

# Chapter 3 Infection

## Chapter aims

After reading this chapter you will be able to:

- describe the main types of microorganism important for human health;
- explain the difference between pathogenic and commensal microorganisms;
- explain the chain of infection and how it may be broken;
- relate the signs and symptoms of infection to the underlying pathophysiology of infection;
- explain how the main anti-microbial drugs work and their main side-effects;
- demonstrate awareness of antibiotic resistance and the steps that can be taken to reduce the risk of antibiotic resistance developing.

## Introduction

Imagine a world in which it is too dangerous to go into hospital for surgery and just cutting your finger could result in death. It seems ridiculous yet according to the World Health Organization (WHO) the threat from bacterial infection due to increasing resistance to antibiotics is making this a real possibility (WHO, 2015).

In this chapter we examine four of the main types of microorganisms important to human health and give examples of the infectious diseases they cause. The microorganisms we have included are: viruses, fungi, protozoa and bacteria. We will examine how microorganisms are passed on in 'the chain of infection' and how this chain may be broken. We then look at the general signs and symptoms of infection and how these are caused. We will consider the drugs used to treat the different types of infections and the side-effects of these. Finally, we will examine how antibiotic resistance occurs and what steps you can take to reduce antibiotic resistance developing.

# Infection

Statistics from the World Health Organization for 2000–2016 place infectious diseases among the top ten causes of death worldwide (WHO, 2018). These infections include lower respiratory tract infections, diarrhoeal diseases and tuberculosis. In low income countries lower respiratory tract infections and diarrhoeal diseases are the top two causes of death. In high income countries, such as the United Kingdom, people predominantly die of chronic diseases, such as cardiovascular disease, cancer and dementia. However, lower respiratory tract infections remain a leading cause of death.

Infectious diseases are caused by microorganisms including bacteria, viruses and fungi. Disease-causing microorganisms are said to be **pathogenic**. A microorganism that causes disease is called a **pathogen**. Infection arises when a microorganism enters the body, resists the innate defences, and invades the tissues. The most common sites of infection are the respiratory and gastrointestinal tracts. The skin can be a site of entry – usually when it is disrupted, for example by a wound. Another important site of entry is the genitourinary tract. Pathogens can spread from person to person, directly or indirectly, or from animals to humans in what is called a **zoonotic** disease. *Salmonella* food poisoning is a classic example of a zoonotic disease, originating from contaminated food, often poultry.

Not all infections with pathogenic microorganisms cause symptoms. An infection is said to be **subclinical** if it produces no symptoms. Infection will result in disease and clinical symptoms if the infection causes tissue injury. Some microorganisms such as viruses cause direct damage to cells because they multiply inside our cells. Many viruses then spread by rupturing or ‘bursting’ the cell and spreading through the tissues or bloodstream (see below under ‘Viruses’). Some bacteria produce toxins which kill or damage cells and tissues. An example is *Vibrio cholera*. This microorganism produces a toxin that damages the gastrointestinal tract leading to severe diarrhoea. However, our immune response and inflammatory responses to invading pathogens can cause additional tissue damage.

## The microbiome

In a healthy person, the internal tissues are normally free of microorganisms. The skin and parts of the body connected to the external environment (for example, the mouth, nose, intestinal and genitourinary tracts) become colonised by microbial species soon after birth. These organisms make up what is called the microbiome. The microorganisms making up the microbiome are commensal, which means they live harmlessly in or on the body. The microbiome prevents more pathogenic microorganisms colonising and infecting us. The microbiome includes some fungi, viruses and protozoa but is mainly made up from bacteria (Goering et al., 2013). The microbiome can contain pathogenic species. For example, *E. coli* bacteria usually live harmlessly in

the gastrointestinal tract but can cause urinary tract infections (UTIs) if they enter the urinary system. Wounds may become infected by microorganisms from the skin microbiome. **Immunocompromised** people (those with a weakened immune response) are particularly susceptible to infections and these infections often originate from the microbiome.

### Activity 3.1 Reflection

Identify five infectious diseases. For each disease write down whether it is caused by a virus, bacteria, fungi or protozoa. Name the microorganism that causes the disease.

*Examples are given at the end of the chapter. As you proceed through the chapter, compare your choices with the infectious diseases discussed.*

Activity 3.1 will have enabled you to connect five infectious diseases with the type and name of the pathogen responsible. We now examine four main types of microorganisms that can cause disease in humans.

## Bacteria

Bacteria are **prokaryotic** organisms. Prokaryote means ‘lacking a nucleus’ (Figure 3.1). Bacteria are all single-celled organisms, and although they do not have a nucleus, they do have genetic material in the form of DNA (deoxyribonucleic acid). Bacteria have their own cellular ‘machinery’ to grow and reproduce. This cellular machinery includes enzymes, and **ribosomes** needed to manufacture proteins. By contrast, **eukaryotic** cells, which includes all human cells, have a more complex structure. Human cells have a cell **nucleus** and other **organelles**, such as lysosomes (Chapter 2). The cellular machinery of human cells is different from that of bacteria. The difference in cellular machinery of human and bacterial cells enables the effective use of antibacterials. When we take antibacterial drugs, orally for example, the drugs circulate throughout the body. However, antibacterial drugs target the bacteria’s unique cellular components and machinery without affecting the cellular components of our own cells. This helps reduce the number of side-effects. Antibacterial drugs are explained further later in the chapter.

Bacteria are free-living organisms. ‘Free-living’ means that bacteria can live independently of the human body (or any other host organism). Most bacteria do not cause human disease but approximately 50 pathogenic species of bacteria exist. As mentioned under ‘The microbiome’, pathogenic species of bacteria may live harmlessly as part of the microbiome of the skin, mouth or intestines. Disease may occur if they invade our body tissues to cause damage. Some clinically common bacteria are identified in Table 3.1.

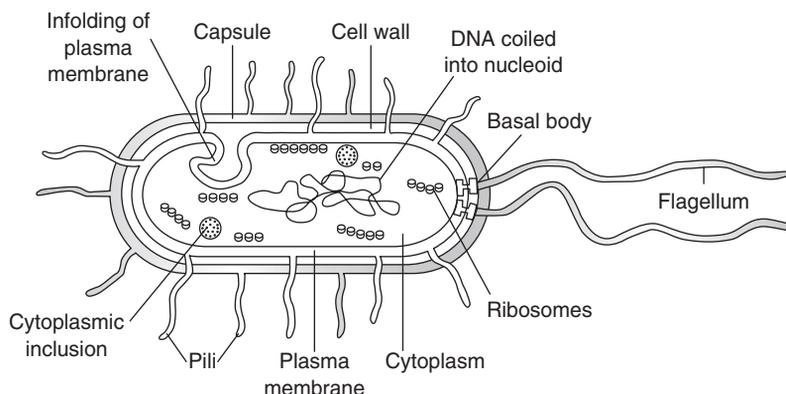


Figure 3.1 A bacterium

Name of bacterium	Disease expression
<i>Staphylococcus aureus</i>	Skin infections, pneumonia, sepsis, endocarditis
<i>Clostridium difficile</i>	Diarrhoea, pseudomembranous colitis
<i>Klebsiella pneumoniae</i>	Pneumonia
<i>Escherichia coli</i>	Diarrhoea, urinary tract infections, respiratory disease, sepsis
<i>Pseudomonas aeruginosa</i>	Sepsis, wound and burn infections
<i>Bacteroides fragilis</i>	Gastrointestinal upset
<i>Mycobacterium tuberculosis</i>	Tuberculosis

Table 3.1 Selected human bacterial diseases

Table 3.1 shows that the same bacterial species may be responsible for more than one type of ‘disease expression’. The disease expression refers to the nature of the disease caused (for example, skin infection or respiratory disease), and depends on the part of the body that is infected.

## Viruses

Viruses are one of the simplest types of microorganism. Viruses are smaller and simpler than cells. Viruses are not free-living and need to infect our cells to multiply. Viruses are described as ‘intracellular parasites’.

Figure 3.2 shows the structure of the human immunodeficiency virus. The simplest viruses are particles made of a protein ‘coat’ or capsid, containing the genetic material. The genetic material can be RNA (ribonucleic acid), or DNA (deoxyribonucleic acid), depending on the type of virus. Some virus particles are more complex and have an envelope surrounding the capsid. For example, HIV and influenza virus are more complex viruses with envelopes. The envelope comes from the host cell membrane as the virus particles are released. The envelope contains viral envelope proteins which are needed for cell infection, and are also important targets of the host immune response (Chapter 4). Virus particles are called virions.

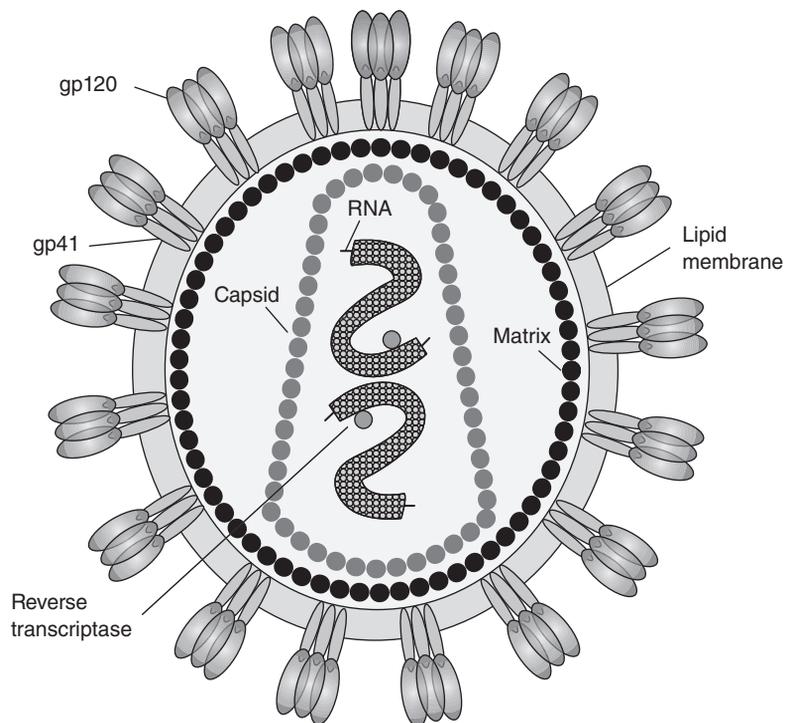


Figure 3.2 The structure of HIV-1

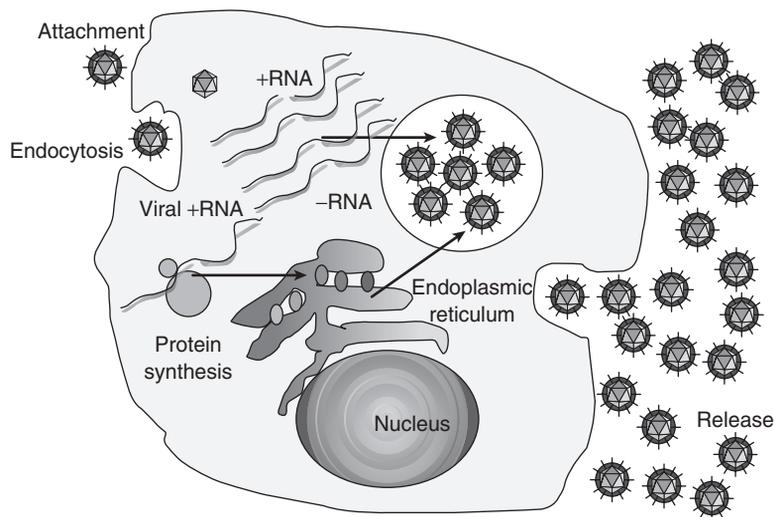


Figure 3.3 Virus replication within a host cell

Viruses lack the cellular ‘machinery’ (such as ribosomes) needed to convert their genetic material into new virus particles. Viruses are therefore reliant on a host cell which they infect in order to make more copies of themselves (‘replicate’). This makes antiviral therapy difficult to develop as any antiviral agent that stops viral replication will also affect the host cell function. Antiviral therapy is considered later in the chapter. The virus life cycle is shown in Figure 3.3.

Viruses show ‘host cell specificity’. This means that they can only usually infect one cell type. Virus infection involves attachment of the virus particle to a cell membrane receptor on the host cell. This interaction needs a specific protein on the surface of the virus particle and a target receptor on the host cell. Only those host cells with the ‘matching’ receptor for the virus surface protein can be infected. For example, HIV uses the virus membrane protein gp120 (Figure 3.2) to infect white blood cells which have a target receptor called CD4. This restricts HIV to infecting only cells with the CD4 receptor on the surface. These cells include T helper lymphocytes and macrophages (Chapter 4). Influenza virus uses the sialic acid receptor which is found on lung epithelial cells and the upper respiratory tract.

Some examples of clinically important viruses are given in Table 3.2.

<b>Viral pathogen</b>	<b>Disease expression</b>
Herpes simplex type 1	‘Cold sores’
Herpes simplex virus type 2	Genital herpes
Human papilloma virus 6, 11, 16, 18	Warty growths, cervical carcinoma
Hepatitis B virus	Hepatitis
Rhinovirus	Upper respiratory tract infections
Varicella-zoster virus	Chickenpox, shingles
Norovirus	Acute gastroenteritis
Human immunodeficiency virus	Acquired immunodeficiency disease (AIDS)

Table 3.2 Selected human viral diseases

## Fungi

Most fungi are multicellular organisms. Not all fungi are considered to be microorganisms. Many fungi grow as thread-like filaments. Other well-known types include single-celled yeast and mushrooms. Fungi are free-living organisms and are important ecologically for breaking down dead plant material. Pathogenic fungi invade tissues and cause damage by releasing digestive enzymes.

Examples of clinically important fungi that cause disease are given in Table 3.3.

Diseases associated with fungal infections are mostly seen in those with compromised immune systems. For example, patients on oral steroids (Chapter 2) or people with

a pre-existing disease may have weakened immunity. Many fungi cause opportunistic infections. These are infections that occur more frequently in those with weakened immune systems. People with healthy immune systems do not usually develop disease when exposed to these pathogens. Oral thrush (candidiasis) is a common side-effect of chemotherapy. Opportunistic infections are the common cause of death for those people with AIDS (Chapter 4).

Fungal pathogen	Disease expression
<i>Candida albicans</i>	Thrush
<i>Aspergillus fumigatus</i>	Lung infection in immunocompromised patients
<i>Trichophyton interdigitale</i>	Athlete's foot
<i>Pneumocystis jirovecii</i>	Pneumonia in immunocompromised patients

Table 3.3 Selected human fungal diseases

## Protozoa

Protozoa are single-celled animals. Many are free-living but some are important parasites of humans. Some free-living species infect humans as opportunistic infections if the person's immune system is weakened.

Examples of clinically important protozoa are shown in Table 3.4.

Protozoan pathogen	Disease expression
<i>Cryptosporidia parvum</i>	Cryptosporidiosis
<i>Giardia lamblia</i>	Giardiasis
<i>Toxoplasma gondii</i>	Toxoplasmosis
<i>Entamoeba histolytica</i>	Amoebic dysentery
<i>Plasmodium vivax</i>	Malaria

Table 3.4 Selected human protozoan diseases

## The chain of infection

The chain of infection (Figure 3.4) illustrates the stages needed for microorganisms to be passed on from one individual to another and cause disease. Prevention of infection is one of the most important roles of nurses and other healthcare professionals. By being aware of each potential link in the chain, infection may be reduced or eliminated within the clinical setting.

Terms used in the chain of infection are given in Table 3.5.

For example: methicillin-resistant *Staphylococcus aureus* (MRSA) is an example of an organism. A reservoir might be a person who is either colonised or infected with MRSA. The portal of exit might be contaminated body fluids such as wound exudate from an infected wound. Mode of transmission might be hands or contaminated equipment. The portal of entry in this case would be by a wound that another person has. That person is the susceptible host. From this scenario we can see that handwashing could break this chain at more than one point.

For further information on the chain of infection, please see the further reading section at the end of this chapter.

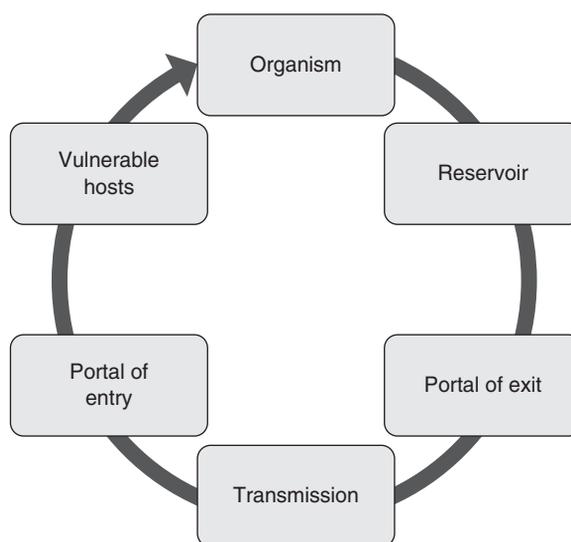


Figure 3.4 Chain of infection

Term	Description	Examples
Organism	The pathogenic microorganism	<i>E. coli</i> , <i>C. difficile</i> , MRSA (meticillin-resistant <i>Staphylococcus aureus</i> )
Reservoir	Source of the infection	A patient/health professional, animal, equipment, food, water
Portal of exit	How the microorganism leaves the body of the host	Faeces, urine, aerosols, droplets from respiratory tract (coughing/sneezing), vomit, blood, wound drainage
Transmission	How the microorganism is passed on	Direct contact, airborne
Portal of entry	How the microorganism enters the body	Break to the skin (wound), injection, needlestick injury, scalpel, animal bite, catheter, mucous membranes
Vulnerable hosts	The person who becomes infected	Any susceptible person, elderly, pre-existing disease, immunocompromised

Table 3.5 Terms used in the chain of infection

In the next section we will look more closely at bacterial infection.

## Bacterial infection

### Scenario

You are the staff nurse on duty when George is admitted to the ward. He is a 72-year-old man who lives alone at home. He is confused and disorientated on admission and has a respiratory rate of 35 breaths per minute. He has a temperature of 38°C and has been expectorating ('coughing up') yellow sputum. He is diagnosed with probable community acquired pneumonia. Sputum samples are taken and empirical antibiotic treatment with amoxicillin is started.

In this scenario, George's symptoms and history have led to a diagnosis of community acquired pneumonia. A 'best-guess' approach is used to consider which microorganism may have caused the infection. Then an antibiotic is selected which is most likely to be effective. This is known as empirical antibiotic therapy. In clinical practice, it is not possible to wait for the results from the sputum sample to confirm the bacteria as this can take some time. However, a sputum sample has been sent for microbiology to confirm the causative bacteria. We will consider how microbiologists use the sputum sample to identify the bacteria.

Microbiologists have a range of tests they can use to identify which bacteria are causing the disease. They might prepare a sample of the sputum and look at this under the microscope to identify the bacteria. Many bacteria can, however, appear very similar. Special stains can help with the identification. A common stain which is used is the Gram stain. Bacteria are described as either Gram-positive or Gram-negative. Gram-positive bacteria take up the stain and appear purple under the microscope. Gram-negative organisms are not stained. In general, Gram-positive bacteria have a simpler cell wall structure than Gram-negative bacteria. This may mean that antibiotics are more able to penetrate and destroy Gram-positive bacteria. The shape and colour of the bacteria can also give vital clues. *Staphylococcus aureus*, for example, is round (coccus = round) and golden in colour (aureus = golden). The microbiologist may also identify the conditions the bacteria need in order to grow. Some grow well with no oxygen (called anaerobic bacteria) while others require oxygen (aerobic bacteria). Some are described as facultative anaerobes. This means that they prefer oxygen but can grow without it. Identifying the bacteria which are causing the disease is very important as different bacteria will be sensitive to different antibacterial drugs. Microbiologists can also test this directly by testing whether the bacteria grow in the presence of certain antibiotics.

The bacteria which could be causing George's community acquired pneumonia are shown in Table 3.6.

In George's case, the microbiology report identified *Streptococcus pneumoniae* and that the bacterium is sensitive to amoxicillin, confirming that the antibiotic choice was appropriate.

Bacterium	Gram staining	Oxygen needs	Shape
<i>Streptococcus pneumoniae</i>	G +ve	Anaerobic but tolerates oxygen	Cocci (round shape)
<i>Haemophilis influenza</i>	G -ve	Facultative anaerobe	Rod shaped
<i>Staphylococcus aureus</i>	G +ve	Facultative anaerobe	Cocci (round shape)
<i>Klebsiella pneumoniae</i>	G -ve	Facultative anaerobe	Rod shaped

Table 3.6 Properties of bacteria associated with community acquired pneumonia

G +ve: Gram-positive; G -ve: Gram-negative.

## General signs and symptoms of microbial infection

In the scenario, we can see that George was exhibiting some signs of a bacterial lung infection, for example rapid respiration, cough, yellow sputum and a high temperature (pyrexia).

Many of the signs and symptoms of infection are due to the body's immune response to the infection. Pyrexia is caused when our temperature control centre, the hypothalamus in the midbrain, is reset to a higher than normal temperature, which in humans is 37°C. This occurs when chemicals called prostaglandins and pro-inflammatory cytokines are released from immune cells as part of the inflammatory response (Chapter 2). Metabolism is increased and tissue oxygen requirements increase resulting in increased respiratory rate. The advantages of pyrexia are unclear as it consumes energy at a time when a person is often eating little. It is thought that higher temperatures might stop some microorganisms multiplying as quickly. Higher temperatures may also stimulate the immune system and tissue repair. In most cases the pyrexia does not need treatment and the temperature will return to normal. Some microorganisms, however, may cause a rise in temperature above 41.5°C. This is considered a medical emergency. The pro-inflammatory cytokines which cause fever, also cause general malaise, weakness and loss of appetite associated with infection.

The course of an illness can be divided into different stages (Table 3.7) which help to explain the pattern of symptoms shown by a patient.

Invading microorganisms can cause tissue injury through a variety of mechanisms. For example, HIV causes the destruction of CD4-positive T lymphocytes during its active replication phase (Chapter 4). CD4-positive lymphocytes are vital for our immune system to work properly. HIV-infection may eventually lead to immunodeficiency.

Stage	Description
Incubation period	Pathogen begins to replicate but symptoms not noticeable.
Prodromal phase	Initial appearance of symptoms but these may be vague and non-specific, for example malaise, fatigue.
Acute stage	Maximum impact of infection. Symptoms are obvious and usually specific for sites of infection.
Convalescent period	Infection is contained and is progressively eliminated.
Resolution	Pathogen is eliminated from the body. No further symptoms.

Table 3.7 Stages of illness

Some microorganisms damage our cells by producing toxins. An example of this is *Vibrio cholera*, the bacterium which results in cholera. *V. cholera* infects the gut and releases a toxin causing severe watery diarrhoea. The toxin is classified as an exotoxin. This means a toxin that is released from the bacterial cells. By contrast, an endotoxin is part of the cell wall of Gram-negative bacteria. It is only released if the bacterial cell disintegrates. At low levels endotoxins are useful and activate our innate immune system. However, at high levels, the immune response to the endotoxin can lead to sepsis (see below, under 'sepsis'). Many microorganisms cause damage indirectly by activating the body's immune system. The immune system responds by killing infected cells. For example, the immune response to hepatitis B virus results in destruction of liver cells through a type IV hypersensitivity response (Chapter 4). The long-term complication of hepatitis B infection can be cirrhosis of the liver or liver cancer.

## Pharmacological management of infections

### Antimicrobial drugs

An antimicrobial is a substance which kills or inhibits the growth of microorganisms. The British National Formulary (BNF) groups these according to which type of microorganism is killed and lists: antibacterials, antifungals, antivirals and antiprotozoal drugs. In general, antimicrobials work by exploiting differences between human cells and those of the microorganism. If the antimicrobial was not selective in this way it would kill human cells as well as killing the microorganism.

### Antibacterial drugs

Antibacterial drugs are used to combat infections caused by bacteria. They will not kill viruses. Antibacterial drugs are sometimes referred to as antibiotics. Antibacterial drugs can be classified in different ways. A common way to group them is by chemical structure. Penicillins, for example, all have a similar chemical structure called a beta lactam ring. Groups of antibiotics may share certain features including the way they

work, side-effects and any contraindications they may have. They may also kill similar bacteria, although this is not always the case. Activity 3.2 will give you an overview of some of the important groups of antibiotics and the names of drugs that belong to each group.

### Activity 3.2 Research

Using the table format below, list one or two drugs for each group of antibacterial drugs. Use the British National Formulary to help you. You should be able to access paper copies from the ward or library. An electronic version is also available for NHS staff.

Antibacterial group	Name of individual antibacterials
Example: Cephalosporin	Example: Cefaclor, Cefalexin
Penicillins	
Macrolides	
Quinolones	
Tetracyclines	

*Suggested answers are found at the end of the chapter.*

Now that you are more familiar with the different antibacterial groups, we will look more closely at how these drugs act to treat infections.

Some antibacterial drugs kill bacteria. These are known as **bactericidal** antibiotics. Examples include penicillins and aminoglycosides. Other antibacterial drugs do not kill the bacteria outright but prevent bacteria replicating. These are known as **bacteriostatic** antibiotics. Examples include tetracyclines. The bacteriostatic action helps the body's immune system kill the bacteria.

**Narrow spectrum** antibiotic drugs kill only very specific bacteria. By contrast, **broad spectrum** antibiotics kill a wide variety of bacteria. Examples of broad spectrum antibiotics include erythromycin, ciprofloxacin and doxycycline. A broad spectrum antibiotic is useful when the cause of infection is unknown. Unfortunately, they tend also to kill bacteria comprising the gut microbiome. The possible consequences of this are illustrated in the scenario below.

*Clostridium difficile* is a Gram-positive bacterium. It can persist in the environment for a long time as it produces tough spores which are resistant to alcohol based cleaning agents. It is found in the gastrointestinal tract of about 5% of the population where it usually causes minimal harm. However, in Edward's case in the scenario below, treatment with the broad spectrum antibiotic ciprofloxacin

### Scenario: *Clostridium difficile*

Edward is an elderly man currently an inpatient on a medical ward. He has recently been taking a course of ciprofloxacin for acute pyelonephritis (a type of kidney infection; in Edward's case due to *E. coli*).

A week later his infection seems to have improved. However, he is now experiencing profuse watery diarrhoea. A diagnosis of *Clostridium difficile* infection is made. You transfer Edward into a single-bedded side room. He is treated with the antibiotic metronidazole in accordance with guidance. You ensure that strict handwashing procedures are in place on the ward.

disrupted his normal gastrointestinal bacteria (microbiome). As a result, *C. difficile* was able to grow without competition from other bacteria. *C. difficile* can lead to **pseudomembranous colitis** as it produces toxins which inflame the bowel. Although still a problem in hospitals, infection control procedures and more careful use of antibiotics have reduced the incidence of *C. difficile* infections.

## Mechanism of action of antibacterial drugs

Antibacterial drugs work in different ways and we can divide them up according to their mechanism of action.

1. **Antibacterials that disrupt cell wall synthesis:** Examples of antibacterial drugs that disrupt cell wall synthesis are penicillins, cephalosporins, carbapenems and monobactams. The bacterial cell wall is made of a substance called peptidoglycan which forms a protective mesh. The antibacterial drugs interfere with the synthesis of peptidoglycans and, as a result, the cell wall is weakened. In the absence of a rigid cell wall, water enters the bacterial cell by osmosis, causing it to swell, burst and die.
2. **Antibiotics that affect bacterial protein synthesis:** Antibacterial drugs that affect bacterial protein synthesis are tetracyclines, chloramphenicol, macrolides and aminoglycosides. Bacterial proteins are manufactured within the bacterial cell using cellular 'machinery' called ribosomes (Figure 3.1). Antibacterial drugs that affect bacterial protein synthesis bind to the bacterial ribosomes and prevent bacteria from making proteins. This stops the bacteria growing or multiplying.
3. **Antibacterial drugs that inhibit bacterial DNA synthesis:** Antibacterial drugs that inhibit bacterial DNA synthesis include quinolones. DNA synthesis is vital for bacterial cell replication.
4. **Antibacterial drugs that affect folic acid synthesis:** Antibacterial drugs that affect folic acid synthesis include Trimethoprim. Bacteria need to manufacture their own folic acid to survive. Some antibacterial drugs interfere with this folic acid synthesis and kill bacteria.

## Side-effects and clinical implications of antibacterial drugs

Many antibacterial drugs cause gastrointestinal upset as a side-effect leading to symptoms of nausea, vomiting and diarrhoea. This is often because the antibacterial has damaged the natural gut bacteria (microbiome). This was seen in the scenario with Edward, above.

## Drug allergies

Many people report that they are allergic to antibiotics. It is important to understand the symptoms that lead to this belief. Some people may have experienced feeling sick which would not be a true allergic reaction. Symptoms such as rashes, difficulty breathing, and swelling, are more indicative of allergy. If a person is truly allergic to an antibacterial it may make their infection much more difficult to treat. Penicillins are especially prone to causing allergies. If patients are allergic to one type of penicillin, for example amoxicillin, they are likely to be allergic to all of them, for example flucloxacillin and penicillin V. This is because they all have the same beta lactam ring which causes the allergy. They may also be allergic to cephalosporins but these can be used as alternatives if people are monitored. A patient with a penicillin allergy would have to be given an alternative from a different group. For example, patients allergic to penicillins are often offered the macrolide erythromycin instead.

### Activity 3.3 Decision-making

A patient on your ward has a drug chart which states that they are allergic to penicillin. The following antibiotic is written up for the patient: Co-amoxiclav 500 mg three times a day. Would this be safe to give?

*An outline answer is available at the end of the chapter.*

Some antibacterial drugs are more toxic and cause more side-effects than others. Aminoglycosides, such as gentamicin for example, are toxic to the kidney and ear. The dose and blood levels need to be closely monitored to prevent toxicity. The full range of side-effects caused by antibiotics can be found in the BNF or the summary of product characteristics for each antibiotic.

## Choosing antibiotics

### Scenario

Josie is a 30-year-old woman who attends your nurse-led clinic appointment. She describes increasing urinary frequency over the last couple of days and a burning

*(Continued)*

(Continued)

sensation on passing urine. She has also felt tired and a bit flu-like since yesterday. She has no drug allergies and is on no other medication. You carry out a mid-stream urinalysis test. This tests positive for nitrite and leucocyte esterase. You suspect a lower urinary tract infection. Josie is prescribed a three-day supply of Trimethoprim tablets 200 mg twice a day.

In order to treat infection an antibiotic has to be chosen which is likely to kill the infective organism. As we can see from the scenario, a diagnosis has been made according to symptoms and the results of the urinalysis test. As the infection is mild, no attempt has been made to identify the microorganism causing the disease and a best-guess has been made as to what the likely microorganism is. You may remember that the same 'best-guess' occurred with Edward. Activity 3.4 should give you an insight into how empirical antibiotic therapy is chosen.

### Activity 3.4 Critical thinking

Do you think that Trimethoprim, at this dose and for this length of time, was an appropriate choice of antibacterial therapy for this urinary tract infection? The BNF contains a summary of antibacterial therapy which you might find useful.

*A suggested answer is given at the end of the chapter.*

Although the BNF gives a useful quick reference guide it is important to be aware of where this information comes from and to be able to compare it to other sources of information. Public Health England have issued a guideline 'Management of infection guidance for primary care for consultation and local adaptation'. It can be accessed from Public Health England's website. A link is provided at the end of the chapter.

You may want to research the evidence for treatment of urinary tract infections and compare the guidance with that in the BNF. NICE also has guidance relating to many different types of infection. Local hospitals often have their own antibacterial policies which take into account local patterns of resistance. We will look at resistance later in the chapter.

## Antifungals

Fungi are eukaryotic and therefore have more similarity to human cells than bacteria. Ensuring antifungals are selective (which means they kill only fungi and not human

cells as well) can be a challenge as many of the targets used by antibacterial drugs do not exist in fungi. Penicillins, for example, would not kill fungi as fungi do not contain peptidoglycans in their cell walls. Luckily, although both human cells and fungi have cell membranes they are slightly different. Antifungal agents act by damaging the cell membrane of fungi. The two most commonly used groups of antifungals are 'Triazole' antifungals and 'Imidazole' antifungals. The name relates to their chemical structure. Some antifungals are available as oral or parenteral formulations but many are also used topically to treat localised infections, for example, clotrimazole cream for vaginal thrush.

## Side-effects and implications for practice

Like antibacterial drugs, common side-effects include gastrointestinal disturbance. Many antifungal agents are toxic to the liver and should be used with care or avoided in patients with liver problems.

Antifungals often interact with other drugs. This is because they inhibit specific enzymes in the liver which are involved in the metabolism of other drugs (Chapter 1). So, for example, a patient on simvastatin should not be given ketoconazole at the same time because the levels of simvastatin could rise leading to toxic side-effects.

## Antivirals

Viruses can be very difficult to kill as they are such simple structures and offer few targets for killing agents. Immunisation with a vaccine is often our best defence against viruses (Chapter 4). However there are some very useful antiviral agents. Aciclovir was one of the first effective antivirals to be developed. It is effective against herpes simplex, which causes cold sores and genital infections. It is also effective against varicella-zoster, which causes shingles and chickenpox. Aciclovir is actually a pro-drug (Chapter 1) and is activated by an enzyme in the virus. This is what makes the drug selective. The active form of aciclovir prevents DNA replication and inhibits this process for viral DNA more effectively than for human DNA. Viruses are therefore prevented from reproducing. Other useful antiviral agents include those used for the treatment of HIV but these are outside the scope of this book.

## Antimicrobial resistance

Resistance is the ability of a microorganism to resist the effects of an antimicrobial drug. It is becoming a serious global health concern. In 2013 the Chief Medical Officer said that 'Antibiotic resistance poses a catastrophic threat' and went on to explain that if we do not act now we could be at risk of dying from ordinary infections we now think of as treatable. Some microorganisms are naturally resistant to some antimicrobials; this is known as innate resistance. We cannot kill a virus with an antibacterial agent such as penicillin, for example. Knowing which microorganism is causing the infection helps us choose the right

antimicrobial and should mean this kind of resistance is not generally a problem. In other cases microorganisms evolve and become resistant to antimicrobials that previously treated the infection they caused. It is this second type of resistance which is the most troubling. Although resistance can occur to many antimicrobials, we will concentrate here on resistance to antibacterials, the drugs that treat bacterial infections, as this is causing the greatest concern. The more that antibacterials are used, the more likely resistant organisms are to emerge. The resistant organisms go on to infect other people and may become widespread in the population.

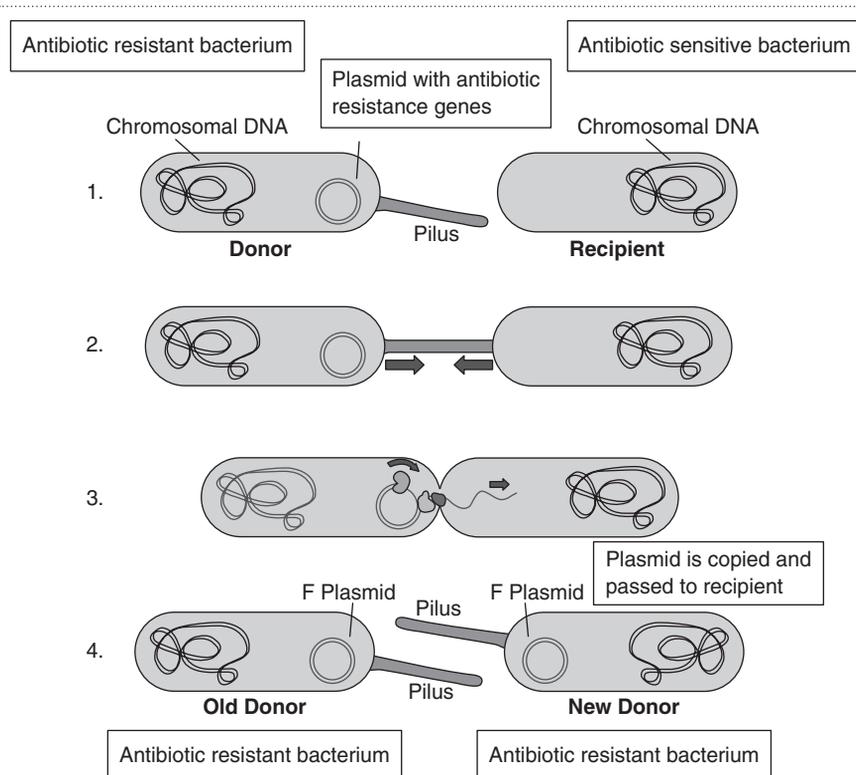
### Scenario

You are a nurse working on a surgical ward. Your patient, Nisa, is going for hip replacement surgery. She had a screen for meticillin resistant *Staphylococcus aureus* (MRSA) earlier and was found to be positive for this bacterium. As a result, you have been asked to ensure that she receives mupirocin nasal ointment and chlorhexidine body wash and shampoo. This will help to reduce the amounts of MRSA present and thereby reduce the risk of infection by MRSA during surgery. If Nisa was infected during surgery, the treatment would be much more complicated than for non-resistant strains of *Staphylococcus aureus*. This is because MRSA is resistant to the antibacterial agent flucloxacillin. This antibacterial would therefore not cure the infection. More toxic antibacterials such as vancomycin might be needed instead.

## Mechanisms of resistance

Bacteria reproduce by binary fission – that is, dividing into two. This is an example of asexual reproduction which, in biology, means without the mixing of genes. One parent therefore gives rise to two identical daughter cells. However, in order to survive in a world with a changing environment, which may include one with the new challenge of antibacterial therapy, bacteria need to mutate, which means they need to change genetically. Spontaneous mutations may occur in a bacteria's genetic make-up as it reproduces. *E. coli*, for example, can replicate itself every 20 minutes. This means that in 7 hours one bacterium can generate over two million bacteria. If a mutation means the bacteria is more able to survive the antibacterial than other bacteria this will quickly be passed on. However, in reality, if an appropriate antibacterial is taken properly the body's immune system will usually mop these resistant bacteria up. The most important way that resistance is passed on is when bacteria pass genes to each other via a process called conjugation (see Figure 3.5). Bacteria have one main chromosome but also contain separate pieces of DNA called plasmids. These plasmids often contain genes for antibacterial resistance. Two bacteria join together using sex pili and pass plasmids from one bacterium to another. The genes that are passed on in the plasmid now enable the bacteria to counteract the antibacterial. Bacterial conjugation enables bacterial antibacterial resistance to spread very rapidly through bacterial populations. The mechanisms bacteria use to counteract antibacterials are outlined below:

- Bacteria may produce enzymes that inactivate the antibacterial.
- Bacteria may actively remove the antibacterial from themselves.
- Bacteria may alter the binding site that the antibacterial usually adheres to so that it no longer 'sticks'.
- Bacteria may begin using different metabolic pathways to those that are being inhibited by the antibacterial.



Antibiotic resistance genes are often carried on circular pieces of DNA called plasmids. A donor bacterial cell joins with a recipient bacterial cell through the pilus. The plasmid is copied and passed on to the recipient cell. Both the donor and recipient cell now have a copy of the plasmid. This process can continue with other bacterial cells and antibiotic resistance genes can be passed on very rapidly through the bacterial population.

Figure 3.5 Conjugation

## Overcoming antibacterial resistance

Resistance is a global issue and needs to be tackled with different approaches. New antimicrobial agents need to be developed which microorganisms are not yet resistant to. However, there has been a decline in the development of new antimicrobials as they are expensive to research and are held in reserve for serious infections which means relatively little money is spent buying them. Countries also need to tighten

control of antibacterial supplies so they are not used for inappropriate infections. Healthcare professionals also have a role to play. The more that antimicrobials are used the faster resistance develops. If infection prevention and control is improved, the need for antimicrobials in the healthcare setting can be reduced. Correct use of antimicrobials is also important. Advice from experts such as microbiologists is important for choosing the correct drug. Narrow spectrum antibacterials are preferable to broad spectrum which was illustrated by the *Clostridium difficile* case study. Patient education is important. Patients should be encouraged not to seek antibacterials for viral infections. It has been shown that people are satisfied to receive reassurance and accurate explanations about their condition compared to antibacterials they do not need (Britten, 1995). The TARGET antibacterials toolkit produced by the Royal College of General Practitioners and others has some useful resources and leaflets for patients. The website can be found at the end of the chapter.

### Activity 3.5 Reflection

List interventions that you have carried out or observed others carrying out which help to prevent the spread of antimicrobial resistance. For each think about how this helps to combat resistance.

*A suggested answer is given at the end of the chapter.*

Having reviewed the general signs and symptoms of infection and the pharmacological management of infections, we turn to examine sepsis which is one of the most important concerns in healthcare today (NICE, 2016).

## Sepsis

Sepsis is defined as ‘life-threatening organ dysfunction caused by a dysregulated host response to infection’ (Singer et al., 2016). This rather technical definition tells us that sepsis is a life-threatening response to infection. Sepsis is estimated to affect 31.5 million people worldwide every year and cause an estimated 5.3 million deaths each year.

Our understanding of sepsis has changed over the years, and its definition has been updated a number of times. The current definition is The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3; Singer et al., 2016). As sepsis is such an important concern in healthcare today, it is worth examining this definition. How sepsis is understood in the healthcare setting affects its recognition and prompt treatment. The box below examines the Sepsis-3 definition.

## Sepsis-3

Our understanding of sepsis has evolved over the years. The 1991 and 2001 consensus definitions were based upon the ‘systemic inflammatory response syndrome’ (Balk, 2014). The systemic inflammatory response syndrome (SIRS) is a widespread (systemic) inflammatory response that can follow a diverse group of injuries. The injuries include not only infection, but trauma, burns, and pancreatitis and other injuries. Within the SIRS framework, sepsis was defined as ‘SIRS with documented or suspected infection’. There were two further categories within a sepsis continuum: severe sepsis and septic shock – of increasing severity.

The Sepsis-3 definition was developed to reflect advances in our understanding of the pathogenesis of sepsis (Singer et al., 2016). In particular, the Sepsis-3 definition focuses on the central role of infection in sepsis. Singer et al. (2016) argue that this is an important development of the previous central focus on the systemic inflammatory response, SIRS. The stronger emphasis on infection, it is argued, helps focus treatment on prompt antimicrobial therapy (see below under ‘Treatment of sepsis’). Sepsis is clearly more complex than the original ‘systemic inflammatory response with infection’ suggests. There is often an anti-inflammatory response, especially in the late stages of sepsis that can make patients susceptible to further infection. There are metabolic dysfunctions which affect cellular respiration and cell function. These advances in the understanding of sepsis pathogenesis have important implications for sepsis management and the development of new treatments.

The Sepsis-3 definition has produced different criteria for recognition of sepsis than the older SIRS criteria. There is ongoing debate about the most appropriate criteria for recognition of sepsis in clinical practice. For example, the British Medical Journal Best Practice: Sepsis in Adults (2018) notes that ‘these changes have prompted much debate and the 1991 definitions remain in widespread clinical use while the controversies are resolved’.

Having examined the Sepsis-3 definition of sepsis in the box above, we will now look at the most common causes of sepsis, the risk factors for sepsis and the pathophysiology of sepsis.

The most common causative agents of sepsis are bacteria – either Gram-negative or Gram-positive. Fungal infections can also cause sepsis. However, the causative agent of sepsis is only isolated and identified in around half of all cases. Of those cases in which the agent has been identified, common agents are Gram-positive *Staphylococcus aureus*, Gram-negative *Escherichia coli* and *Pseudomonas* spp. Common fungal agents include *Candida* spp. and *Aspergillus* spp. In the UK, sepsis is the most common direct cause of maternal death. In the 6-week postnatal period, group A *Streptococci* are the most common causative agent. Many causes of sepsis in the community setting are likely to be from the patient’s microbiome and are described as **endogenous** (or ‘from within’).

NICE (2016d) provides guidelines for early recognition, diagnosis and treatment of sepsis. The guidelines state: ‘Think “could this be sepsis?” if a person presents with signs or symptoms that indicate possible infection’. Assessment includes a person’s risk of infection, and in a face-to-face assessment includes assessing temperature, heart rate, respiratory rate, blood pressure, level of consciousness and oxygen saturation. The details of risk stratification tools can be found within NICE (2016d).

Knowledge of risk factors for sepsis are pivotal in early recognition (NICE, 2016d). Table 3.8 lists some of the main risk factors for sepsis.

<b>Risk factor</b>
Underlying malignancy
Age > 65 years
Haemodialysis
Alcoholism
Diabetes mellitus
Recent surgery or other invasive procedures
Breached skin integrity
Indwelling lines or catheters
Intravenous drug use
Pregnancy or recent pregnancy

*Table 3.8* Key risk factors for sepsis

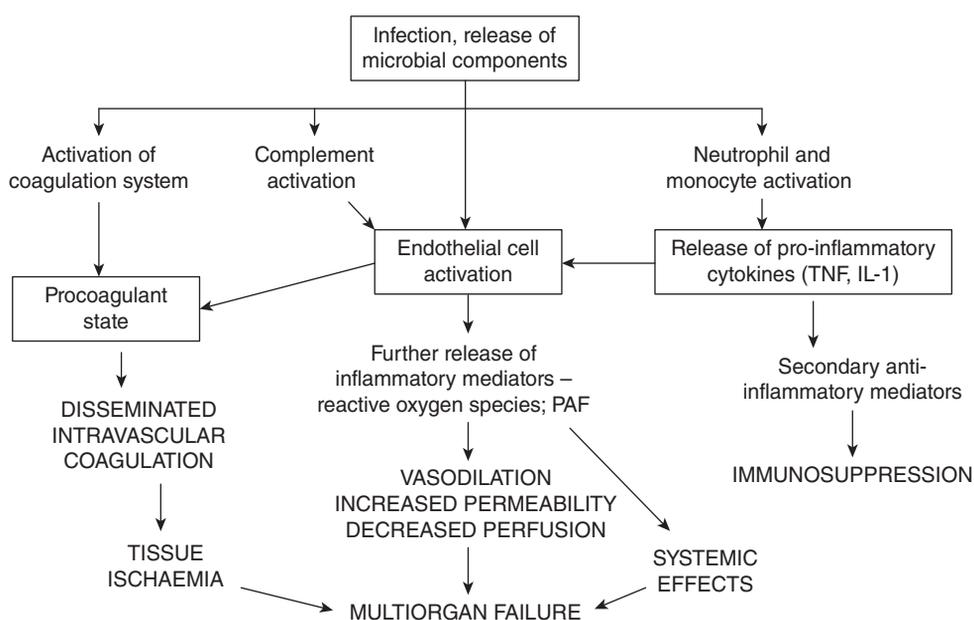
As can be seen from Table 3.8, many risk factors involve a pre-existing medical condition, such as a malignancy, alcoholism or diabetes. These may be associated with a weakened immune system and a greater susceptibility to infection. Other risk factors include breached skin integrity and indwelling lines or catheters. These again increase the risk of infection.

The common sites of infection in sepsis include the respiratory tract, the bloodstream, the abdomen, the skin and urinary tract. However, infection at any site in the body can potentially lead to sepsis. To help with the recognition and management of sepsis, an understanding of the pathophysiology of sepsis is essential. We turn to describing this below, building from the Sepsis-3 consensus definition.

## Pathophysiology of sepsis

Sepsis-3 defines sepsis as a dysregulated host response to infection which can lead to life-threatening organ dysfunction. ‘Dysregulation’ refers to impairment of normal regulatory responses. In sepsis, the dysregulated host response to infection has components which will be explained shortly. These responses are often described as the ‘sepsis cascade’ and can occur very rapidly in some patients, in some cases over a period of hours. Multi-organ failure can result and possible death.

Figure 3.6 shows the main components of the ‘dysregulated host response’ to infection that are found in sepsis. Many of these responses have been described in Chapter 2 within the sections on acute inflammation. In an acute inflammatory response, the responses were noted as being localised, well-regulated and offering a protective effect. By following the description below, you will see the contrast between a well-located and well-regulated response and the ‘dysregulated’ response which constitutes part of the host response in sepsis. This, in turn, can cause widespread life-threatening organ dysfunction.



*Figure 3.6* Pathophysiology of sepsis. PAF, platelet activating factor; TNF, tumour necrosis factor; IL-1, interleukin-1. Adapted from Mitchell et al., 2016.

An infection and/or the presence of microbial products from disrupted bacterial cells causes a widespread host response. Part of this host response includes activation of:

- innate immune cells – especially white blood cells called neutrophils and monocytes;
- the complement system (a set of plasma proteins which help fight infection);
- the coagulation system (another set of plasma proteins which lead to blood clotting);
- the endothelial cells (these cells make up the ‘endothelium’ or inner lining of the blood vessels).

These responses result in the widespread release of ‘pro-inflammatory cytokines’ and other mediators of inflammation (Chapter 2). Pro-inflammatory mediators and complement components cause further endothelial activation and further activation of immune cells. The activated immune cells and the endothelium continue to produce mediators of

inflammation. These include IL-6, IL-8, nitric oxide, platelet activating factor, and reactive oxygen species. There is a counter-balancing production of anti-inflammatory mediators, which paradoxically, may lead to immunosuppression.

The activation of the endothelium is key to understanding the progression to low blood pressure (hypotension) and organ failure in sepsis. Activation of the endothelium results in widespread vasodilation, and an increased permeability of blood vessel walls. Increased vascular permeability causes excessive fluid loss from the vascular compartment (from the circulation) and a reduced blood volume. Vasodilation and reduced blood volume together reduce blood pressure (hypotension) and may lead to reduced tissue perfusion, potentially leading to organ failure.

Activation of the endothelium also activates the coagulation system in the blood. A 'procoagulant state' may be reached in which microthrombi (small 'blood clots') form in small blood vessels. This is known as disseminated intravascular coagulation (DIC) and can lead to tissue ischaemia.

The inflammatory mediators also cause systemic effects including fever. There is evidence that mediators and reactive oxygen species directly affect cell metabolism. This includes a reduction in contractility of the myocardial cells of the heart. Sepsis is also characterised by insulin resistance and hyperglycaemia. This has been attributed to the production of stress hormones glucagon, adrenaline and cortisol.

Multi-organ failure may result. This is due to the multiple impacts of hypotension, oedema, and disseminated intravascular coagulation. There are direct metabolic effects from inflammatory mediators and cytokines, leading to anaerobic metabolism and cell dysfunction. In many cases the lungs are the first organs affected. This manifests as acute respiratory distress syndrome and acute lung injury. There is often cardiovascular instability and deteriorating renal function. Acute kidney injury can result (Chapter 14).

The magnitude of a patient's response and hence the outcome and severity of sepsis depends upon a range of factors: the virulence of the infecting microorganism, the host's immune status and other co-morbidities (Mitchell et al., 2016). The nature and level of mediators and cytokines released has a significant effect.

## Treatment of sepsis

As we have seen sepsis is a complicated condition. Early recognition and treatment is vital for the patient. Treatment guidelines suggest that a range of interventions are needed to stop a patient deteriorating. One bundle of therapies is known as the 'sepsis six bundle'. This has been shown to improve patient outcomes (Daniels et al., 2011). These interventions are:

1. **Administer oxygen:** Oxygen should be given to all patients with sepsis. In sepsis oxygen saturation of the tissues falls. This is because blood pressure is reduced leading to hypoperfusion of tissues. In addition, leaky capillaries lead to oedema which means oxygen must diffuse further to reach tissues. Small blood clots can occur in the capillaries which reduces oxygen delivery.
2. **Take blood cultures:** This should be done before antibiotic therapy is started where possible. Blood cultures help to identify the causative pathogen and antibiotics can be adjusted accordingly.
3. **Give IV antibiotics:** Sepsis is usually triggered by a bacterial infection and it is important that the infection is treated as soon as possible. Intravenous antibacterial drugs should be given within one hour of a sepsis diagnosis (NICE, 2016d). At the beginning it may not be clear which bacteria is causing the infection. Broad-spectrum antibacterial drugs are therefore often prescribed as they kill a wide variety of bacteria. The exact antibacterial prescribed will vary depending on local resistance patterns and the likely causative pathogen. It is also important that any potential sources of infection, such as urinary catheters, are removed.
4. **Give intravenous (IV) fluids:** During sepsis a patient's blood pressure may fall leading to reduced tissue perfusion. Intravenous fluid replacement such as Hartmann's solution would be given. Fluid replacement increases the circulating volume and restores blood pressure.
5. **Check serial lactate levels:** High lactate levels indicate anaerobic metabolism due to reduced tissue perfusion; this means the patient is in shock. Monitoring lactate helps to show how effective oxygen therapy and IV fluids are.
6. **Monitor hourly urine output:** Urine output falls when renal perfusion is reduced. This is a useful way of monitoring cardiac output which again helps to monitor response to treatment.

It is now time to review what you have learned within this chapter by undertaking some multiple choice questions.

### Activity 3.6 Multiple choice questions

1. What is the definition of a commensal microorganism?
  - a) A microorganism that causes disease
  - b) A microorganism that is transmitted from animal to human
  - c) A microorganism that usually lives harmlessly on our bodies
  - d) A microorganism that needs other microorganisms to survive

*(Continued)*

(Continued)

2. For each of the following state whether the answer is TRUE or FALSE.
  - a) *Candida albicans* is a bacterium
  - b) Hepatitis B is a virus
  - c) *Toxoplasma gondii* is a protozoan
  - d) *Escherichia coli* is a fungus
3. Bacteria are prokaryotic cells and differ from human, eukaryotic cells because:
  - a) They have no nucleus
  - b) They have no DNA
  - c) They have no cell wall
  - d) They have no ribosomes
4. Symptoms of infection can be caused by
  - a) Our immune system
  - b) Toxins produced by microorganisms
  - c) The death of invaded human cells
  - d) All of the above
5. Which of the following statements about *Clostridium difficile* is TRUE?
  - a) It is a type of virus which infects the gastrointestinal tract
  - b) It is one of the leading causes of pneumonia
  - c) It can occur after the use of broad spectrum antibiotics
  - d) It is spread by droplets which are inhaled by patients
6. If a patient is allergic to penicillin which of the following antimicrobial drugs can they take? Answer TRUE or FALSE for each drug.
  - a) Flucloxacillin
  - b) Trimethoprim
  - c) Co-amoxiclav
  - d) Fluconazole
7. Which of the following is NOT an example of how an antibacterial agent works?
  - a) Inhibition of cell wall synthesis
  - b) Inhibition of mitochondrial respiration
  - c) Disruption of protein synthesis
  - d) Inhibition of DNA synthesis
8. For each of the following statements about antimicrobials state whether the answer is TRUE or FALSE.
  - a) Aciclovir is an antiviral agent
  - b) Clotrimazole is an antibacterial agent

- c) Oxytetracycline is an antifungal agent
  - d) Metronidazole is an antibacterial agent
9. As part of a strategy to combat antibiotic resistance, patients may be given a leaflet explaining why they are not being given an antibiotic and explaining how long symptoms of their illness might last. A cough usually lasts:
- a) 4 days
  - b) 7 days
  - c) 14 days
  - d) 21 days
10. Which of the following are useful strategies for preventing antibiotic resistance? Mark each answer as TRUE or FALSE.
- a) Using broad spectrum antibiotics where possible
  - b) Preventing infections by good hygiene
  - c) Ensuring doses of antibiotics are not missed
  - d) Ensuring courses of antibiotics continue for at least two weeks

## Chapter summary

There are many different types of microorganisms but many live harmlessly in the environment and on our body. Microorganisms include bacteria, viruses, protozoa and fungi. However sometimes microorganisms are pathogenic and cause diseases. The body has many defences against disease, but infectious diseases can still be lethal. Different medicines have been developed to fight infections. These usually work by exploiting differences between human cells and the cells of the invading microorganism. Resistance to antimicrobial agents is an increasing problem. Microorganisms are constantly evolving different ways to survive the antimicrobials that we design to kill them. If we do not use the antibacterials we have very carefully and invent new ones, then we could one day be faced with dying from simple infections. Understanding the importance of correct antibacterial choice and administration can help nurses prevent resistance spreading. The cycle of infection can be used to identify infection control measures nurses can undertake to prevent infections in the first place.

Sepsis is a life-threatening response to infection and is an important concern in healthcare today. Early recognition and management of sepsis are essential. Sepsis results from complex poorly regulated host responses to infections. It can lead to septic shock, multi-organ failure and death.

## Activities: Brief outline answers

### Activity 3.1 Reflection (p60)

List five infectious diseases. For each disease write down whether it is caused by a virus, bacteria, fungi or protozoa. If you can, name the microorganism that causes the disease.

There are many examples you could have used – here are a few:

The common cold is caused by a virus. The name of the virus is *rhinovirus*.

Meningitis can be caused by bacteria, viruses or fungi. Bacteria causing meningitis include *Neisseria meningitidis* and *Streptococcus pneumoniae*. Viruses causing meningitis include enteroviruses and mumps virus. *Cryptococcus neoformans* is a fungus that can cause meningitis.

### Activity 3.2 Research (p69)

For each of the groups of antibacterials list one or two medicines that belong to this group. Use the BNF to help you.

Antibacterial group	Name of individual antibacterials
Example: Cephalosporin	Cefaclor, cefalexin
Penicillins	Amoxicillin, flucloxacillin
Macrolides	Erythromycin, clarithromycin
Quinolones	Ciprofloxacin, moxifloxacin
Tetracyclines	Doxycycline, oxytetracycline

### Activity 3.3 Decision-making (p71)

A patient on the ward has a drug chart which states they are allergic to penicillin. The following antibiotic is written up for the patient. Co-amoxiclav 500 mg three times a day. Would this be safe to give?

No. Co-amoxiclav consists of clavulanic acid and amoxicillin. Amoxicillin is a penicillin and could cause an allergic reaction in this patient.

### Activity 3.4 Critical thinking (p72)

Trimethoprim is an appropriate choice. A three-day course may be enough for women with uncomplicated infections.

### Activity 3.5 Reflection (p76)

List interventions that you have carried out or observed others carrying out which help to prevent the spread of antimicrobial resistance.

There are many examples you could give. These might include ensuring correct dose, route frequency, not missing doses, keeping to administration times for antibiotics on drug charts. These all help to kill microorganisms most effectively and prevent resistant organisms occurring. You may have seen pharmacists checking charts and querying doses, times, frequencies. You may have seen prescribers referring to guidelines, local policies or microbiologists. You may have had to ensure samples were sent to labs quickly to allow early identification of microorganisms. Washing your hands after seeing each patient prevents the spread of infections and hence the need for antimicrobials. Explaining to patients how to take their antimicrobials or educating

them about what antibiotics can and cannot treat is also useful. Involvement in antimicrobial audits is another example.

### Activity 3.6 Multiple choice questions (pp81–3)

1. What is the definition of a commensal microorganism?
  - c) A microorganism that usually lives harmlessly on our bodies
2. For each of the following state whether the answer is TRUE or FALSE.
  - a) *Candida albicans* is a bacterium False
  - b) Hepatitis B is a virus True
  - c) *Toxoplasma gondii* is a protozoan True
  - d) *Escherichia coli* is a fungus False
3. Bacteria are prokaryotic cells and differ from human, eukaryotic cells because:
  - a) They have no nucleus
4. Symptoms of infection can be caused by:
  - d) All of the above
5. Which of the following statements about *Clostridium difficile* is TRUE?
  - c) It can occur after the use of broad spectrum antibiotics
6. If a patient is allergic to penicillin which of the following antimicrobial drugs can they take? Answer TRUE or FALSE for each drug.
  - a) Flucloxacillin False
  - b) Trimethoprim True
  - c) Co-amoxiclav False
  - d) Fluconazole True
7. Which of the following is NOT an example of how an antibacterial agent works:
  - b) Inhibition of mitochondrial respiration
8. For each of the following statements about antimicrobials state whether the answer is TRUE or FALSE.
  - a) Aciclovir is an antiviral agent True
  - b) Clotrimazole is an antibacterial agent False
  - c) Oxytetracycline is an antifungal agent False
  - d) Metronidazole is an antibacterial agent True
9. As part of a strategy to combat antibiotic resistance, patients may be given a leaflet explaining why they are not being given an antibiotic and explaining how long symptoms of their illness might last. A cough usually lasts:
  - d) 21 days
10. Which of the following are useful strategies for preventing antibiotic resistance? Mark each answer as TRUE or FALSE.
  - a) Using broad spectrum antibiotics where possible False
  - b) Preventing infections by good hygiene True
  - c) Ensuring doses of antibiotics are not missed True
  - d) Ensuring courses of antibiotics continue for at least two weeks False

## Further reading

**Appelbaum, PC** (2007) Microbiology of antibiotic resistance in *Staphylococcus aureus*. *Clinical Infectious Diseases*, 45 (Supplement 3): S165–70. Available at: [http://cid.oxfordjournals.org/content/45/Supplement\\_3/S165.full/](http://cid.oxfordjournals.org/content/45/Supplement_3/S165.full/)

**Goering, R, Dockrell, H, Zuckerman, M, Roitt, I and Chiodini, P** (2018) *Mims' Medical Microbiology* (6th edition). Oxford: Elsevier.

A very accessible textbook on medical microbiology.

**Gotts, and Matthay, M** (2016) Sepsis: pathophysiology and clinical management. *BMJ*, 353: i1585. Available at: [www.bmj.com/content/353/bmj.i1585/](http://www.bmj.com/content/353/bmj.i1585/)

This is a comprehensive review of sepsis.

**Health Protection Agency** (2009) *MRSA Screening and Suppression: Quick Reference Guide for Consultation and Local Adaptation*. Available at: [www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/330793/MRSA\\_screening\\_and\\_suppression\\_primary\\_care\\_guidance.pdf/](http://www.gov.uk/government/uploads/system/uploads/attachment_data/file/330793/MRSA_screening_and_suppression_primary_care_guidance.pdf/)

**Public Health England** (2013) *Primary Care Guidance: Diagnosing and Managing Infections*. Available at: [www.gov.uk/government/collections/primary-care-guidance-diagnosing-and-managing-/](http://www.gov.uk/government/collections/primary-care-guidance-diagnosing-and-managing-/)

**Public Health England** (2017) *Clostridium difficile: Guidance, Data and Analysis*. Available at: [www.gov.uk/government/collections/clostridium-difficile-guidance-data-and-analysis/](http://www.gov.uk/government/collections/clostridium-difficile-guidance-data-and-analysis/)

**Royal College of General Practitioners, Public Health England and The Antimicrobial Stewardship in Primary Care**. TARGET antibiotic toolkit. Available at: [www.rcgp.org.uk/TARGETantibiotics/](http://www.rcgp.org.uk/TARGETantibiotics/)

## Useful websites

For further information on drugs, their uses, side-effects and patient information leaflets:

[www.medicines.org.uk/](http://www.medicines.org.uk/)

Summary of product characteristics.

[www.earthlife.net/prokaryotes/welcome.html](http://www.earthlife.net/prokaryotes/welcome.html)

Website for more information on microorganisms.

<https://sepsistrust.org/professional-resources/education-resources/>

Educational resources from the UK Sepsis Trust.