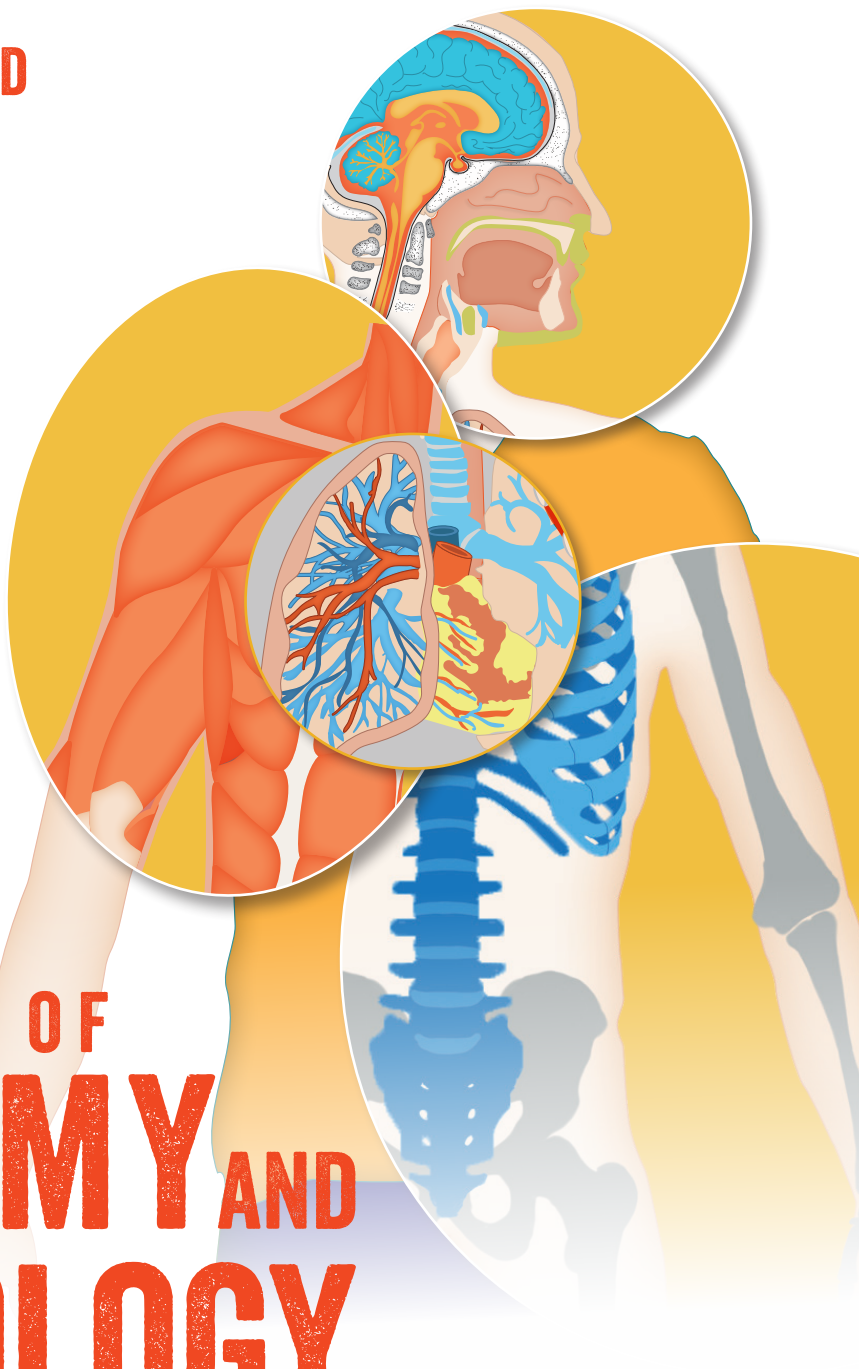
Applying your learning alongside the person-centred nursing framework

NEAL COOK
ANDREA SHEPHERD

FOREWORD BY
BRENDAN MCCORMACK
AND TANYA MCCANCE



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1 Oliver's Yard
55 City Road
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2455 Teller Road
Thousand Oaks
California 91320

Unit No 323-333, Third Floor, F-Block
International Trade Tower
Nehru Place, New Delhi – 110 019

8 Marina View Suite 43-053
Asia Square Tower 1
Singapore 018960

Editor: Laura Walmsley
Associate editor: Sahar Jamfar
Production editor: Sarah Sewell
Copyeditor: Clare Weaver
Proofreader: Christine Bitten
Marketing manager: Ruslana Khatagova
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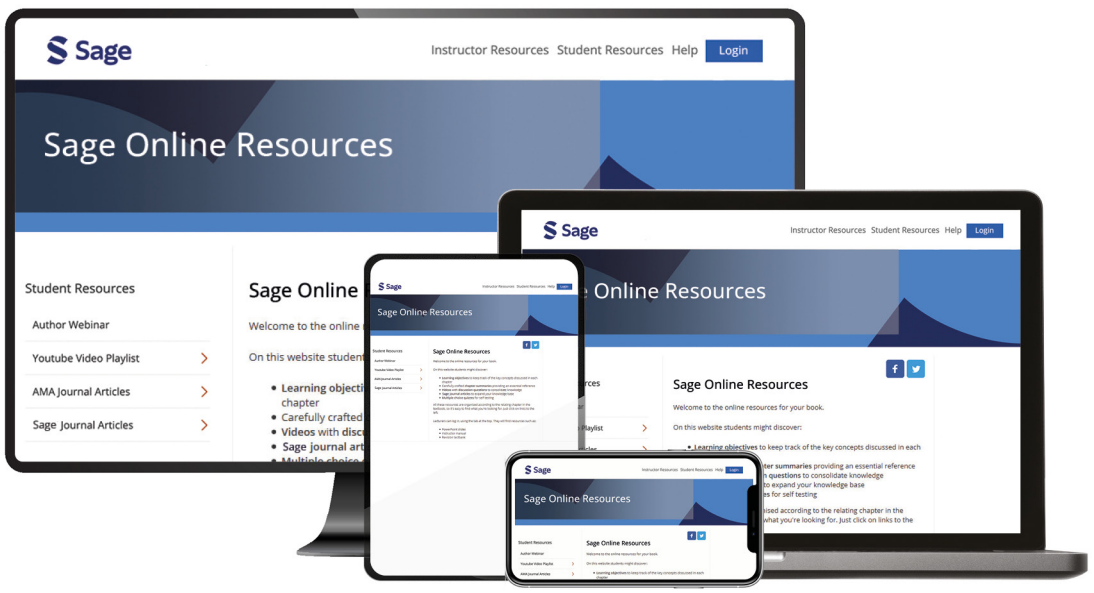

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Online resources help to improve your understanding and bring each chapter to life. Access the online resources by visiting https://study.sagepub.com/essentialap3e

Visualise essential concepts, theory and practice with curated video links. *See below for how to access the videos*.

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ABOUT THE AUTHORS

Neal Cook is a Professor of Nursing and Head of School at the School of Nursing and Paramedic Science, Ulster University and a Principal Fellow of the Higher Education Academy. Neal is also President of the European Association of Neuroscience Nurses and an Executive Board Member of the British Association of Neuroscience Nurses. Neal has taught anatomy, physiology and pathophysiology to undergraduate and post-graduate nursing students across a number of courses since he commenced working in higher education. Neal is also passionate about person-centred practice, a key focus of his research, practice and educational activities. He has worked in the fields of neurosciences and critical care since registering as a nurse, becoming a specialist practitioner and subsequently moving into education and research. Neal has published clinical, research and education papers in the fields of education and neurosciences and remains very active in these endeavours. He remains clinically active in neurosciences and remains a Registered Nurse with the Nursing and Midwifery Council (UK).

Andrea Shepherd is a Senior Lecturer in Nursing and Associate Head of School at the School of Nursing and Paramedic Science, Ulster University, a Senior Fellow of the Higher Education Academy and Board Member of the British Association of Neuroscience Nurses. She has taught anatomy, physiology and pathophysiology to undergraduate nursing students across a number of courses since she commenced working in higher education. Andrea is also an Advanced Life Support Instructor, teaching life support courses in Health and Social Care Trusts and in the University. She has worked in the fields of critical care and orthopaedics since registering as a nurse, becoming a specialist practitioner and subsequently moving into education. She currently takes a lead role in adult pre-registration nursing, is clinically active in critical care and remains a Registered Nurse with the Nursing and Midwifery Council (UK).

The School of Nursing and Paramedic Science at Ulster provides pre-registration and post-registration nursing and paramedic science education across two campuses in Northern Ireland and internationally.

THE HUMAN MICROBIOME AND HEALTH

4

UNDERSTAND: CHAPTER VIDEO

In working through this chapter, you might find it useful to have an overview of the human microbiome.

The following video may be useful in enhancing your understanding. This can be easily accessed via **http://study.sagepub.com/essentialap3e**

Activity 4.1: Understand has further resources to enhance your understanding.

LEARNING OUTCOMES

When you have finished studying this chapter you will be able to:

1. Identify the major groups of microbes found in different parts of the body
2. Describe the normal structure of the prokaryotes (single-celled microbes – bacteria)
3. Understand how the body acquires its microbiota (the microorganisms of a particular site) and how this varies in different parts of the body (intrapersonal) and between different people (interpersonal)
4. Discuss the importance of the normal flora in maintaining health of the human body and factors that may alter this flora
5. Consider potential implications of variations in the normal flora
6. Outline the implications for health of pathogenic microorganisms and the importance of appropriate use of antibiotics

INTRODUCTION

You have learned quite a lot about the human cell, but more than 90% of the cells in the human body are not human in origin but microbial, that is, only visible under a microscope. In a book about the human body they deserve some attention. They form the microbiome, which has been defined as the 'ecological community of commensal,[1] symbiotic,[2] and pathogenic[3] microorganisms that literally share our body space and have been all but ignored as determinants of health and disease' (Lederberg and McCray, 2001: 8) and have been described as the 'forgotten inner organ represented by the enteric microflora' (O'Hara and Shanahan, 2006: 692). The individual organisms comprising the normal flora (microbiota) interact with one another and with the host. That is, they are an integral part of the human body.

Following the Human Genome Project, The National Institutes of Health (USA) are funding the Human Microbiome Project (HMP) involving around 80 research institutions to study the role of microbes in human health and disease (NIH HMP Working Group, 2009); this is a relatively recent area of work and its importance is growing. The human microbiome has been described as 'our second genome' (Grice and Segre, 2012: 151).

In this chapter we are going to look at the major groups of microbes within and on the human body, their structure and requirements for metabolism and life, and the importance of the normal flora (also called the 'indigenous microbiota') of the body. It is now clear that the microbiota, both internal and external, play a major role in maintaining health (Leo et al., 2023). This chapter will include an outline of the microbiological content of the gastrointestinal tract, skin, mouth, upper respiratory tract and reproductive tract, and the development and factors which alter the nature of the flora. The importance of the human microbiome in health will be the main focus. However, the potential implications for health of some pathogenic organisms and approaches to minimising risk will be introduced.

ACTIVITY 4.1: UNDERSTAND

Watch the following video clips online to help develop your understanding of the human microbiome.

These online videos can be accessed via https://study.sagepub.com/essentialap3e.

Context

Within the Bodie family, the different individuals will have different microbiota. Danielle, the baby, is still being breast-fed and will have acquired most of her microbes during and since birth from her mother. The microbiota of the adults will have developed over time, influenced by the different environments, foods and drink ingested, individuals with whom they have contact and hygiene practices. While close family members are likely to have a degree of similarity in their microbiota, they will also have considerable variation.

[1]Living on or within another organism, deriving benefit without harming or benefiting the host.
[2]A relationship between different species where both organisms benefit from the presence of the other.
[3]An agent causing disease or illness to its host.

MICROBIAL STRUCTURE AND FUNCTION

Introduction

The number of microbial cells normally living on and in the human body is in the region of 10^{14} (100 trillion) bacteria and 10^{15} (a quadrillion) viruses compared to about 10^{13} (10 trillion) human cells comprising the body.[4] Other microbes are present in smaller numbers. Each person's microbiome is unique, varying between individuals, between different parts of the body and over time. Most of the focus on microbes in healthcare education is on those that cause disease, which is not the emphasis here: in this chapter we are considering microbes and human health. However, the types of organisms involved in both contexts are similar in structure and much of their function: this section provides an overall introduction.

There are a number of different types of microbes that may be found in the human body: most are prokaryotes, both bacteria and some archaea, a few eukaryotes – fungi, protozoa (protists) and helminths (worms), and many viruses (mostly bacteriophages – i.e. that attack bacteria). Table 4.1 indicates the main types of microorganisms found in humans. Their metabolism may be:

- Obligate aerobes: can only grow in presence of oxygen.
- Facultative aerobes: can grow if oxygen is available or not.
- Obligate anaerobes: cannot grow if any oxygen is available.

Table 4.1 Main types of microbial organisms

Microbe type	Class of organism	Structure	Metabolism	Additional information
Bacteria	Prokaryotes	DNA or RNA within cell without membrane surrounding organelles. No nucleus	Varied oxygen requirements	(Figures 4.2–4.4)
Archaea	Prokaryotes			Much research still required
Viruses	'At the edge of life'	RNA or DNA (genetic material), surrounded by a protein coat, sometimes with a lipid coat	Dependent on host cell metabolism for replication	Non-active outside host Replicate only inside living cells of host using materials of cell to produce proteins encoded in RNA or DNA and form viruses Each virus restricted to specific number/type of cell. Those that infect bacteria are known as 'phages' (Figures 4.7 and 4.8)

(Continued)

[4]Understanding the numbering of microbial cells is complicated by the different systems seen in various publications. Until fairly recently British and German publications used the long scale (each new term a million times larger than the previous one) and American and French ones used the short scale (over one million, each new term one thousand times larger than the previous one). Modern British use is normally the short scale and is used in this text.

Long Scale	Short Scale
10^{15} = 1,000,000,000,000,000 = 1000 billion	10^{15} = 1,000,000,000,000,000 = 1 quadrillion
10^{14} = 100,000,000,000,000 = 100 billion	10^{14} = 100,000,000,000,000 = 100 trillion
10^{13} = 10,000,000,000,000 = 10 billion	10^{13} = 10,000,000,000,000 = 10 trillion

Table 4.1 (Continued)

Microbe type	Class of organism	Structure	Metabolism	Additional information
Fungi	Eukaryotes	Separate from animals and plants with some characteristics of both Cell nuclei surrounded by membrane	Rely on carbon fixed by other organisms	Most grow from their tips as tubular filaments (hyphae), which branch producing a network of hyphae. Some grow by budding or binary fission as single cells: includes moulds, yeasts Some produce spores dispersed for reproduction. Further research to clarify role in microbiota needed (Figure 4.9)
Protozoa/ protists	Eukaryotes	Eukaryote that is not animal plant or true fungus Independent cells or non-differentiated into tissues	Some use sunlight, others rely on organic compounds	Some are pathogens of animals, some of plants, some non-pathogenic (Figure 4.10)
Helminths	Eukaryotes	Worm-like parasites living in animal hosts	Feed on living hosts	Can cause weakness and disease but can also reduce incidence of allergy and autoimmune conditions (Johnston et al., 2014). Uncommon in developed countries (Figure 4.11)

Relationship between microbes and host

Microbes have differing relationships with their hosts. In this section, we will look at some of these relationships, specifically for microbes that are transients, commensals, opportunists and pathogens.

Transients

These microbes get incorporated briefly into the microbiota from the diet or environment. However, they do not remain long and are unable to colonise the body because:

- the normal flora have already taken up the available sites,
- the immune system eliminates them,
- physical or chemical characteristics of the body prevent their growth.

Commensals

Commensals are the normal flora of the body in symbiosis with their host. They live harmlessly in or on their selected site and gain nutrients from their host. They may be beneficial to the individual carrying them as they prevent potentially harmful microbes becoming established. In addition, many of them have a positive effect by, for example, forming particular vitamins or influencing the immune system (discussed later) though these may be described as symbiotic.

Opportunists

These are microbes which are normally harmless within the body but can cause disease when the host's immune system defences are lowered by other disease or by therapy (e.g. radiotherapy, chemotherapy or

GO DEEPER

Classification of microbes

It will be easier to understand this chapter with some knowledge of the classification of microbes. In the 18th century, the Swedish botanist, physician and zoologist, Carl Linnaeus, developed the scientific taxonomy still used today, with some modifications (Figure 4.1). However, growing understanding of microorganisms leads to frequent changes in their classification. Staining (particularly Gram staining), used for visual recognition of bacteria, and distinctive aspects of metabolism have been used in classification. More recently, DNA and RNA fingerprinting have become important in microbial classification. At present there are 11,940 different species names for bacteria but only 451 for archaea – an area in which there is much research yet to be completed.

In this chapter phylum and genera (plural of genus) will be mainly used when discussing microbes in the human microbiome.

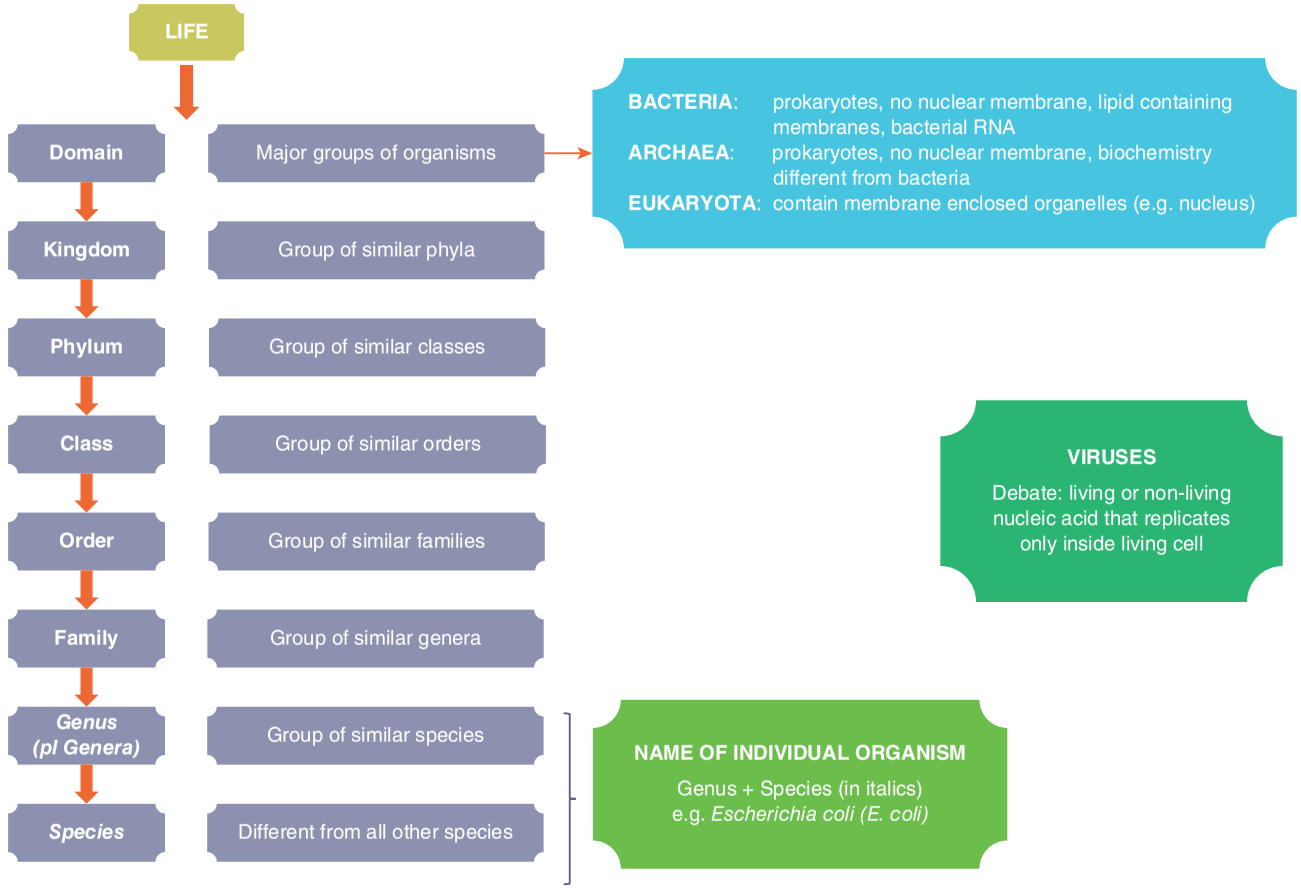


Figure 4.1 Classification of life

various drugs). They can also cause infection when they gain access to a part of the body where they are not usually found (such as *Escherichia coli* normally found in the gut, causing urinary tract infection if it gains access to the bladder). This is endogenous (self) infection when the organisms originate from the same person. Exogenous (or cross) infection is when the microbes come from someone or somewhere else.

Pathogens

Pathogens can cause disease, although the virulence (severity of the disease it causes) depends on both the host and the organisms. Some microbes are highly virulent and even in small doses will almost always cause disease (e.g. plague or the Ebola virus), while others are less virulent and will only cause disease in large quantities or when the host is susceptible (see opportunists).

Types of microbes

Prokaryotes

Bacteria

We will start by looking at bacteria which are the most important microbes in the context of the human microbiome. They are single-celled prokaryotes and a typical bacterium is shown in Figure 4.2, although they differ in size and shape. The major difference from eukaryotes is that the cell organelles in bacteria are not enclosed by cell membrane but lie directly within the cytoplasm: they do not have an enclosed nucleus. It is considered that the mitochondria in eukaryotes are bacteria that, during evolution, took up residence and a major role in energy metabolism within the organism (archaea) that developed into the ancestor of present eukaryotes (Chapter 2).

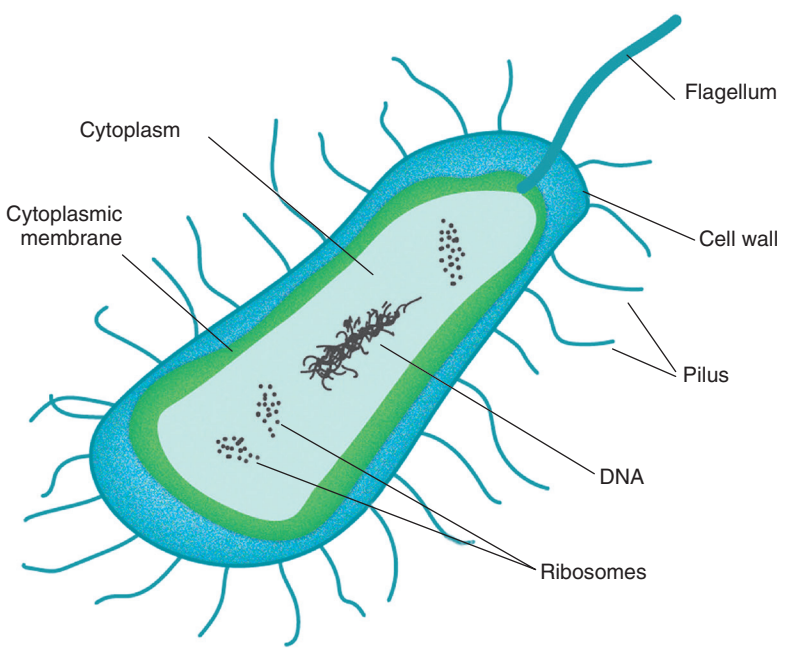


Figure 4.2 A bacterium

The following characteristics are used to describe bacteria:

1. Shape and organisation (Figure 4.3):
   i. Round (coccus) which exist individually and in pairs, chains and clusters.
   ii. Rod (bacillus) which also exist individually and in chains.
   iii. Curved (vibrio) individuals.
   iv. Spiral (spirochaete) individuals.

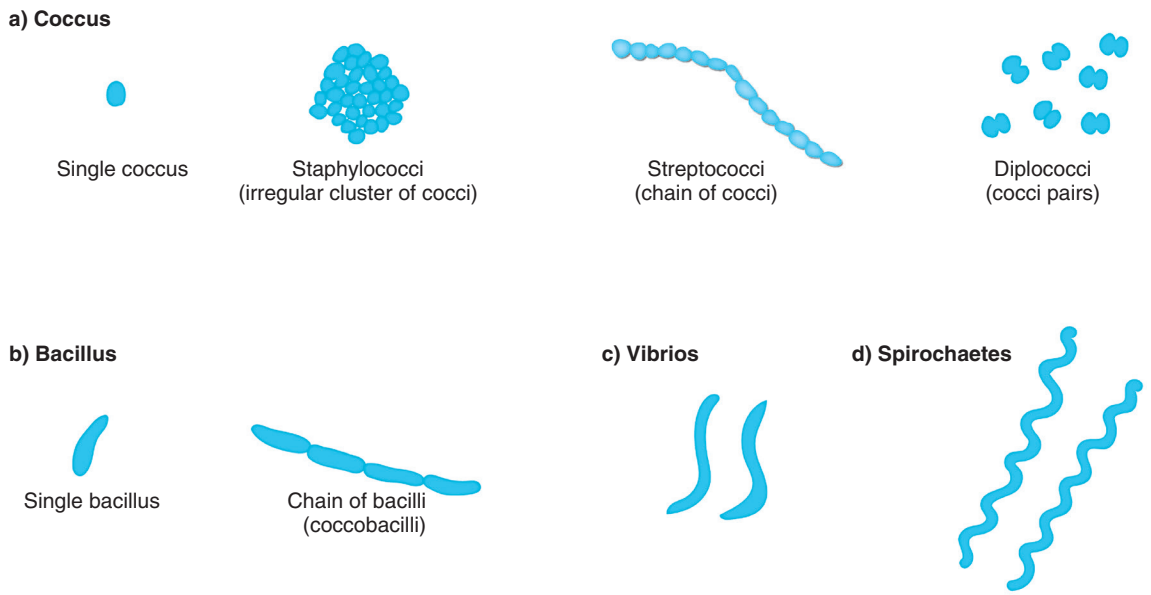


Figure 4.3 Shapes of bacteria

2. Structure: presence or absence of specialised structures in different bacteria (Figure 4.4):
   i. Mucous capsule protects against dehydration and desiccation in dry conditions.
   ii. Flagella enable bacteria to move.
   iii. Spore formation occurs in some bacteria under adverse conditions with germination and cell division recommencing when conditions improve.
   iv. Pili provide attachment to the host.

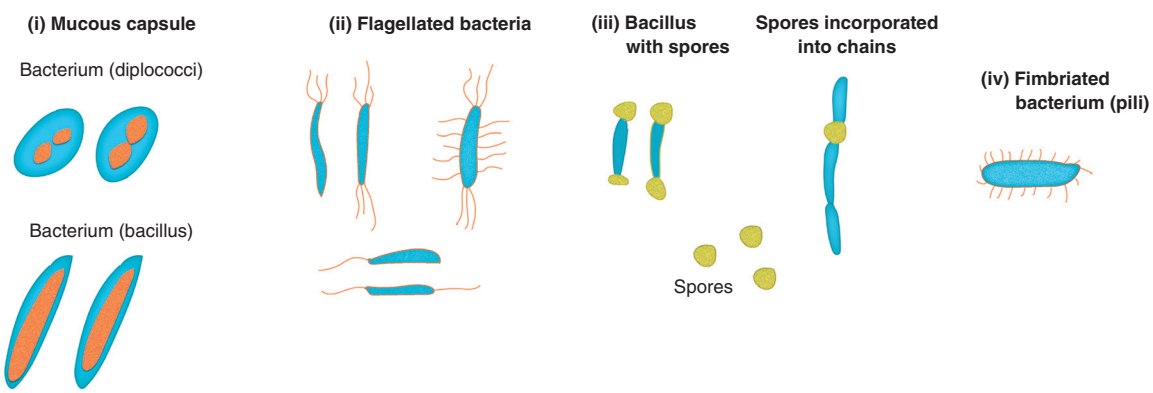


Figure 4.4 Specialised structures in bacteria

3. Effect of dyes on microbial specimens fixed on microscope slides. Bacteria are colourless and thus need to be stained in order to be viewed. There are a variety of stains but the Gram stain is a frequently used one that differentiates bacteria according to the physical and chemical structure of the cell wall. Bacteria are either Gram-positive (stained by the crystal violet dye) or Gram-negative (stained red or pink by a counter stain) when the dark Gram stain is not absorbed by the cell wall. Some bacteria are Gram-variable due to variation in the thickness and structure of the cell wall.
4. Conditions of growth. Within the human microbiome there are a large number of commensal bacteria, some of which are opportunists. Some species of bacteria can be pathogenic or non-pathogenic depending on the environment, and some pathogenic species are similar to those within the normal flora. The conditions for growth of bacteria vary with individual species but must meet their needs in relation to:
    - Temperature – 35–40°Celsius.
    - Moisture.
    - pH level – Neutrophiles – optimum pH 7; Acidophiles – optimum below pH 5; Alkophiles – optimum above pH 8.
    - Oxygen – Obligate aerobes – absolute requirement for oxygen in aerobic respiration, e.g. most environmental bacteria; obligate anaerobes – cannot use O_2 and can be killed by O_2 metabolites. They produce energy by anaerobic respiration/fermentation, e.g. inhabitants of large intestine. Facultative anaerobes – can grow in either the presence or absence of O_2. Use aerobic respiration if O_2 available but use fermentation or anaerobic respiration if O_2 unavailable (growth more rapid in O_2), e.g. *E.coli.*
    - Energy source – Phototrophs – use sunlight as energy source, e.g. plants, algae, photosynthetic bacteria; chemotrophs – use chemical compounds as energy source (metabolism), e.g. mammalian cells, fungi, many types of bacteria.

Bacterial division

Different organisms will grow at different speeds and demonstrate exponential growth through binary fission as the DNA replicates and separates, and the cell divides into two identical daughter cells (Figure 4.5). The time taken for this process to occur is known as the generation time and varies with different species. *Escherichia (E.) coli* has a generation time of 20 minutes, thus the number of bacteria double in each 20 minutes.

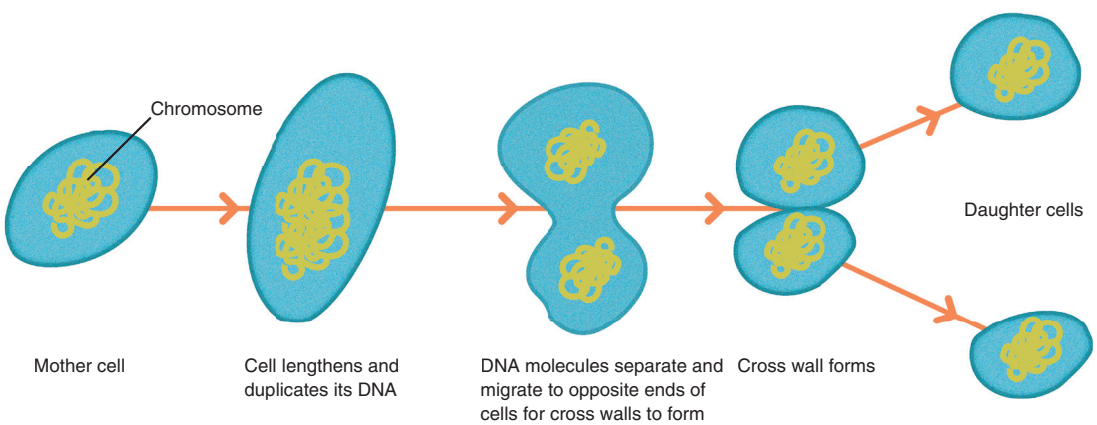


Figure 4.5 Binary fission

Binary fission continues with the cell numbers doubling on each occasion, until the limits of the supplies of requirements for cell division are reached. Figure 4.6 illustrates the four phases of bacterial cell division:

- **Lag phase** is the period during which the bacteria are adjusting to the environment and preparing for cell division.
- **Log phase** is when the bacterial cell numbers are doubling at a constant rate and the population increases very rapidly. With pathogens, it is usually during this phase that symptoms develop.
- **Stationary phase** is when the bacterial numbers level off as cell growth and cell death are equal. This occurs as the nutrients are used up and waste products of metabolism (toxins) begin to accumulate.
- **Death phase** has a steady fall in cell numbers as there is an inadequate nutrient supply or high toxin levels.

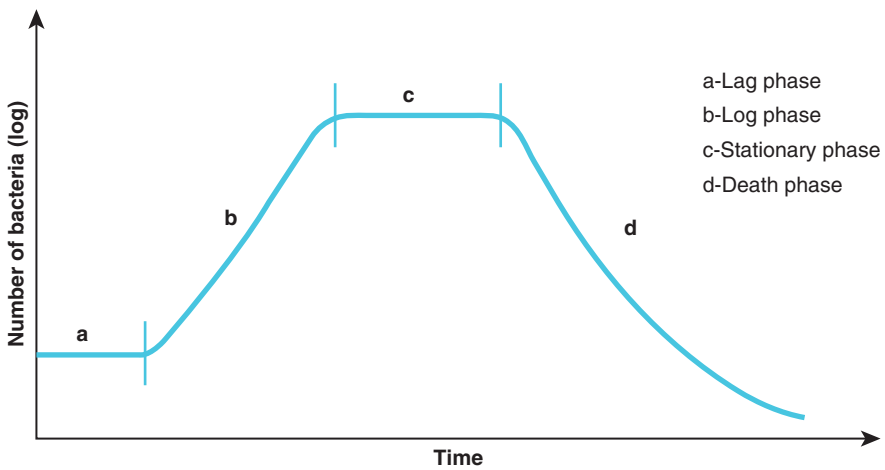


Figure 4.6 Bacterial growth

Archaea

These are similar in appearance to bacteria in that they have no membrane-bound organelles. However, some of their genes and metabolic pathways are more similar to those of eukaryotes although some other aspects of their metabolism are unique. They only reproduce asexually and do not form spores. These were initially thought to live only in extreme environments such as hot springs and salt lakes but are now known to exist within a wide range of habitats, including the human colon.

Methanogens are one type of archaea which produce methane as a by-product of metabolism in anaerobic conditions, such as in the Gastrointestinal Tract (GIT) of humans (and ruminants – contributing to greenhouse gases and global warming) (Djemai et al., 2022).

Neither prokaryotes nor eukaryotes

Viruses

Viruses are intracellular parasites without independent life outside the cells they infect; all life is host to one or more viruses. Whether or not these are living organisms and their classification as a separate kingdom is appropriate is an ongoing debate. Viruses vary in shape and size (Figure 4.7 illustrates two

types) and, in their simplest form, consist of the genetic material of nucleic acid (either DNA or RNA) surrounded by a protein capsule. Some are further surrounded by a membrane envelope. Viruses have generally been considered to be causes of disease, although the HMP and other research is amending this view. Most of the viruses in the human microbiome are bacteriophages, that is, they infect bacteria.

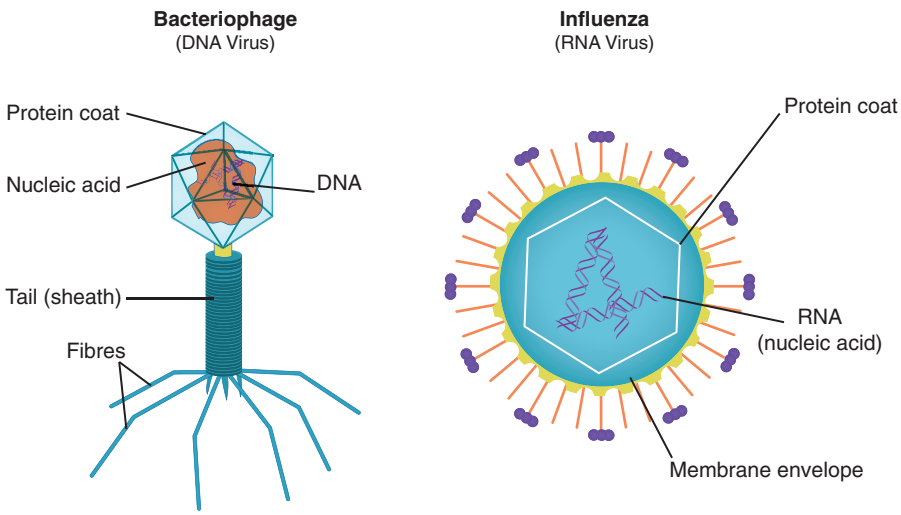


Figure 4.7 Examples of viruses

Viruses multiply within the cells of their host and are then released into their environment. Figure 4.8 illustrates the life-cycle.

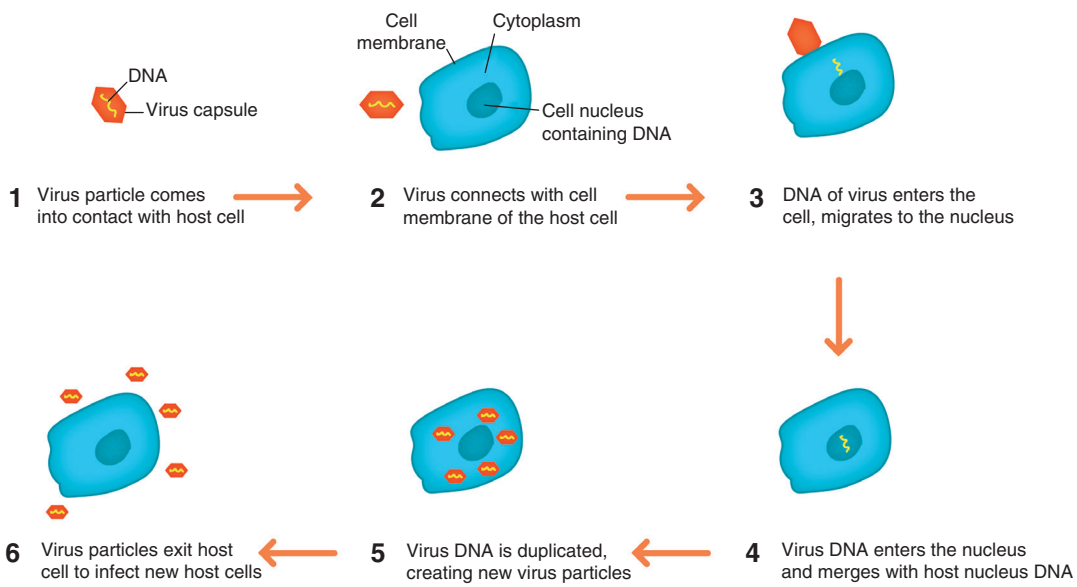


Figure 4.8 Life-cycle of a virus

The virome (i.e. the viruses within the microbiome) has been found to be relatively stable in an individual, although even people eating the same diet had differences in viral composition. However,

alteration in diet resulted in changes in the proportion of a particular virus so that the viromes in those on similar diets were more similar than in those eating differently. Study of the human virome is continuing but there is still much to discover.

Eukaryotes

These all have an identifiable nucleus and other organelles surrounded by membrane.

Fungi

These are eukaryotes but are neither plants nor animals. Some have a simple structure and exist as unicellular organisms, for example yeasts. Others are more complex and exist as a mycelium, an interwoven mat of tubular filaments or hyphae. Figure 4.9 illustrates these.

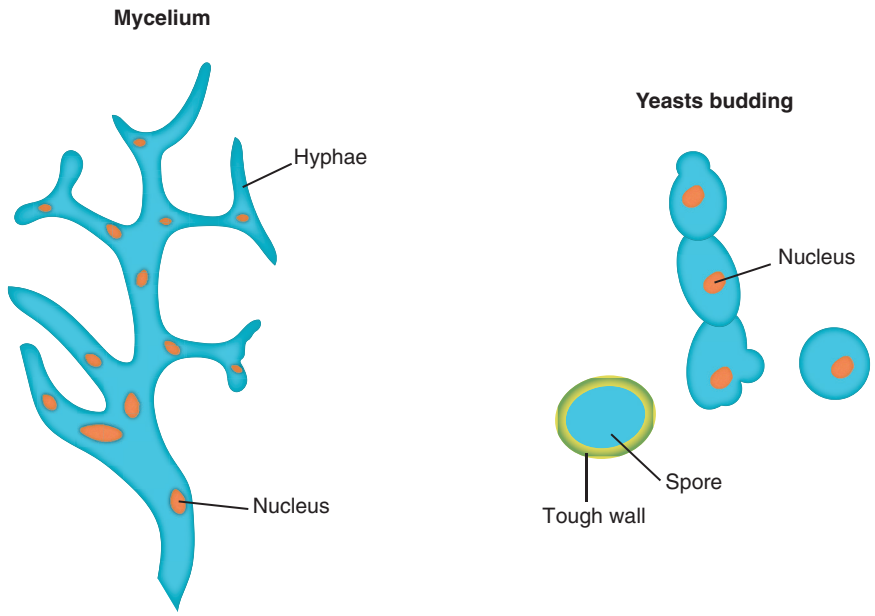


Figure 4.9 Fungi

Some fungi are found in healthy individuals but can cause disease if the environment becomes compromised. For example, commensal *Candida* can become pathogenic because:

> defects in the immune system, genetic predispositions, breaches in skin and mucosal barrier integrity, as well as microbial dysbiosis *(imbalance)* can all be factors predisposing to *Candida* infection and invasion. (Iliev and Underhill, 2013: 369)

The evidence of benefit to the host of resident fungi is still sparse – further research is required and there is increasing data that show resident fungi can contribute to both health and disease (Spatz and Richard, 2020).

Protozoa/protists

These are unicellular microorganisms most of which are harmless, but some are pathogens or opportunists. Examples of particularly unpleasant GIT pathogens are *Cryptosporidium* and *Giardia*. Figure 4.10 illustrates some protozoa.

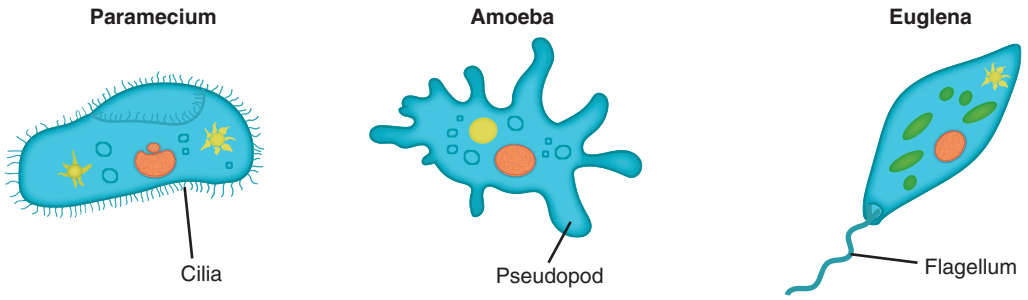


Figure 4.10 Examples of protozoa

Helminths (worms)

Helminths (Figure 4.11) are uncommon residents of the human gut in developed countries but more common where contamination of water and food is prevalent. While the idea of having worms resident in one's gut is unpleasant, some may have certain health benefits particularly in relation to allergic disorders (Erb, 2009); recent evidence would suggest this not to be the case (Arrais et al., 2022). One paper highlights the relationship between helminth infections and reduced incidence of allergic conditions, mainly in underdeveloped countries where such infections are more common than in more advanced countries (Johnston et al., 2014). However, the results from studies are varied and further research is required.

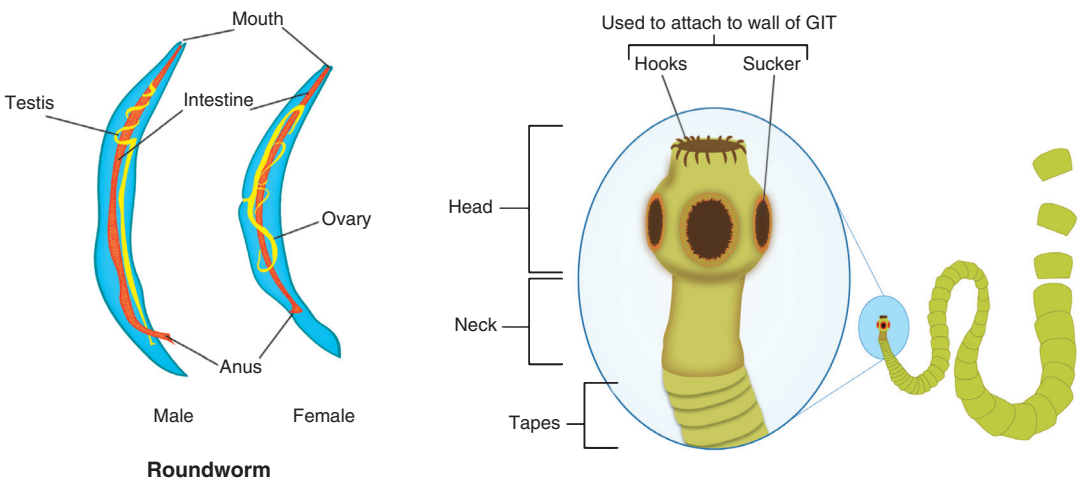


Figure 4.11 Examples of helminths

HUMAN MICROBIOME

Introduction

In-depth study of the human microbiome began with the Human Microbiome Project in 2008 using many of the methods developed within the Human Genome Project, which aimed to map the genes on the human chromosomes. The understanding of the role of the microbiome in contributing to human

health is growing but it is already clear that it plays an important part in a number of host physiological activities which impinge on health status.

Pathogenic microbes in disease are discussed in detail in pathophysiology, clinical microbiology and nursing books in the context of infection control. Here we are primarily focusing on microbes in relation to the major sites of the human microbiome and health. Many different species of microbes live in and on the human body and are thought to account for 1–3% of total body mass. They exist on all surfaces exposed to the external environment particularly:

- **Gastrointestinal tract**: in essence a long tube joining the external environment at either end, it contains the majority of microbes.
- **Skin**: the largest organ of the body, which protects the internal organs from exposure to the external environment.
- **Mouth**: exposed to a wide range of microbes through food and drink.
- **Upper respiratory tract**: exposed to microbes in the air.
- **Vagina**: exposed to microbes from other individuals during sexual activity.

The makeup of the microbiota of the different sites is now being defined by genomic analysis, identifying the DNA composition of the site using similar techniques to those in the Human Genome Project. However, it is clear that there is much research still to be undertaken.

Development of the microbiome

In a review of the impact of the gut microbiota, Clemente et al. (2012) discuss how the microbiota develops through life with the major changes occurring within the early years. The functions carried out by the microbiome alter according to the bacterial (and other microbial) composition and these have a significant impact on health (Leo et al., 2023).

Early development

Until recently it had been thought that the fetus was sterile and only acquired microorganisms after birth. However, there is now some evidence that a limited number and type of bacteria are present in the amniotic fluid surrounding the fetus (Jiménez et al., 2008; Vemuri and Herath, 2023).

The microbiota proper begins rapid development at birth as the infants are exposed to the microbes in their environment. Dominguez-Belloa et al. (2010) studied the influence of the mode of delivery of an infant on its microbial residents. A small sample of mothers and babies delivered vaginally (four) or by Caesarean Section (CS) (five mothers and six babies) had microbial smears taken as follows:

- **Mothers**: skin, oral mucosa, vagina – 1 hour before delivery.
- **Babies**:
  - skin, oral mucosa, nasopharyngeal aspirate – within five minutes,
  - meconium (earliest stool passed) – within 24 hours of delivery.

The mothers' results varied and showed that the microbial communities at the different sites examined on the body were different, but the infants' results were completely different. Each infant showed little variation across the body, but the bacteria identified were different for the two groups of babies. All the infants delivered vaginally had bacteria from all parts of their body that were similar to the vaginal microbes of the mother. Those born by CS had no maternal vaginal bacteria but had bacteria similar to

those on the mother's skin. These differences may result in persistent differences and delays in the development of the adult microbiome.

In early life when the diet is primarily milk, the microbiome contains microbes with the ability to utilise lactate, and the composition of the gut microbiota begins to change to utilise plant foods even before solid food is introduced to the infant's diet. Initially, the microbes in the gut are oxygen tolerant, but are replaced by anaerobic bacteria as found in adults. The number of different types of bacteria and viruses in the newborn infant is relatively low, but with solid food the infant microbiota diversifies further. Gradually over time it becomes more like that found in adults.

APPLY

The microbiome in early life

Danielle was born naturally, and at two months, her microbiota is still similar to her mother's vaginal microbes. As she reaches six months she will be introduced to solids, which may be in the form of pureed food from her parents' diet. She is likely to develop a microbiota similar to her parents.

The makeup of the initial microbiota may influence functions associated with nutrition and immune systems. It has been reported that CS delivered infants are more liable to develop allergies and asthma than those vaginally delivered (for example: Bager et al., 2008; Tollånes et al., 2008). However, this has been disputed by Maitra et al. (2004) in a large Dutch study and in a more recent study by Liu et al. (2023).

Later development

By the first birthday, the microbiota is beginning to resemble that of adults and normally reaches this state by two-and-a-half years of age. Usually it then remains stable during adulthood if diet, disease, environment, etc., remain constant. In older people there is greater variability in the proportions of types of microbes than in younger adults. This may be due to changes associated with ageing and the effects of medication use. The microbiota of the same site in different individuals are more similar than of different sites in the one individual, fitting the microbiological concept proposed in 1934 by Baas Becking and Beijerinck (cited by De Wit and Bouvier, 2006) of 'Everything is everywhere, but the environment selects'.

MICROBIOME, HEALTH AND DISEASE

The microbiome, the overall genetic makeup of the microbiota, plays an important role in maintaining health through interaction between the different microbes and with their host. Most microbes in and on us are commensals and some perform functions that our own cells have not evolved to undertake themselves. While we specify some microbes in this chapter, more important is understanding the functions that they perform – as many different species can play identical roles.

Gastrointestinal tract (GIT)

Within an individual the makeup of the microbiota remains relatively stable. The level of bacterial content varies through the gut with the stomach virtually sterile and the content increasing through the

small intestine to the highest level in the colon (Canny and McCormick, 2008; Lin and Medeiros, 2023). Although there is variation between individuals, the gut microbiota is inherited from the mother and is similar in closely related individuals (Ley et al., 2006; Tian et al., 2023). However, it is suggested that 'each host has a unique biological relationship with its gut microbiota and this influences an individual's risk of disease' (Kinross et al., 2011: 14).

GO DEEPER

Gut microbiota

The gut microbiota can include several hundred species which tend to be relatively stable in any one individual although they vary between people. The main groups of bacteria identified (Eckburg et al., 2005; cited by Matsuki and Tanaka, 2014) are:

- two dominant bacterial groups:
  - firmicutes,
  - bacteroidetes;
- followed by:
  - actinobacteria,
  - proteobacteria,
  - verrucomicrobia,
  - and others.

It is also useful to note that the microbial diversity in the lumen varies compared to that of the surface of the intestine.

Functions of the gut microbiota

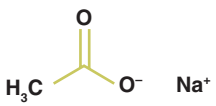
The relationship between gut microbes and host is a symbiotic one in which both sides benefit. Research with germ-free animals has helped to clarify the contribution to health of the microbiota. Functions carried out by the GIT microbiome are numerous and include energy and drug metabolism, formation of vitamin K and enhancing the immune response in the body.

Energy metabolism

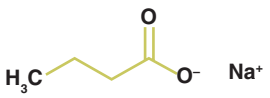
This involves the metabolism of carbohydrates and formation of Long Chain Fatty Acids (LCFAs). The microbiota of the GIT plays an important role in utilisation of 'resistant' starch foods. Essentially these are high-fibre carbohydrates derived from plants which are not digested effectively within the small intestine, but undergo fermentation and assimilation in the large intestine, meeting perhaps 10% of the calorie needs of the body.

The metabolic activity of gut microbes creates a range of Short Chain Fatty Acids (SCFAs) with acetate, butyrate and propionate being the three most common, occurring in varying proportions in different people (Figure 4.12).

a. (Sodium) Acetate $CH_3COO^-(Na^+)$



b. (Sodium) Butyrate $CH_3CH_2CH_2COO^-(Na^+)$



c. (Sodium) Propionate $CH_3CH_2COO^-(Na^+)$

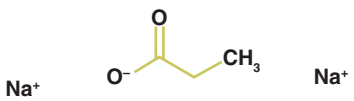


Figure 4.12 Main short chain fatty acids (SCFAs)

GO DEEPER

Short chain fatty acids and metabolism

Acetate is produced by most anaerobic bacteria, while the bacteroides and firmicutes are the main producers of butyrate and propionate. These have an important effect on the quality of the environment of the large intestine and absorption from the gut into the internal environment. These three SCFAs play important but different roles in metabolism (Russell et al., 2013; Yao et al., 2022) although all are utilised by the colonic mucosa:

- Acetate reaches the highest levels in the plasma and is used in lipogenesis (formation of lipids, Chapter 9) in both liver and fat cells.
- Butyrate is important as an energy source for the epithelium of the colon, but it also appears to help prevent inflammation, and possibly prevents colorectal cancer by inhibiting cellular division and promoting apoptosis (Fung et al., 2012; Hajjar et al., 2021). Decreased numbers of butyrate-producing bacteria are found in those with Crohn's disease (Gasaly et al., 2021).
- Propionate is used in gluconeogenesis (formation of new glucose, Chapter 9). It is thought to have an important role in satiety, protection against diet-induced obesity and improving insulin sensitivity (Chapter 7) (Arora et al., 2011; Deehan et al., 2022).

Formation of vitamin K

Vitamin K is a fat soluble vitamin that plays an important role in blood clotting and a deficiency can result in low prothrombin levels and haemorrhage. While deficiency is rare in adults, it is common in newborn babies who have low levels of vitamin K, which is used up fairly quickly and leaves the baby at risk of haemorrhage. In the UK they are usually routinely administered vitamin K by injection. Microbes in the gut also manufacture vitamin K which is then absorbed into the body. However, in someone who has large amounts of antibiotics the microbes in the gut may be altered leading to a reduction in the amount of vitamin K formed, and this can result in hypoprothrombinaemia and increase the risk of bleeding.

There is also some evidence that vitamin K plays a role in bone density (Bügel, 2008; Salma et al., 2022) with insufficiency associated with low bone density and increased fractures. Human studies have demonstrated that vitamin K increases bone mineral density in people with osteoporosis and reduces fracture rates particularly in combination with vitamin D (Weber, 2001; Kuang et al., 2020).

UNDERSTAND

Hypoprothrombinaemia

Hypo- = lower than normal,

prothrombin = the precursor to thrombin,

-aemia = in the blood.

hypoprothrombinaemia = low levels of prothrombin in the blood

Drug metabolism

Some drugs and other xenobiotic substances (i.e. not normally found in the body) are metabolised by microbes in the gut (Kinross et al., 2011; Pant et al., 2022), which may reduce the efficacy of the drugs.

APPLY

Digoxin and gut microbiota

Digoxin is an example of a drug shown to be influenced by the gut microbiota. In about 10% of people, a particular bacterium in the gut was found to convert a significant amount of digoxin to an inactive substance; antibiotic treatment was also found to increase plasma digoxin levels (Gulnaz et al., 2023).

Development of intestinal structure

Although more research is needed, it appears that substances produced by the gut microbiota regulate the formation of the normal structure of the intestinal epithelium (Chapter 8). In addition, these microbes stimulate the formation of Paneth cells (endocrine cells in the crypts of the epithelium), which stimulate the formation of the intestinal capillary network.

Maturation of the immune system

The microbiota is constantly in contact with the intestinal mucosa and helps to define the barrier between the external and the internal environment. The microorganisms interact with the immune system and stimulate the development of the Peyer's patches (aggregations of lymph tissue within the lower part of the ileum) (Chapters 8 and 13) and lymphoid tissue. The commensal microorganisms play an important part in the maturation of the gut and its immune system, as well as influencing the immune system more widely.

Prevention of pathogenic infection

The commensals in the intestine fill various 'ecological niches' and compete with transient pathogens for nutrients, thus inhibiting them from becoming resident. *Lactobacilli*, common in the GIT, secrete lactic acid and other molecules which also inhibit growth of competing microbes. Microbial diversity varies between the lumen of the gut and the surfaces of the intestine.

Illness and the gut microbiota

In recent years, researchers have identified relationships between the human microbiome and a variety of human diseases. Not unexpectedly, some relationships between the microbiome and some intestinal disorders, for example, Inflammatory Bowel Disease (IBD), have been identified. However, a number of other disorders have also been linked to the gut microbes (Figure 4.13).

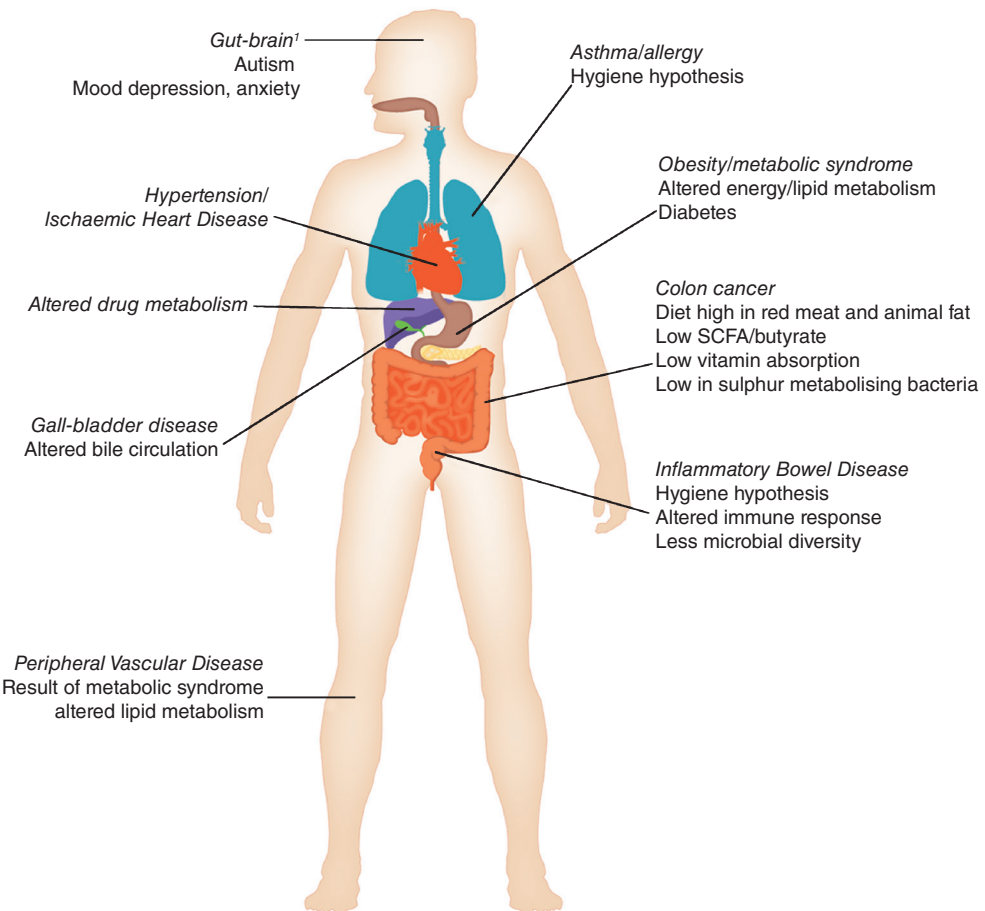


Figure 4.13 Gut microbiota and disease

Adapted from: Kinross et al. (2011: 14) by permission of Springer Nature. Gut microbiome-host interactions in health and disease, *Genome Medicine*, Kinross et al. © 2011.

[1]This refers to the gut-brain axis in which there is communication between the gastrointestinal tract and the brain, including the intestinal microbes, through neural, endocrine and immune pathways. This is important in promoting healthy brain function and behaviour.

While we all know about GIT disorders caused by a specific microbe, it has also been suggested that there is another circumstance which can cause disease. The microbiota as a community may be pathogenic in combination with other risk factors such as host genotype, behaviour and diet. For example, the microbiota can influence metabolic pathways and eating behaviours through the gut-brain axis, resulting in obesity (Asadi et al., 2022).

Changes in diet can alter the microbiome remarkably fast with clear differences occurring within 24 hours when human subjects changed their diets from high-fat/low-fibre to low-fat/high-fibre. However, one of the difficulties in this area is relating changes in species type and abundance with change in function: the genetic plasticity of bacteria means that this is not necessarily the case.

Antibiotic use is one of the factors that has most effect on the gut microbiota in particular, tending to result in reduced diversity in the bacteria present and slow return to normal. This can allow colonisation by 'foreign' bacteria with permanent changes in the structure of the microbiota and, potentially, increased occurrence of disease. Use of broad-spectrum antibiotics has been associated with development of *Clostridium difficile* associated disease. It is important to note that antibiotics are ineffective against viral infections.

GO DEEPER

Antibiotics and resistance

Repeated use of antibiotics in human medicine is considered to be the main cause of the development of microbial antibiotic resistance. Antibiotics will kill many of the normal microbiota (as well as the pathogens) leaving behind those that are resistant to the antibiotic. These multiply and there is also some transfer of the antibiotic resistant genes across species.

However, in 1969 the Swann Report hypothesised that the use of antibiotics as growth factors in animal husbandry would result in the development of antibiotic resistant bacteria that could enter the human food chain. Some action was taken on this, including antibiotic use in animals being restricted to those drugs not used in humans, resulting in some reduction in antibiotic resistance. However, the similarity in structure between some antibiotics used in animals and humans was not foreseen and this use of antibiotics is still a matter of concern in the worrying growth of antibiotic resistance (Marshall and Levy, 2011).

One major example of antibiotic resistance is Methicillin-resistant *Staphylococcus aureus* (MRSA), sometimes known as a 'superbug'. This particular bacterium is resistant to a number of different antibiotics and thus causes a number of particularly difficult to treat infections. The general public are less likely to develop nosocomial infections (cross infection) than those in places where people have invasive devices, open wounds and weakened immune systems including hospitals, prisons and nursing homes. Careful hygiene practice is essential to minimise infection spreading.

Management of altered gut microbiota

A number of approaches involving the microbiome are being used to enhance health, including the use of probiotics, prebiotics and faecal transplants.

Advertisements for food or food supplements often mention probiotics or prebiotics in promoting health. These are defined as:

- **Probiotics**: Live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host (e.g. yogurt containing live bacteria).

APPLY

Probiotic supplementation

The use of probiotics with premature babies is now recommended by the Cochrane Collaboration. It appears to reduce the incidence of Necrotising Enterocolitis (NEC) (affecting the bowel), which can occur in premature babies during the early weeks of life. A review by AlFaleh and Anabrees (2014) found that probiotics (supplements containing potentially beneficial bacteria or yeasts) reduced NEC and death in premature babies less than 1,500 grams in weight. However, the data on babies less than 1,000 grams in weight is not conclusive. A systematic review and meta-analysis in 2022 concluded that probiotics could reduce the incidence of severe NEC, reduce mortality in underweight premature children and reduce the incidence of feeding intolerance (Liu et al., 2022).

- **Prebiotics**: A food ingredient not digested in the small intestine (e.g. some fruits and vegetables, beans, unrefined grains) or that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria that can improve the host health (Erhardt et al., 2022).
- Faecal transplants involve the introduction of a colony of microbes from a healthy donor to a recipient's colon. This treatment has now been tested in a number of studies and appears to be beneficial in a number of disorders including: multiple sclerosis, chronic fatigue syndrome, idiopathic thrombocytic purpura, ulcerative colitis, irritable bowel syndrome and diabetes mellitus (Vrieze et al., 2013; Lu et al., 2022). Recurrent diarrhoea caused by *Clostridium difficile* has been successfully treated by faecal microbiota transplantation (Orenstein et al., 2013; Baunwall et al., 2022).

ACTIVITY 4.2: UNDERSTAND

Watch the following video online to help develop your understanding of resistant starch and health.

This online video can be accessed via https://study.sagepub.com/essentialap3e.

APPLY

Understanding diet for health

Hannah and Richard Jones of the Bodie family both enjoy wholemeal bread and plenty of fruit and vegetables in their diet. As one of his roles as a schoolteacher, Richard has been given responsibility for the introduction of free school meals for all school children in their first few years of primary school. He is aware that this is not just about ensuring that the children receive a good diet but also about their beginning to learn about the food they should be eating. He is ensuring that the menus supplied will provide good balanced diets with adequate prebiotic food every day and some probiotic foods during the week.

Skin

The skin is the body's largest organ (approximately 1.8–2 m^2) and, as the interface with the external environment, we need to consider how it interacts with the external environment. The skin has its own ecosystem with a wide range of resident microbes including bacteria, viruses, fungi and, sometimes, mites. The rough texture of the epidermis means that many microbes can be resident in the different grooves of papillae, in hair follicles and in ducts of sweat glands (Figure 4.14). Most of these are commensals and protect against invasion by non-resident flora through action on sweat, partly by producing fatty acids which inhibit growth of fungi.

Mites reside in the areas where hair covers the skin and are considered part of the normal flora, although they can sometimes cause skin disorders. The average adult has approximately 1,000 species of bacteria colonised on their skin, amounting to about 1 trillion bacteria, but the good news is that, largely, we are immune to our own skin microflora (Zulkowski, 2013). At the slightly acidic pH of skin (approximately 5.5) the normal flora of the skin is maintained, whereas an alkaline environment associated with urinary or faecal incontinence can result in skin irritation, dermatitis and excoriation (Andrews, 2012; Babino and Argenziano, 2022).

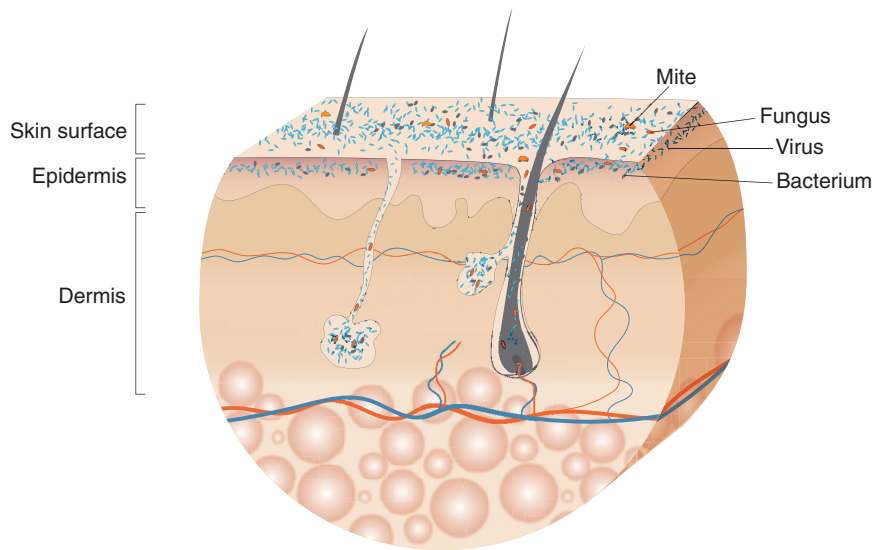


Figure 4.14 Microbiota of skin

Adapted by permission from Springer Nature: Grice, E.A. and Serge, J.A. 'The skin microbiome', *Nature Reviews Microbiology*, 9(4): 244-253, © 2011.

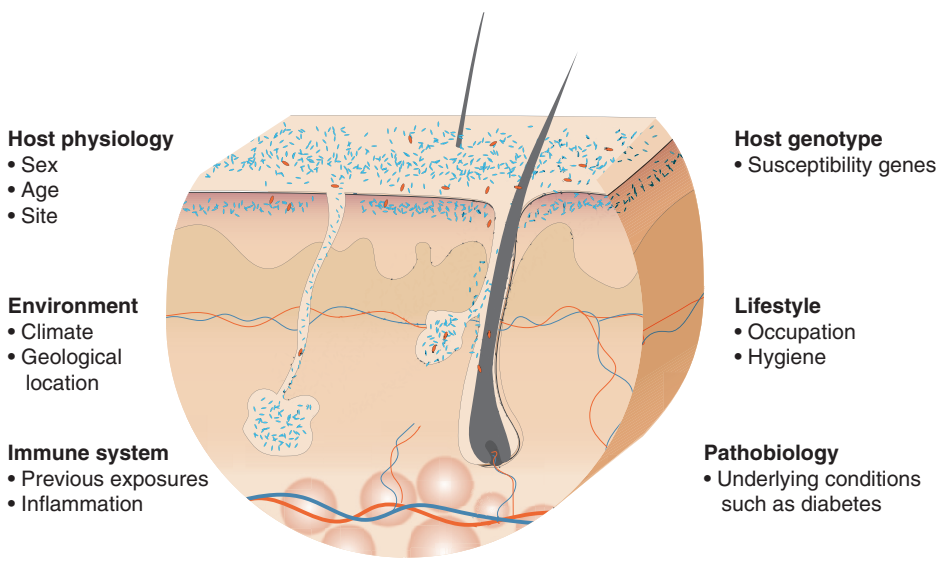


Figure 4.15 Environmental factors influencing skin microbiota

Adapted by permission from Springer Nature: Grice, E.A. and Serge, J.A. 'The skin microbiome', *Nature Reviews Microbiology*, 9(4): 244-253, © 2011.

The microbial community varies with the environmental differences of the various sites of the body due to the range of factors identified (Figure 4.15). A major factor in bacterial variation seems to be moisture and warmth, with such areas as the axillae and groins being more likely to have higher levels of microflora. Other sites have considerably lower microbial counts with most found in the sweat glands. An outline of the most common bacteria of the skin microbiota is given in Table 4.2. Further research is required to identify the fungi and viruses in the skin microbiota.

Table 4.2 Microbes in different areas of skin

Skin environment	Skin sites	Common microbes present	Notes
Moist	Umbilicus, axilla, groin areas, soles of feet, gluteal crease (between buttocks), popliteal fossa (behind knee), antecubital fossa (inner elbow)	Most abundant organisms are: • *Staphylococcus* species • *Corynebacterium* species	The actions of these microbes in sweat results in unpleasant odour
Dry	Forearm, buttocks, parts of hand	Mixed microbiota from bacterial phyla • *Actinobacteria* • *Proteobacteria* • *Firmicutes* • *Bacteroidetes*	Greater diversity than gut or oral cavity of same individual
Sebaceous (sebum [lipid-rich substance] secreting glands)	Forehead, behind ear, the back, side of nostrils	Dominant microbes are lipophilic (lipid-liking) • *Propionibacterium* species	Diversity lowest

Adapted by permission from Macmillan Publishers Ltd: Grice, E.A. and Serge, J.A. 'The skin microbiome', *Nature Reviews Microbiology*, 9(4): 244–253, ©2011.

APPLY

Preventing self-contamination

Considering that we have bacteria residing on our skin, there is a necessity to consider how to remove such bacteria in certain situations. For example, those going for surgery are at risk of self-contamination from their skin flora getting into open wounds. Few studies have been conclusive in identifying how to effectively decolonise the skin. Darouiche et al. (2010) influenced the Department of Health (2011) when they identified that 2% chlorhexidine in 70% isopropyl alcohol is more effective than povidone–iodine in reducing the risk of post-operative wound infection.

In addition to the normal skin flora which generally do not give rise to infection or cause cross contamination, transient microbes are those we pick up in everyday activities which can be pathogenic. Once a person becomes immunocompromised, commensals also have the potential to become pathogenic.

ACTIVITY 4.3: APPLY

Skin care and infection control

We know from different studies that people with chronic conditions such as diabetes, chronic renal failure and dermatitis have an increased likelihood of *Staphylococcus aureus* skin colonisation (Young, 2011; del Rosal et al., 2020). People in hospital are also likely to have Gram-negative bacteria on their skin with an increased likelihood of transient and pathogenic bacteria available for cross contamination. When we shed dead skin cells, they also house bacteria. Some people in hospitals may be immunocompromised, and the above issues create a particular risk.

Task

Many things we do in practice can minimise or exacerbate these risks. As a person-centred nurse, you need to manage these aspects of practice without diminishing someone's sense of self-worth. To be knowledgeable and informed, take some time now to check out the impact of the following on managing skin flora and preventing cross contamination. What is the evidence telling you in relation to how effective the following are in reducing cross contamination?

- The use of paper towels to dry hands after washing them.
- Use of air hand dryers.
- The effectiveness of soap when used to cleanse skin.
- The effectiveness of skin wipes when used to cleanse skin.
- The effectiveness of hand washing by healthcare staff.
- The effectiveness of changing bed linen in care settings (hospitals, nursing homes, people's homes).

You may need to use academic literature databases such as Ovid™ or Medline™ to source the evidence, or you can also try using Google Scholar™.

Mouth

The oral microbiota is the second most complex (after the GIT) containing mainly bacteria, archaea, viruses and fungi (see Table 4.3). We have already discussed the development of the microbiome in general, but the mouth has some distinct characteristics. Toothless infants already have a diverse microbiota but once teeth erupt there are considerably more ecological niches open to colonisation by a greater range of microbes (Zaura et al., 2014; Duque et al., 2023).

APPLY

Oral hygiene

Some of the microbes (of a single or mixed species) in the mouth form biofilms in which bacteria stick to a surface (teeth, dentures, etc.) and secrete a slimy, glue-like substance which sticks to the surface. This protects the bacteria from harm and forms the plaque which dental hygienists clean off to prevent gum disease, gingivitis (early stage) or more severe periodontitis in which the supporting tissues of the teeth may become affected.

Good mouthcare including regular brushing of the teeth, flossing between the teeth and use of mouthwashes all help to remove the biofilms and reduce development of gum disease. If it does develop, chemical agents in the toothpaste, etc., will kill the bacteria in the biofilm.

Table 4.3 Oral microbiota

Microbe	Number and type(s)	Comments
Bacteria	Around 1000 species: about half still to be cultured Diverse collection of obligate aerobes, facultative and obligate anaerobes Six phyla contribute 96% of species: firmicutes, bacteroidetes, proteobacteria, actinobacteria, spirochaetes, fusobacteria Three distinct bacterial communities distributed as follows: 1. Buccal mucosa, gingivae, hard palate 2. Saliva, tongue, tonsils, throat 3. Supra- and sub-gingival plaque	No significant differences across geographical sites A lot of fermentable carbohydrates results in bacteria that create acid and cause caries (dental) Oral microbiota inhibits pathogenic colonisation – few binding sites for pathogens Conversion of nitrate to nitrite (converted to nitric oxide) Help keep blood vessels flexible resulting in anti-hypertensive effect
Viruses	Mainly bacteriophages (i.e. attack bacteria) – fits with range of bacteria	Primarily associated with disease
Fungi	*Candida* species carried by about half the population without symptoms 85 fungal genera reported	
Protozoa/protists	Mainly *Entamoeba gingivalis* and *Trichomonas tenax*. Harmless saprophytes Numbers raised in those with poor oral hygiene	Nutritional link with oral disease – food debris is food source for protozoa
Archaea	Minor part of microbiome. All species are methanogens (form methane)	Numbers raised in those with periodontitis

Adapted from: Wade (2013) and Grice and Segre (2012).

APPLY

Oral microbes and illness

We can understand that the oral microbiota could be linked to disorders of the mouth, but it also has health effects unrelated to the GIT, possibly through its influence on the immune system or on inflammation. Diabetes and atherosclerosis are examples. Bacterial types and numbers in the mouth correlate with those found in atherosclerotic plaque (fat and other substances that are laid down in the lining of the artery wall) (Koren et al., 2011; Tan et al., 2023). They can also result in infectious endocarditis (inflammation of the lining of the heart), and brain and liver abscesses.

While airborne bacteria are the commonest cause of lung infections in those with cystic fibrosis, oral microbes have also been found in the lungs of these people (Wade, 2013; Santos-Fernandez et al., 2023).

Respiratory tract

A large number of different species of microbes inhabit the Upper Respiratory Tract (URT), some of which are shared with the mouth. *Staphylococcus epidermidis* and corynebacteria are common in the nose, and

Staphylococcus aureus (pathogenic) is not uncommonly carried here. The throat (pharynx) microbiota usually includes a range of different streptococci and other microbes.

APPLY

MRSA

MRSA (Methicillin Resistant *Staphylococcus aureus)* is often carried in the nose without causing an infection. It used to be acquired in hospital settings but is now also found in some healthy individuals in the community. However, it is a major cause of cross-infection in health facilities.

It used to be considered that the Lower Respiratory Tract (LRT) was sterile. However, it has now been demonstrated that, in health, organisms similar to those in the URT, but in much smaller numbers, are present (Charlson et al., 2011; Hernández-Terán et al., 2023). The ciliated epithelial cells of the LRT play an important part in minimising the numbers of microbes in the lungs by wafting mucus containing transient microorganisms up to the URT from which they are eliminated.

APPLY

Microbiota of the respiratory tract and illness

When the efficiency of pulmonary defence mechanisms is diminished, for whatever reason, inhaled or resident microorganisms can proliferate and cause disease – acute or chronic infections. Predisposing causes can include inherent defects as in cystic fibrosis. Impairment of normal airway function can occur from inhaled particles or smoke (e.g. from cigarette smoking) and, over the long term, can lead to Chronic Obstructive Airway Disease (COAD) also known as Chronic Obstructive Pulmonary Disease (COPD).

Vagina

The microbiota of the vagina changes through the different stages of the reproductive life of a woman because of variations in hormone levels, sexual activity and hygiene, and it plays an important role in minimising disease. A considerable number of different bacteria are found colonising the vagina in different combinations, although lactobacilli are the most important.

Childhood

During a vaginal birth a girl baby acquires lactobacilli in her vagina as bacteria are transferred from the mother's vagina. She also has some oestrogens left from her mother enabling the lactobacilli to thrive, but these diminish as the oestrogen levels fall. During childhood the pH of the vagina is slightly alkaline or neutral. A mixed colony of microbes has been described with some bacteria at fairly high levels and others lower. Lactobacilli were found more often among older girls (in 88% of those aged 11), while this was lower in younger children (in 45% of those under two years) (Hammerschlag et al., 1978; cited by Farage et al., 2010).

At puberty the rising levels of oestrogen promote division of the epithelial cells and an increase in intracellular glycogen at the mid-point of the menstrual cycle. The lactobacilli metabolise the glycogen, produce lactic acid and lower the pH of the vagina as it changes towards the microbiota of adult women.

Reproductive years

In the reproductive years, eight different *Lactobacillus* species are the commonest strains found but 92% of women studied only carried one of these. A range of other bacteria can be part of the normal flora for each woman. These bacteria maintain the pH of the vagina at 4.0–4.5 (acidic) by forming lactic acid, which maintains the health of the vaginal epithelium (Farage et al., 2010). *Lactobacillus* species stick to the epithelial cells of the vagina and thus prevent pathogens colonising this site. The levels of oestrogens vary during the menstrual cycle causing variation in the lactobacilli. During healthy pregnancy the microbiota is more stable than at other times and it is suggested that this protects against vaginal infections during pregnancy (Romero et al., 2014; De Siena et al., 2021).

Post-menopausal years

During the menopause, as oestrogen levels drop, the glycogen content of the vaginal cells also falls leading to diminishing lactobacilli numbers. The resulting fall in lactic acid results in a rise in vaginal pH which facilitates the growth of pathogenic bacteria. Women taking Hormone Replacement Therapy (HRT) have lower pH levels than those without. In addition, of those not taking HRT only 20% had lactobacilli in their vaginas while 83% of those on HRT did carry these microbes (Farage et al., 2010).

CONCLUSION

This chapter has introduced the importance of the microbiome in human health. This is a topic that has received little attention in most anatomy and physiology books for nurses but is now of growing importance in research and in understanding how the body maintains health. Approaches to maintaining the health of the microbiome, with particular emphasis on the potential damage that can be caused by the incorrect use of antibiotics, have been reviewed. We hope this understanding will be useful in achieving person-centred practice.

This chapter has mentioned some disorders where alteration in the microbiome is implicated. However, it has not attempted to cover all the material relevant to pathogens and disease. These will be examined later in your course.

GO DEEPER

Further reading

Burton-Shepherd, A. (2015) 'Prebiotics and probiotics as novel therapeutic agents for obesity', *Nurse Prescribing*, 13(3): 136–9.

Capone, K., Nikolovski, J., Stamatas, G., Green, M., Cox, S. et al. (2012) 'Exploration of bacteria comprising the human skin microbiome throughout the first year of life', *Journal of Obstetric, Gynecologic and Neonatal Nursing*, 41: S147–8.

Ferranti, E., Dunbar, S., Dunlop, A. and Corwin, E. (2014) 'Things you didn't know about: the human gut microbiome', *Journal of Cardiovascular Nursing*, 29(6): 479–81.

KEY POINTS

1. There are a wide range of different types of microbes that occur in the human microbiota, a number of which are similar in structure to some pathogens, and which protect the body from colonisation by pathogens. Understanding this will help you to protect people from infections.
2. The development and the intrapersonal and interpersonal variability of the human microbiome occur due to diet, hygiene practices and environmental factors, and this understanding will help you to realise person-centred practice.
3. The value of diet in enhancing the microbiota has been introduced.
4. Understanding the appropriate use of antibiotics provides the background for patient education in relation to completing courses of treatment and will be valuable in providing care.

REVISE

TEST YOUR KNOWLEDGE

This chapter covers a lot of material and it is best to break your revision into components. Consider revising in the following areas:

1. The different relationships that can occur between microbes and the human body.
2. The structure of the different types of microbes.
3. The microbiome of the different systems of the body.
4. The development of the human microbiome throughout life.
5. The microbiome in health and disease in the different systems.
6. Approaches to promoting health of the GIT.

In order to help you revise, consider the following questions.

Test yourself by revising the chapter first, and then answer these questions without looking at the book. Afterwards compare your answers with the text and with the notes you made. Did you miss anything in your notes? Have you looked at the figures? Here are the questions:

1. Describe the relationship between man and microbe in the following:
   - Transients.
   - Commensals.
   - Opportunists.
   - Pathogens.
2. What are the major groups of organisms and the major differences between them?
3. What are the main environments inhabited by the human microbiome?
4. What are the types of microbes found in the different areas inhabited by the human microbiome?

5 List and write brief notes on the major functions of the microbiome in the gastrointestinal tract (GIT).

6 Write brief notes on the implications of antibiotic use for human health.

7 What approaches can be used in the management of altered GIT microbiota?

8 Outline how the vaginal microbiota varies throughout life.

REVISE

For additional revision resources visit: **https://study.sagepub.com/essentialap3e**.

ACE YOUR ASSESSMENT

- Revise key terms and practise pronunciation with interactive flashcards.
- Test yourself with quizzes and multiple-choice questions.
- Access the glossary with audio to hear how complex terms are pronounced.

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