of the microbiota and an increase in pathogenic bacteria, leading to a decrease in gut microbiota diversity and dysbiosis. The pathogenic bacteria can contribute to the intestinal lining becoming more permeable, which can trigger inflammation in the gut wall. Figure 17 shows a colonoscopy of healthy, pale pink colon on the left with clear folds in the gut wall, and a swollen, red inflamed colon on the right.

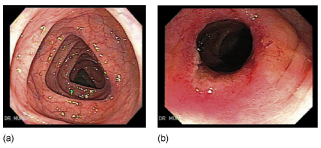


Figure 17 (a) Healthy colon; (b) Inflamed colon

The altered blood flow in chronic stress also affects gut motility and is linked to irritable bowel syndrome (IBS). Recent research has shown that there is altered gut diversity in patients with IBS, but whether this is a cause or effect is not yet known (Kim, 2023).

As you may be starting to see, the optimal functioning and health of the human host and gut microbiome are intertwined. In the next few sections you are going to learn about some of the factors affecting the health of the gut microbiome. You will then explore more about how imbalances in the gut microbiome can lead to several common health conditions.

3 Factors affecting the gut microbiome

There are many factors which can affect the diversity and health of the gut microbiome. Some of these factors are *non-modifiable*, such as our genetics and age. However, other factors affecting the health of our gut microbiomes are *modifiable*, that is, it is possible to alter the health of our gut microbiomes through lifestyle changes. These include diet, exercise and stress. In the next few sections, you will explore some of the modifiable and non-modifiable factors which affect the diversity and health of the gut microbiome.

3.1 Genetics of the human host

Recent research has identified that the genetic make-up of the human host can directly influence the microbiome, and vice versa.

As you will see in Video 2 below, human genetic material is composed of extremely long molecules of **deoxyribonucleic acid (DNA)**, located in the nucleus of the cell. Within the DNA molecules are shorter sequences, called **genes**, which form the 'recipe' for the manufacture of proteins, which control many of the essential processes within the human host. However, the proteins that the human host produces can also affect the functioning of the gut microbiome. What's particularly interesting is that recent evidence has shown that the gut microbiome can actually change which proteins are made by the human host cells. For example, the gut microbiome can affect which proteins are made by the cells of the gut wall, and this has an impact on digestion of food and the immune response to pathogens that enter the gut. Exactly how the microbiome is controlling which proteins are made by the human host cells is still not very well understood, but evidence suggests that this is through **epigenetics** (Alenghat, 2013). As Video 2 explains, epigenetics is the addition or removal of chemical groups from the DNA molecule, which helps to control which proteins are made in a cell at any given time.

View at: youtube:_aAhcNjmvhc

Video 2 Summary of epigenetics (TED Ed talk)

The finding that the microbiome can affect epigenetic regulation of the human DNA is important for health. Epigenetic changes are highly dynamic and known to be important in regulating numerous important processes within the cells. Altered epigenetic regulation of genes is also linked to a number of health conditions, such as cancers, autoimmune disorders, neurodegenerative disorders, stress and mental health disorders. It is also well known that changes in epigenetic control of the DNA can pass down through successive generations within a family, so this may be an important target for improving health of not only the individual but their subsequent offspring.

3.2 Early exposure to microorganisms

The gut microbiome starts to develop in a fetus during pregnancy and continues to change rapidly during the first 2-3 years of life (Roswall et al., 2021).

There are several factors which affect the microbiome of the developing fetus during pregnancy, including:

- maternal microbiota

- diet
- maternal genetics and epigenetics
- medications
- infections.

The mode of delivery can affect the microbiome of the newborn. Vaginal delivery can result in transference of the microorganisms from the mother's vagina to the newborn, while caesarean section leads to exposure to microorganisms on the mother's skin. A shorter or longer exposure time to the maternal microbiome during gestation can also influence the newborn's gut microbiome, so gestational age can be important.

Finally, during childhood both maternal and environmental factors play an important role in the development of the gut microbiome. These include:

- breastfeeding versus formula feeding
- maternal diet if breastfed
- child's genetics
- child's environment (e.g., microorganisms on toys, family)
- family lifestyle (including stress)
- geographical location.

Figure 18 highlights some of the main factors during the three stages thought to influence a child's microbiome.

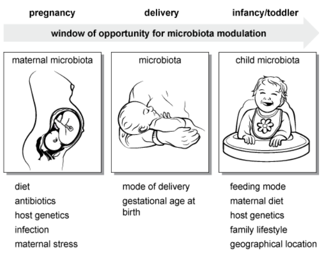


Figure 18 Microbiota development in early life

3.3 Geographical location and microbiome diversity

- **Question 12**

  Thinking back to an earlier section of this course, which are the two most common bacterial groups of the gut microbiome?

- Firmicutes and Bacteroidetes.

Interestingly, the ratio of these two groups has been found to consistently change depending on the geographical latitude of the human hosts.

The further North humans live, the more Firmicutes they have in their microbiome, whereas humans living nearer to the Equator have more Bacteroidetes (Suzuki and Worobey, 2014). As you will learn in Section 4, the ratio of Firmicutes to Bacteroidetes is important in several health conditions, such as Crohn's disease and obesity. So, this difference in the diversity of microbiota within the microbiome may in part explain the geographical difference in some health conditions. However, it is still unclear why there is this difference, but possible contributing factors include:

- ethnicity
- diet
- Bergmann's rule (populations at higher latitudes have on average a higher body mass to withstand colder conditions)
- climate
- other microorganism distribution, especially pathogens/parasites.

While the reasons for the geographical variations in the diversity of the gut microbiome are still not clear, and much research is underway, geographical effects do appear to play an important role in the diversity of the microbiome. However, an important consideration is that human geography is complex, and may be linked to factors such as socioeconomic status. Additionally, differing diet in different geographical regions may have a significant impact and you are going to learn more about this next.

3.4 The impact of diet

As you learnt previously, the gut microbiota digest nutrients from the diet of the human host for their own growth and survival, as well as providing the human host with important nutrients. Undigested fibre and protein results in the preferential growth of bacteria that can use these substances, and this in turn increases the production of SCFAs by these bacterial groups. SCFAs are not only important in the health of the gut itself but also throughout the body of the human host (Zhang, 2022).

As humans typically eat a diverse diet, having good bacterial diversity is also important to be able to digest and metabolise the wide range of nutrients required for good health. Dietary fibre in particular is known to be essential for maintaining a good diversity of bacteria in the gut. However, Westernised diets often contain low amounts of fibre and protein, with high levels of fat, sugar and ultra processed foods (UPFs). In contrast, diets such as the Mediterranean diet and Japanese diets, which are higher in fresh ingredients, particularly fruit and vegetables, are known to be beneficial to the health of the gut microbiome and promoting good bacterial diversity.

Interactive content is not available in this format.

Figure 19 (interactive) The effect of the Mediterranean diet compared with the Western diet on gut microbiota

Not only does high fibre maintain the diversity of the bacteria within the gut microbiome, but it also helps to reduce colonisation by pathogenic bacteria and improve the mucus barrier of the gut wall. Diets which are low in fibre increase the risk of a number of health conditions, including obesity, heart disease, some cancers, and diabetes.

Another important aspect of diets high in fresh food, particularly fruit and vegetables, are higher levels of micronutrients (vitamins and minerals). This helps to increase the proportion of Firmicutes (and so SCFA-producing bacteria). For example:

- Vitamins A, B6, B12, D and E – increases Firmicutes compared to Bacteroidetes, which helps SCFA-producing bacteria thrive.

- Calcium with phosphorous increases SCFA-producing bacteria.
- Vitamin C has antioxidant properties to protect against damage to cells by some metabolites.

Both high sugar levels and UPFs found in Westernised diets can change the gut microbiome diversity and are associated with inflammation of the gut wall (Shi, 2019).

Question 13

What is the name of an imbalanced gut microbiome, or one lacking diversity?

Dysbiosis.

Microbes and additives in the UPFs have been found to lead to dysbiosis of the microbiome. This results in an increase in pathogenic bacteria, reduced structural integrity of the gut wall with increased permeability, inflammation of the gut wall and altered signalling via the microbiota-gut-brain axis. This has been linked to several immune conditions, such as Crohn's disease, ulcerative colitis and rheumatoid arthritis.

Introduction of beneficial bacteria or their products, such as SCFAs, can help to reverse these effects. However, prolonged consumption of a Westernised-type diet or UPFs can lead to permanent changes in the microbiome, gut wall and wider responses to the microbiome throughout the body. This is at least partly due to epigenetic changes of the human host which, as you learnt earlier, can also be passed down through the generations (Zinocker, 2018).

3.5 Exercise

Exercise is well known for having multiple health benefits, for both physical and mental health. Despite this, finding time and motivation to exercise can sometimes be challenging. While finding time for exercise may remain elusive, recent research has shown that the gut microbiome may actually play a role in increasing motivation. Certain metabolites made by the gut microbiome can relay signals to the pleasure/reward centre of the brain via the microbiota-gut-brain axis. This improves motivation to exercise, as well as exercise performance, and may help to explain why there is variability between individuals around motivation and pleasure from exercise (Dohnalová, 2022).

Conversely, exercise can help to improve the health of the gut microbiome. Higher intensity or prolonged exercise improves cardiorespiratory fitness. This leads to improved oxygen intake and transport around the body in the bloodstream, including to the gut wall, which is beneficial to the health of the gut bacteria (Mailing, 2019). In fact, the distance runners regular undertake can correlate to the ratio between Bacteroidetes and Firmicutes!

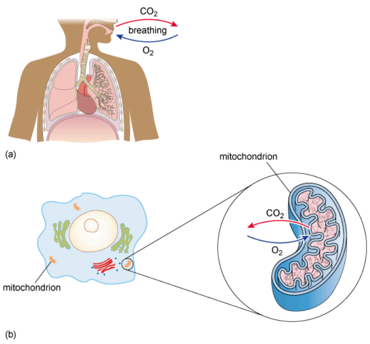


Figure 20 (a) Breathing in (inspiration) and breathing out (expiration) allows the exchange of oxygen and carbon dioxide; (b) The cells use the oxygen to generate energy in the mitochondria. Carbon dioxide is produced as a waste product.

Recent research has shown that some elite endurance runners have an increase in a bacterial species called *Veillonella*. This species is thought to increase the amount of lactate that the athlete can tolerate, which in turn is linked to the function of mitochondria in the cells. Mitochondria are often called the 'powerhouses of the cell' as they produce the majority of the body's energy (Figure 20). The metabolites produced by the microbiome, such as SCFAs, can improve the health and number of the mitochondria (Damman, 2024).

Lower intensity exercise helps to reduce transit time of the stool, that is, the stool passes through the GI tract faster. This reduces the amount of time pathogenic bacteria can come into contact with the gut wall and potentially displace the microorganisms of the microbiome. There is also an increase in SCFAs produced during low intensity exercise, which reduce the risk of colorectal cancer and Crohn's disease. Exercise is also known to reduce the risk of both of these conditions (Monda, 2017).

However, exercise should not be considered in isolation. High intensity exercise combined with a diet high in UPFs has been linked to increased gut permeability and an increase in musculoskeletal injuries (Álvarez-Herms, 2023). This indicates that there is an important balance needed between a healthy diet and exercise, in order to maintain the optimal health of the gut microbiome.

Interestingly, the benefits of exercise on microbiome health are more pronounced during childhood, so it has been proposed that children who exercise more frequently will have a better microbiome diversity. This results in better brain development, more lean mass, and better energy regulation.

3.6 Medications

As you learnt earlier, the gut microbiome is now known to affect how different medications, recreational drugs and other chemicals are processed in the body and this can contribute to IVDR.

- **Question 14**

  From earlier in this course, can you remember what IVDR stands for?
- Individual variability of drug response.

Recreational drugs, medications and other chemicals can also directly affect the gut microbiome.

- **Question 15**

  From your general knowledge, which type of pathogenic organisms are treated by using antibiotics?

- Antibiotics are given for the treatment of bacterial infections (they are sometimes prescribed as a preventative manner too, if an individual has particular health conditions or illness).

- **Question 16**

  How might antibiotics affect the gut microbiome?

- Antibiotics might change the number and diversity of the bacterial groups within the gut microbiome.

Indeed, antibiotics and non-antibiotic drugs, such as proton-pump inhibitors (PPIs) (which are often used to treat acid reflux), statins (which can lower cholesterol in the blood), laxatives, and chemotherapies can change the composition of the gut microbiome. These are typically associated with a reduction in the biodiversity of the bacteria within the gut microbiome (Weersma, 2020). However, often individuals who are taking these medications need to do so for significant health reasons, so an important balance needs to be achieved to maintain good overall health.

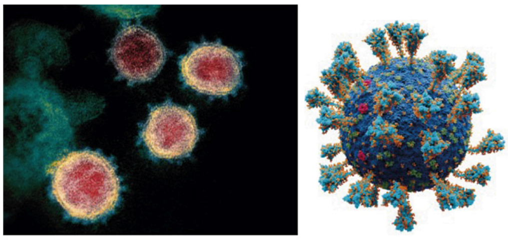
Figure 21 Medication packages

It can therefore be helpful for individuals who regularly take antibiotics or certain groups of non-antibiotic medications to use pre- or probiotics (as you'll explore later in this course).

3.7 Infection and disease

One of the important functions of the gut microbiome is to reduce the risk of harmful pathogenic bacteria from colonising the gut. A reduction in healthy bacteria can lead to infection caused by the pathogenic bacteria, such as *Clostridium difficile (C. difficile)* and *Helicobacter pylori (H. pylori)*. Both of these infections can have significant impact on health, and *H. pylori* is an important cause of stomach ulcers.

Changes in the gut microbiome has also been shown to be associated with the severity of the response to infection with the SARS-CoV-2 virus – the virus which causes COVID-19 (Figure 22).



(a) (b)

Figure 22 (a) A transmission electron micrograph shows four red-orange coloured SARS-CoV-2 coronaviruses, with the typical 'corona' appearance around the virus; (b) A 3D representation of the SARS-CoV-2 virus with the spike proteins, which have a key role in enabling the virus to enter host cells and cause infection.

Yeoh et al. (2021) found that in patients with COVID-19, there was a reduction in the gut bacterial groups which would usually promote a good immune response. The more severe the disease, the more significant the changes in the gut microbiome. The researchers also found that these changes persisted for more than 30 days after the symptoms had resolved and proposed that dysbiosis may play a role in the development of post-COVID syndrome (more commonly known as long COVID). In some individuals, symptoms such as breathlessness, fatigue and pain persist for a prolonged period – in some instances even years – following initial infection.

3.8 Age and the menopause

The composition of the gut microbiome changes with age, and this is particularly noticeable after the age of 65 years. The changes that occur can reflect the physical fitness, frailty, and longevity of the individual. In healthy ageing, there is consistently a depletion of some of the core bacterial groups, particularly Bacteroidetes. In contrast, individuals assessed as having a higher degree of frailty have an increase in the levels of Bacteroidetes (Wilmanski, 2021). The decrease in Bacteroidetes seen in healthy ageing also appears to be associated with longevity, and individuals over 100 years of age typically have fewer Bacteroidetes and an increase in rare bacterial groups.

Often these changes in gut microbiome diversity reflect the environmental and personal factors that an individual has been exposed to during their lifetime. As we age, there is age-related decline in the structural integrity of the gut wall, to our internal physiology, and there are many molecular and cellular changes, such as epigenetic changes, all of which can have an impact on the gut microbiome. As a result, an important area of scientific research is exploring the impact of environment, diet, exercise, disease, medication and societal factors and their impact on the ageing gut microbiome (Ghosh, 2022). A better understanding of these factors will hopefully help to promote better health and longevity in ageing (Figure 23).

(a) (b)

Figure 23 (a) Ernestine Shepherd and (b) Toshisuke Kanazawa, body builders aged 80 and 81 years, respectively, at the time of these photos, demonstrate that it is possible to maintain good physical health and fitness in the later decades of life

One particular period of life that affects females is the menopausal period.

Fun fact: are perimenopause and menopause the same thing?

In everyday language, the two terms are often used interchangeably, however, the scientific terminology is more precise. From the age of approximately 40–44 years onwards, most females will enter the perimenopause, which is a transitional period which can last several years. During perimenopause, hormone levels fluctuate and there are often changes in the pattern of menstruation. The menopause is a specific moment in time, defined by the NHS as being when there has been no menstruation for a year in females over 50 years, or for two years, if under 50 years of age. The average age of the menopause in the UK is 51 years of age.

There is a sex-related difference in the microbiomes of males and females, however, during the perimenopause and post-menopausal period there is a reduction in diversity and the gut microbiome in females becomes more similar to males (Peters, 2022). At present, there is very little research into the changes in the gut microbiome during the menopausal period, and how hormonal changes contribute to this alteration in bacterial diversity. There are many health-related risks associated with the menopause, and it is unclear whether modification of the gut microbiome after the menopause may help to reduce the risk of developing some of these conditions. Therefore, more research into this area will be essential to try to improve the health and wellbeing of post-menopausal females.

4 Impact of dysbiosis on health

As you have seen from the previous sections, the relationship between the gut microbiome and human host is truly symbiotic. The anatomy, physiology and health of the human host affects the composition and functioning of the microbiome, which in turn has an impact on many different structures and processes within the human body.

It is becoming increasingly clear that an alteration or reduction in the diversity of microbiota, or dysbiosis, is linked to several very common health conditions. These health conditions can often be debilitating or life-threatening, so understanding the role of the microbiome in their development will not only improve the design of better treatment plans but may also help to reduce the risk of developing these conditions in the first place.

In the next few sections, you will explore some of the conditions known to be linked to dysbiosis in more detail. You will then finish this course by looking at some of the current ways that the microbiome can be modified to improve patient outcomes and some potential future treatment options.

Two common conditions affecting the GI tract are **inflammatory bowel disease (IBD)** and **irritable bowel syndrome (IBS)**. Sometimes, these two terms are used interchangeably among the general public, and although some symptoms may overlap, they are very different disorders, with very different treatments and prognosis, as you will learn next.

4.1 Inflammatory bowel disease – Crohn's disease and ulcerative colitis

IBD is a group of two chronic inflammatory diseases which includes Crohn's disease and ulcerative colitis (UC). These two immune conditions can be identified using diagnostic testing and imaging techniques. Genetics, environmental factors, and dysfunction of the individual's immune system are important in the development of both Crohn's disease and ulcerative colitis.

In addition, recent research has shown that many individuals with IBD have dysbiosis, which may be a key step in the early development of the disease. Dysbiosis in the gut microbiome leads to the colonisation of opportunistic harmful pathogens and increased permeability of the gut wall. This in turn triggers an immune response by the host, which can lead to extensive and damaging inflammation in the gut.

Inflammation in the gut wall in Crohn's disease and ulcerative colitis can be seen using an **endoscope**. An endoscope is a long thin tube with a camera on the end, that is passed through the mouth or via the anus, to view the gut wall. Viewing of the upper GI tract is by **gastroscopy**, which enables observation of the stomach and first part of the duodenum. Viewing of the large intestine (colon), rectum and anus is via **colonoscopy**. In a healthy individual, the surface of the gut is smooth, and you can see the blood vessels. In IBD the gut wall becomes red, swollen, and raised in patches due to inflammation and ulceration.

Interactive content is not available in this format.

Figure 24 (interactive) Endoscopic images of a healthy gut wall and inflamed gut walls in ulcerative colitis in the large intestine (colon)

While Crohn's disease and ulcerative colitis are both considered IBD, they differ in the severity, location and extent of the damage to the GI tract by the inflammation (Table 1)

Table 1 Comparison of Crohn's disease and ulcerative colitis

Crohn's disease	Ulcerative colitis
Inflammation and ulceration in any part of the GI tract, from the mouth to the anus.	Inflammation and ulceration only found in the large intestine, rectum and anus (colitis = inflammation of the colon).
Ulceration occurs in patches.	Ulceration tends to be continuous.
Inflammation penetrates and leads to destruction of the entire thickness of the gut wall.	Inflammation only affects the inner layer of cells lining of the gut wall.
Widespread damage to other abdominal organs and cavity can occur.	Damage localised to the GI tract.
Multiple other parts of the body outside of the GI tract can be affected, both within the abdominal cavity and other tissues/organs throughout the body.	Inflammation also affects other body parts, such as eyes, skin, liver and joints.

Common signs and symptoms of both diseases are persistent diarrhoea, blood and mucus in faeces, abdominal pain and cramps, bloating and swelling, weight loss and extreme tiredness. Both conditions are often associated with poor digestion and absorption of nutrients, causing deficiencies that can affect other parts of the body. These deficiencies are normally dependent on the location and extent of the damage to the gut wall and tend to be worse in Crohn's disease due to small intestine involvement, which is the main site of nutrient absorption.

Both Crohn's disease and UC have been linked with dysbiosis. You may recall from earlier that in a healthy gut microbiome, there is a balanced ratio of Firmicutes and Bacteroidetes with typically slightly more Bacteroidetes than Firmicutes (although this varies by individual, age, and geographical region). However, in IBD there is often an increase in Bacteroidetes, which results in significantly more Bacteroidetes than Firmicutes. The Firmicutes/Bacteroidetes (F/B) ratio influences other microorganisms within the microbiome and is important for maintaining normal intestinal function and protecting against inflammation.

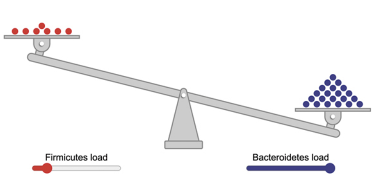


Figure 25 The Firmicutes to Bacteroidetes ratio in inflammatory bowel disease is altered

Question 17

What important molecule do Firmicutes produce in the gut microbiome? (Look back over Section 3 for a reminder.)

- SCFAs, which protect against inflammation and help maintain the gut integrity.

There is currently no cure for either disease. However, treatments which modify the immune system to reduce inflammation and to alleviate the symptoms can be effective. Research into the benefits of taking probiotics in IBD are still very limited. A study by Stojanov, Berlec and Štrukelj (2020) suggests that orally administered, pharmaceutical-grade probiotics could help restore the F/B ratio in IBD by increasing the amount of Firmicutes and achieving a more balanced F/B ratio. While there is some early evidence to suggest that it may reduce inflammation and trigger remission (a reduction in disease pathology) in ulcerative colitis, to date there has been no evidence of a benefit in Crohn's disease (Limketkai et al., 2022).

4.2 Irritable bowel syndrome and small intestinal bacterial overgrowth

In contrast to IBD, the causes of irritable bowel syndrome (IBS) are currently poorly understood, but it is thought to be a collection of disorders rather than one single disease, all of which affect the functioning and motility of the GI tract. IBS is characterised by abdominal pain, change in stool consistency and stool frequency (diarrhoea or constipation). The different subtypes of IBS are based on stool consistency.

Historically, IBS was thought to be primarily due to altered gut motility and gut-brain interactions, which was triggered by psychological stressors. However, recent research has indicated that there are other factors involved in the development of the condition, including alterations in gut permeability, immune response and gut microbiome.

It is thought that dysbiosis leads to inflammation and increased permeability of the gut wall. Often this is triggered by an infectious episode of gastroenteritis, irrespective of the cause of the infection (e.g. bacterial, viral, or fungal). This infection then affects the stability and diversity of the microorganisms of the microbiome (Menees, 2018). However, the infection alone is unlikely to be enough of a triggering factor, and the individual may need to have other susceptibilities in order for IBS to develop.

Another potential risk factor that links dysbiosis of the gut microbiome and IBS is **small intestinal bacterial overgrowth (SIBO)**.

- **Question 18**

  In which part of the GI tract are the majority of gut microbiome found?

- The majority of the gut microbiome reside within the large intestine.

However, it is possible to get an overgrowth of the healthy bacterial groups from the microbiome or pathogenic bacteria (or a combination of both) in the small intestine. This leads to excessive usage of nutrients by the bacteria so fewer nutrients are absorbed into the human host. This is termed SIBO. SIBO can trigger an immune response, increase intestinal permeability, and alter carbohydrate digestion and absorption. All of these are similar to the effects of dysbiosis in IBS. In SIBO, the bacterial overgrowth often produces higher quantities of gas, causing bloating and flatulence, symptoms often described in IBS patients. This overlap of signs and symptoms suggests that SIBO may play an important role in IBS. However, it is currently unknown whether SIBO could be a cause of IBS or a consequence of the condition (Figure 26).

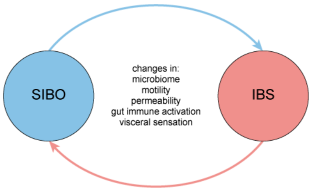


Figure 26 Small intestinal bacterial overgrowth: the chicken or the egg?

Several studies have reported promising results on the benefits of pre- and probiotics in improving the quality of life and reducing symptoms in IBS, but more work needs to be done to identify which substances and strains are most beneficial for which subtypes. You will learn more about pre- and probiotics in the final section.

4.3 Obesity and Type 2 diabetes

The World Health Organisation (2022) defines obesity as abnormal or excessive fat accumulation that presents a risk to health. Obesity is a complex, multifactorial condition linked to a wide range of genetic and non-genetic factors, including environmental, lifestyle, socioeconomic and psychological factors. The primary cause of obesity is an imbalance between the energy consumed by an individual and the energy they expend.

The gut microbiome is involved in energy usage and digestion of carbohydrates for the human host, so the gut microbiome is thought to play a key role in energy balance. Dysbiosis is a frequent finding in obesity, which may affect how those individuals extract and use energy from food (Boccuto, 2023).

You may recall that the ratio of Firmicutes to Bacteroidetes (F/B ratio) is important for a healthy microbiome and human host.

Question 19

In inflammatory bowel disease (IBS – Crohn’s and UC) there is an imbalance in the F/B ratio. Is there a shift towards more Bacteroidetes or more Firmicutes?

- ○ Bacteroidetes
- ○ Firmicutes

In contrast, in obesity there is again a loss of the healthy F/B ratio, but this time with a shift towards more Firmicutes and less Bacteroidetes (Figure 27).

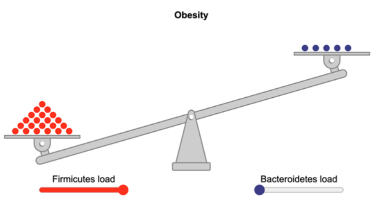


Figure 27 The F/B ratio in obese individuals typically shows an increase in Firmicutes and reduction in Bacteroidetes

Fun fact: complex interactions

Research has shown that specific types of bacteria are linked to obesity. However, perhaps unsurprisingly, research suggests this is highly complex! For example:

- *Christensenellaceae* – associated with weight loss
- *Akkermansia muciniphila* – associated with weight loss
- *Lactobacillus paracasei* – associated with a reduction in obesity
- *Lactobacillus reuteri* and *Lactobacillus gasseri* – increase in obesity
- *Bifidobacterium* – increase in obesity

As you can probably tell, unpicking the role of the different bacterial species in obesity is challenging as there are an estimated 500-1000 different types of bacteria in the gut microbiome! As the bacterial species also influence each other, trying to identify the role of a single bacterial species in obesity may not give true understanding of what happens when you combine all the influences of the entire gut microbiota, microbiome and human host. However, this is still a promising area of research into obesity and understanding some of challenges that individuals may face in losing weight. Finding a way to improve the gut microbiome may also help some individuals with their weight loss goals.

One of the conditions commonly linked with obesity is Type 2 diabetes (T2D). In T2D, the body has poor sensitivity to insulin, the hormone which helps to reduce blood glucose (sugar) levels.

Question 20

In T2D, are blood glucose levels likely to be higher than normal or lower than normal?

- ○ Higher than normal
- ○ Lower than normal

Higher than normal.

In T2D the prolonged unregulated blood glucose sugar levels can result in damage to multiple parts of the body.

Dysbiosis is a common finding in diabetics and is related to poor sensitivity to insulin and poor control of blood glucose levels (Sadagopan, 2023).

Obesity and Type 2 diabetes are rising at a rapid rate, with both being among the ten most common health conditions globally. So, addressing gut dysbiosis to improve the health of the gut microbiome raises the possibility of providing a fairly cheap and easy mechanism to reduce the impact of these conditions, both for the individual and globally.

4.4 Colorectal cancer

Colorectal cancer (CRC – cancer of the colon and/or rectum) is the third most common cancer worldwide and is often associated with dysbiosis of not just the gut bacteria, but also other microorganisms found in the gut microbiome, such as viruses, fungi, and Archaea (World Health Organization, 2023).

Question 21

What role does the gut microbiome have in the fibre consumed in the diet?

Fibre cannot be digested by the human host but is digested by some of the bacterial species of the gut microbiome (particularly Firmicutes). These bacteria then produce SCFAs as a by-product, which are beneficial for the other bacteria of the gut microbiome and human host.

SCFAs produced by the gut microbiome are also protective against colorectal cancer cells, helping to destroy them.

A study found that in colorectal cancer, the more fibre (particularly from cereal fibre and whole grains) consumed, the lower the estimated risk of developing colorectal cancer (Aune et al., 2011). This can be seen in Figure 28. As fibre consumption increases, the risk of developing colorectal cancer decreases.

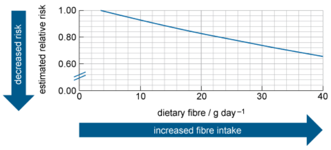


Figure 28 Colorectal cancer risk decreases as the consumption of dietary fibre in grams per day (g day^{-1}) increases

Question 22

From Figure 28, what is the estimated risk of developing colorectal cancer if you consume around 20 g of fibre a day?

The relative risk is just above 0.80. This equates to an approximate 20% reduction in the likelihood of developing colorectal cancer.

A diet high in fibre helps to ensure that the Firmicutes bacteria survive and thrive to produce lots of beneficial SCFAs, but is also thought to be beneficial in reducing CRC risk in other ways:

- Fibre increases the bulk of the stool, so it travels through the gut more rapidly, reducing contact of the gut wall with cancer-causing substances (carcinogens).
- Fibre increases the feelings of fullness which helps to prevent overeating. Obesity is also linked to colorectal cancer, as well as 12 other types of cancer (Cancer Research UK, 2022).

As you may recall from earlier, the gut microbiome also affects how individuals respond to medications and recreational drugs. This includes chemotherapeutic agents and immunotherapy often used in the treatment of colorectal and other cancers. Therefore, the gut microbiome may have an impact on both the risk of developing CRC and how well an individual responds to the treatment (Wong, 2023).

4.5 Kidney disease

The kidneys are two bean-shaped organs, found on either side of the spine, below the ribcage. Each kidney contains approximately 1 million specialised tubes, known as **nephrons** (Figure 29).

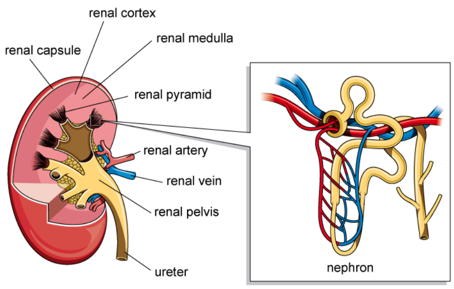


Figure 29 Schematic of a single kidney; here an enlarged nephron is shown, in reality, individual nephrons can only be seen with the aid of a microscope

The kidneys contribute to the balance of several aspects of body function. As part of the urinary system, the nephrons within the kidneys filter the blood plasma. Blood plasma is the yellowish liquid component of blood. A variety of substances are suspended within plasma, including red blood cells, several types of white blood cell and platelets (involved in blood clotting). The plasma also contains some waste materials or toxins that need to be filtered out from the plasma and removed from the body. The nephrons filter the blood plasma, and regulate the excretion of the filtered substances. The urine produced as a result of this process reflects the role of the kidneys in balancing the composition of the blood plasma and clearing substances such as metabolites and drugs from the body. The kidneys are also involved in the production of various hormones and play an important role in regulating blood pressure.

Chronic kidney disease is a long-term condition, where the nephrons become damaged, leading to a gradual loss of function. If kidney function falls to 10-15% of normal function, dialysis or transplantation are the only treatments available for the patient. It is estimated that currently 7.2 million people in the UK (Kidney Research UK, 2023) and 1 in 10 adults worldwide are believed to suffer from chronic kidney disease (Li et al., 2021).

Dysbiosis has been observed in patients with chronic kidney disease. The relationship between the gut microbiome and kidney disease is complex and is an active area of research. In kidney disease, the damaged nephrons fail to filter plasma appropriately, which changes plasma composition. Research suggests that this may alter the number and diversity of gut microbiota.

- **Question 23**

  You learnt earlier that dysbiosis changes the structure of the gut wall. What is the name of the junction between the gut wall cells that are affected and what are the implications of this in terms of permeability?

- In dysbiosis, the tight junctions between cells of the gut wall become weakened and substances that normally would not be able to cross the gut wall can enter the local tissue or bloodstream. Dysbiosis is associated with increased permeability of the gut wall.

Due to the ‘leaky’ gut wall, some products of metabolism and toxins from food pass into the bloodstream and this has been linked to the onset and progression of kidney disease, and increased mortality risk. Conversely, other metabolites from the gut microbiome, such as SCFAs, appear to protect the kidneys and may increase survival rates of chronic kidney disease patients.

Although more research is needed, current understanding of the complex interactions between the gut microbiome and kidney function suggests that there may be the potential for improvements in patient outcomes, based on microbiome-based treatments.

4.6 Mental health

As well as having physical consequences to the health of the body, dysbiosis has been linked to a number of mental health conditions.

- **Question 24**

  What is the name given to the interaction between the gut microbiome and brain?

- Microbiota-gut-brain axis.

Recent studies suggest that the microbiota-gut-brain axis plays a key role in depression and anxiety (Zhu, Tu and Chen, 2022). You may recall that the gut microbiome communicates with the brain via a number of routes, but particularly via:

- Nerves – nerve endings in the gut wall are triggered by substances produced by the gut microbiome and signals are relayed to the brain via the vagus nerve.
- Hormones, neurotransmitters, and other molecules (such as serotonin, SCFAs, and other important neurotransmitters involved in signalling in the brain and nervous system) – which are made by the gut microbiome and enter the bloodstream to travel to the brain (and other organs).

An altered F/B ratio, with a reduction in Firmicutes and increase in Bacteroidetes, is frequently seen in individuals with anxiety, while the reverse is more common in individuals experiencing depression. Other mental health disorders such as bipolar disorder, schizophrenia and post-traumatic stress disorder are associated in changes in the amount of other bacterial species (Xiong et al., 2023).

Some studies have suggested that dietary modifications are particularly beneficial in improving the symptoms of anxiety, even more so than pharmaceutical-grade probiotics (Yang et al., 2019). Prebiotics, dietary fibre and particularly probiotics (which you will learn about in the next section) are considered a potential therapeutic strategy for reducing anxiety, depression or improving dysbiosis (Bibbò et al., 2022; Cooke, Catchlove and Tooley, 2022).

5 Restoring/maintaining the balance of the gut microbiome

As you learnt earlier in this course, there are many genetic, environmental and lifestyle factors which can have an impact on the health of the gut microbiome and consequently the health of the human host. Dietary factors, such as reducing consumption of UPFs and increasing fresh foods and dietary fibre can reduce the risk of developing some diseases and/or improve the severity of the condition.

However, two additional means of improving the health of the gut microbiome are medical interventions: consumption of pre- and probiotics and faecal transplant.

5.1 Prebiotics and probiotics

One way in which the health of the gut microbiome can be improved is through the use of prebiotics and probiotics. Although these have similar names, they contain quite different substances designed to improve the health of the gut microbiome.

Prebiotics act as a food source for the beneficial bacteria in the gut microbiome and help those bacteria to thrive in order to improve the balance of bacteria within the microbiome. Prebiotics are typically substances that cannot be broken down by human enzymes, that can withstand the acidic environment of the stomach, and which are not absorbed in the upper GI tract.

Question 25

Why might a prebiotic need these characteristics?

A substance that is broken down in the acidic environment of the stomach, by human enzymes, or be absorbed in the upper GI tract, might not reach or be available to the majority of the gut microbiome, located in the large intestine.

Prebiotics are typically complex carbohydrates, and can be found naturally in high quantities in lots of different food sources, but especially:

- legumes, beans, and peas
- oats
- bananas
- berries
- Jerusalem artichokes (not the same as regular artichokes)
- asparagus
- dandelion greens
- garlic
- leeks
- onions.

In contrast, **probiotics** are a collection of live, beneficial microorganisms, often bacteria or yeasts, that are ingested with the aim of colonising the gut to improve the quality and diversity of the gut microbiota. Probiotic bacteria are found in fermented foods, such as live yoghurt, kimchi, sauerkraut, and pickled vegetables, but there are many other commercial mixtures and dietary supplements available too, such as probiotic yoghurt drinks and kefir.

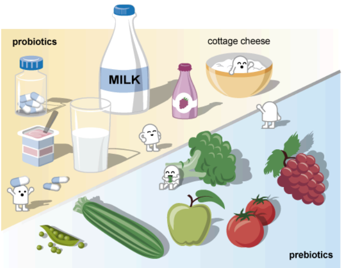


Figure 30 Prebiotic and probiotic foods. The cartoon figures represent the microorganisms in the microbiota that use the pre- and probiotics to thrive and replicate. The tablets represent probiotic supplements (dried or desiccated bacteria products)

Pharmaceutical-grade probiotics, which contain very high amounts of microorganisms, have been shown to have some benefit in clinical trials (NHS, 2022). The high number of microorganisms in pharmaceutical-grade probiotics is thought to result in some of the bacteria being able to survive the highly acidic stomach and beyond. The benefits of commercially-bought probiotic supplements are still controversial, as they contain low concentrations of the microorganisms, the majority of which will most likely be destroyed by the highly acidic environment of the stomach. However, there is still some anecdotal evidence (i.e. not scientific, based on personal accounts) that these may provide some benefit in specific intestinal disorders. To date, there has been no scientific evidence to indicate that there is any benefit to healthy individuals taking probiotics (Jabr, 2017).

You are going to finish off this OpenLearn course by learning about a slightly less palatable way to improve the health of the gut microbiome – faecal transplant!

5.2 Faecal transplant

You learnt earlier that IBS can be triggered by an episode of gastroenteritis by pathogenic bacteria, such as *Clostridium difficile (C. difficile)*. Unfortunately, *C. difficile* is highly resistant to treatment, and can extensively colonise the gut which damages the health of the gut microbiome. A chronic *C. difficile* infection can have a devastating impact on the health of the individual.

One of the functions of the gut microbiome is prevention of colonisation of the gut by pathogenic bacteria, however in a *C. difficile* infection the individual's own gut microbiota get overwhelmed. So, they may need help from another individual via a faecal microbiota transplant (FMT) to reestablish a healthy balance of bacteria in the gut.

Volunteers are rigorously screened for infections, gastrointestinal diseases, antibiotic use in the past 6 months and not being immunocompromised before donation of the faecal matter (Johns Hopkins, n.d.).

Figure 31 Scientist at work in the laboratory

The screened and processed FMT is then delivered by one of four main routes:

- Colonoscopy – the most common method, where the donor faecal matter is distributed along the length of the large intestine.
- Upper endoscopy – typically only used if an individual cannot have a colonoscopy, but is less effective.
- Enema – donor faecal matter is placed in the rectum.
- Tablet – freeze-dried but live microbiota organisms.

While the idea of FMT may be challenging, the impact of recurrent *C. difficile* that is not responding to treatment can be debilitating. However, FMT results in an estimated 87-90% cure rate of recurrent *C. difficile*, so for most individuals it provides significant relief and improvement in their health (Gupta, 2016).

Fun fact: the importance of FMT

At the time of writing, FMT is only approved for treatment of recurrent *C. difficile* infection, but there is a lot of active research into the potential benefits of FMT in other chronic health conditions, such as IBD, IBS, obesity, high blood pressure and depression.

6 Quiz

We hope that you have enjoyed studying about the fascinating subject of the gut microbiome! Below are a series of questions for you to assess your understanding and knowledge gained while studying this OpenLearn course.

Question 1 Microbiomes

Select from the drop-down lists to complete the following paragraph.

Interactive content is not available in this format.

Question 2 Bacterial profiles

Select the two correct statements from the following:

- ☐ Firmicutes and Bacteroidetes are the most abundant bacteria in the gut microbiome
- ☐ Bacteroidetes and Actinobacteria are the most abundant bacteria in the gut microbiome
- ☐ An individual's unique community of bacterial groups is known as their enterotype
- ☐ Most individuals have a similar profile of bacteria in their gut microbiomes

Question 3 Functions of the gut microbiome

One of the important functions of the gut microbiome is digestion of foods, in particular certain fibres. This results in the production of metabolites, which are then used by the human host. An important group of metabolites are short chain fatty acids. Select which of the following are functions of SCFAs.

- ☐ Protect against dysbiosis
- ☐ Destroy colorectal cancer cells
- ☐ Regulate appetite
- ☐ Reduce obesity
- ☐ Provide energy for the body and other microbiota
- ☐ Communicate with the brain

Question 4 Dysbiosis

There are three main mechanisms which cause dysbiosis. Select from the drop-down lists to describe each mechanism.

Interactive content is not available in this format.

Question 5 Health

Several health conditions have been linked to dysbiosis, and a change in diversity of the microorganisms of the gut microbiome. The ratio of Firmicutes to Bacteroidetes is thought to be particularly important in health. Drag the correct statement to the matching description.

Balanced ratio of Firmicutes to Bacteroidetes

Increase in Firmicutes compared to Bacteroidetes

Increase in Bacteroidetes relative to Firmicutes

Match each of the items above to an item below.

Healthy individual

Obese individual

Individual with Crohn's disease

Question 6 Exercise

Exercise is well known for having both physical and mental health benefits. Identify the true statements from the following:

- ☐ Certain metabolites made by the gut microbiome have been linked to increased motivation to exercise
- ☐ Certain metabolites made by the gut microbiome have been linked to improved exercise performance
- ☐ The bacterial species *Veillonella* has been shown to increase the amount of lactate athletes can tolerate
- ☐ The benefits of exercise on microbiome health are pronounced in childhood
- ☐ Exercise is known to reduce the risk of colorectal cancer and Crohn's disease

Question 7 Obesity

Obesity is a complex, multifactorial condition linked to a wide range of genetic and non-genetic factors, including environmental, lifestyle, socioeconomic and psychological factors. Select from the drop-down lists to complete the following paragraph.

Interactive content is not available in this format.

Question 8 Medications

Antibiotics are given for the treatment of bacterial infections and have undoubtably saved millions of lives worldwide. The graph below shows research investigating gut bacterial diversity before and after taking a course of antibiotics. The key in the graph indicates the type of antibiotic used.

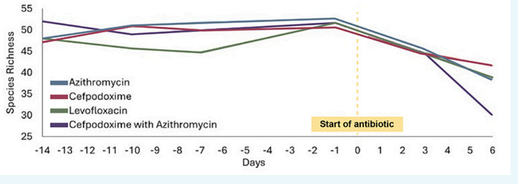


Figure 32 Antibiotic perturbation of gut microbiomes in healthy volunteers

Looking at the graph, which of the following statements is correct?

- ○ The lines on the graph suggest that antibiotic use does not seem to impact bacterial diversity
- ○ Prior to antibiotic use, species richness fluctuates but remains below 45
- ○ Three days after antibiotic use, species richness has decreased
- ○ Six days after antibiotic use, species richness has returned to normal levels

Question 9 Age

The graph below illustrates gut microdiversity over a typical human lifespan. The graph explores stability (i.e. whether the gut microbiome experiences lots of changes) and also gut diversity (i.e. the proportions of different types of bacteria in the gut microbiome). Look carefully at the graph and then answer the following questions.

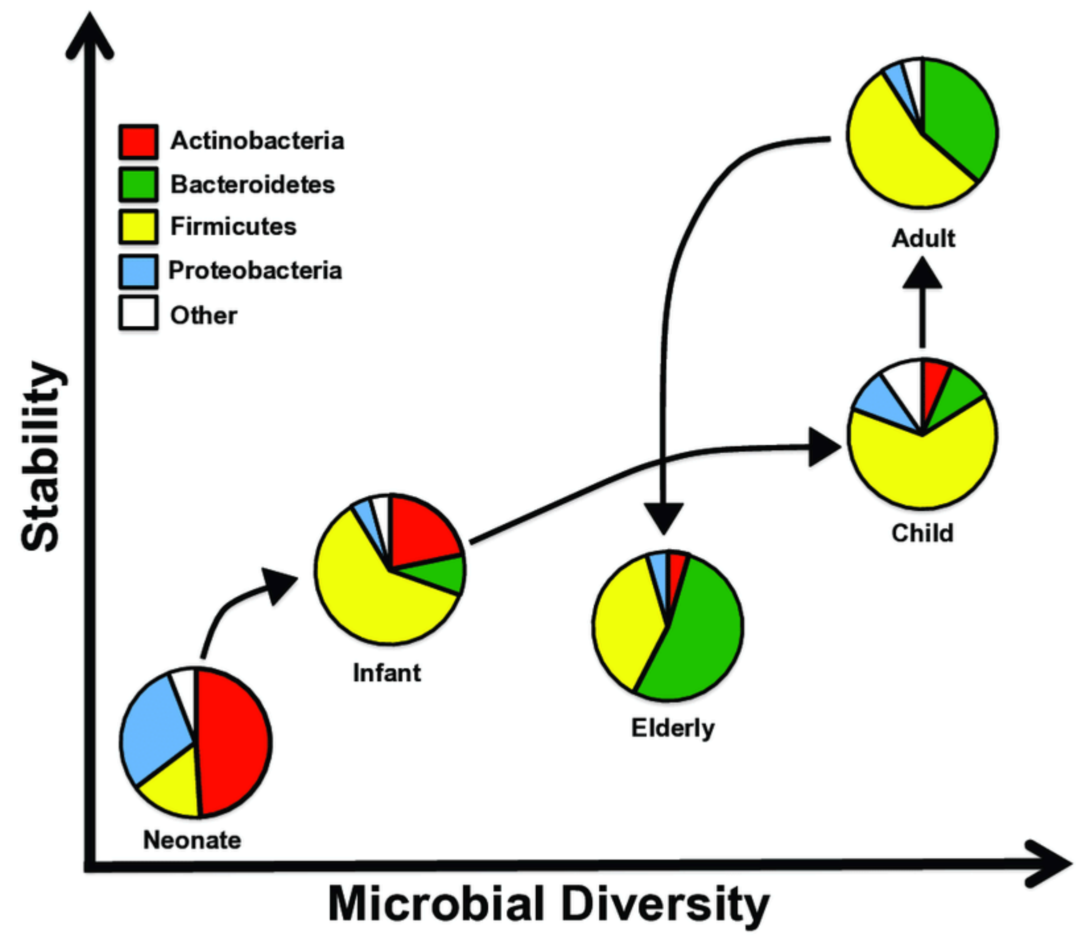


Figure 33 Human gut microbiome composition across the life cycle

From examining the graph, determine whether the following statements are true or false.

The pie charts show there are no changes in gut diversity over the lifespan

- True
- False

The gut microbiome is least stable in neonates

- True
- False

The stability of the gut microbiome decreases in the transition from adult to elderly life

- True
- False

Question 10 Diet

A balanced diet helps provide nutrients for the gut microbiome and the host. Select from the drop-down lists to describe the following food items.

Interactive content is not available in this format.

Now consider the diets which typically incorporate these food items, and complete the sentences below.

Interactive content is not available in this format.

7 Summary

In this course you have learnt about the composition and functions of the human gut microbiome. In particular, you have looked at the role of the gut microbiome in metabolism of nutrients, gut structure and function, in protection against pathogens, in communication with the body (including the microbiota-gut-brain axis, and hormonal signalling) and its role during stress.

You have explored how the gut microbiome interacts with different parts of the body and considered how the gut microbiome can be altered by factors related to the human host (such as genetics, age, and the menopause) and through lifestyle factors (such as diet, exercise, and medications).

You have also explored how altered composition of the gut microbiome, called dysbiosis, is associated with various health conditions, including inflammatory bowel disease (Crohn’s disease and ulcerative colitis) and irritable bowel syndrome (and small intestinal bowel overgrowth), as well as obesity and Type 2 diabetes, colorectal cancer, kidney disease and mental health.

Finally, you learnt about strategies for improving the health of the gut microbiome to restore balance, such as prebiotics and probiotics, and faecal transplants.

Hopefully, you now feel that you have enough knowledge to be able to confidently hold a conversation with other people about the importance of the gut microbiome in health and some disease conditions.

This OpenLearn course is an adapted extract from the Open University course SK190 *Human biology: a body in balance*.

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Figure 31: Belova59 / Pixabay

Figure 32: adapted from Figure 1(c) of Anthony et al. (2022), *Cell Reports*, 39(2): 110649. DOI: 10.1016/j.celrep.2022.110649

Figure 33: Ozdemir, T. (2018) ‘Design and construction of therapeutic bacterial sensors in Escherichia coli Nissle 1917’, Doctoral thesis (Ph.D), UCL (University College London)

Video

Video 1: Overview of body systems affected by the acute stress response. sk299_T12_Video1.1_Slidecast_1_Mixed race teenage couple watching a movie at home, LaraBelova / Getty Images; sk299_T12_Video1.1_Slidecast_4_The brain, Trifonov_Evgeniy / Getty Images; sk299_T12_Video1.1_Slidecast_6_Immune System Concept, wildpixel / Getty Images; sk299_T12_Video1.1_Slidecast_3_Cuisine Culinary Buffet Dinner Catering Dining Food Celebration, _jure / Getty Images; sk299_T12_Video1.1_Slidecast_2_Beating heart, 3DME PTY LTD / Science Photo Library; sk299_T12_Video1.1_Slidecast_5_There are decreases in reproductive hormone production, Claus Lunau/Science Photo Library; sk299_T12_Video1.1_Slidecast_5_Female fighter with injured knee in gym, Dean Mitchell / Getty Images.

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Glossary

colonoscopy

A procedure using a colonoscope or scope (a long thin flexible tube with a camera) inserted into the rectum and colon to view the colon wall tissue.

deoxyribonucleic acid (DNA)

Large molecules present in almost all cells. In humans, DNA is packed into structures called chromosomes. DNA carries genetic information.

dysbiosis

Disruption of the microbiome resulting in an imbalance of microbiota and diversity, which changes the function and metabolic activities of the microbiome.

endoscope

A long thin flexible tube with a camera that is passed through the mouth or into the anus, to view the gut wall.

enteric nervous system (ENS)

Responsible for communicating information about and within the digestive system.

enteroendocrine cells (EECs)

Specialised epithelial cells found scattered along the epithelium of the gastrointestinal tract. Secretes a wide range of hormones into the blood in response to the presence (or absence) of dietary nutrients and mechanical stimuli.

enterotype

The community of bacterial groups or species in an individual, that is often classified based on their predominant bacterial species.

enzyme

A biological molecule that speeds up the rate of chemical reactions (i.e. a catalyst), but is not itself destroyed in the process. Most (but not all) enzymes are proteins.

epigenetics

Modifications of DNA that do not change the DNA code but alter the pattern of gene expression.

gastroscopy

A long thin flexible tube with a camera that is passed through the mouth to view the throat, oesophagus, stomach and first part of the duodenum i.e. the upper part of the digestive system.

genes

A gene is a sequence of nucleotides in DNA, that is transcribed to produce RNA; it can be considered as the basic unit of heredity.

gut-associated lymphatic tissue (GALT)

Collections of lymphatic cells and tissue in or around the digestive system, that support the immune response of the gut.

gut-brain axis

The cross talk between the digestive system and the brain.

individual variability in drug response (IVDR)

The difference in how one individual compared to another may respond to a drug, including serious adverse reactions.

inflammatory bowel disease (IBD)

A collection of two conditions, Crohn's disease and ulcerative colitis, associated with a chronic immune response resulting in severe inflammation, ulceration and damage to the GI tract, abdominal cavity and other body systems.

irritable bowel syndrome (IBS)

A collection of disorders associated with altered gut motility, inflammation and permeability for which the cause and pathology is not fully understood.

lymphatic system

The lymphatic organs (lymph nodes, spleen, tonsils, thymus and bone marrow) and the network of fine tubules that connect them and extend throughout the body. Leukocytes, antibodies and other specialised chemicals involved in the immune response to infection circulate between the lymphatic system, the tissues and the blood, and the lymphatic capillaries collect fluid draining from the tissues and return it to the blood stream.

microbiome

A population of viruses, bacteria and eukaryotic microbes, e.g. in the digestive tract, where it is termed the 'gut microbiome'.

microbiota

A community of microorganisms on or in the body.

microbiota-gut-brain axis

A communication network between the microorganisms of the gut microbiome, vagus nerve, bloodstream, and brain.

nephron

The functional unit of the kidney, composed of tubules and blood vessels which produce the urine.

pathogens

Infectious agents (e.g. parasites, protists, bacteria, fungi, viruses, prions) that cause infectious diseases.

prebiotics

Substances that are eaten or drunk to promote the growth of beneficial gut microbes.

probiotics

One or more live microbial species eaten or drunk to promote gut health.

short-chain fatty acids (SCFAs)

Fatty acid molecules each consisting of 6 or less carbon atoms. It is produced by bacteria within a microbiome by digesting fibre and releasing the fat as SCFAs. Examples are butyrate, propionate and acetate. SCFAs can be used by the host's body or by other bacteria as an important energy source.

small intestinal bacterial overgrowth (SIBO)

Excessive and abnormal growth of either healthy bacteria from the gut microbiome or pathogenic bacteria in the small intestine.

symbionts

An organism that lives with another for mutual benefit.

vagus nerve

The tenth cranial nerve that is a key mediator of the parasympathetic nervous system that extends from the brain down to the majority of organs within the thorax, abdomen and pelvis.

villi

Small, finger-like projections of tissue. Typically these are thin, consisting of only a few layers of cells. Villi are important for increasing the surface area of the tissue which is in contact with surrounding material, such as in the placenta or in the gut. This serves to increase the area of surface over which transport of substances can take place.