

Session 1: Introducing human infectious diseases

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Session 1

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Introduction

Most people on Earth experience at least one episode of an infectious disease every year. Although the majority recover, hundreds of millions suffer severe or long-term health effects as a direct result of an infection and around 10 million people – many of them children – lose their lives. In the 1960s, it was widely believed that the threat to health from infectious diseases would be overcome by advances in methods of prevention and treatment. Unfortunately these predictions have proved to be optimistic because of the rapidly increasing threat from ‘emerging infectious diseases’.

This first session of the course presents an overview of infectious diseases and discusses emerging infectious diseases.

In the following video, Dr Claire Rostron, Senior Lecturer in Health Sciences at The Open University, and one of the course authors, will introduce some exciting concepts to be covered in the course.



Before you start, The Open University would really appreciate a few minutes of your time to tell us about yourself and your expectations of the course. Your input will help to further improve the online learning experience. If you'd like to help, and if you haven't done so already, please fill in this optional survey.

1.1 What are infectious diseases?

Infectious diseases are distinguished from other illnesses and disorders because they can be transmitted from someone who is ill either directly or indirectly to other individuals, who then develop the same infectious disease and are also able to pass it on. A familiar example is the 'common cold' which almost everyone has experienced at some time in their lives (Figure 1). Non-human animals and plants also suffer from infectious diseases, which cause massive losses to food crops and livestock, but our focus in this course is on infection in humans.



(a)



(b)

Figure 1 The common cold affects children and adults all over the world: (a) Vietnam. (b) United Kingdom.

By contrast, health problems that cannot be transmitted between individuals, such as heart disease, diabetes, lung cancer, arthritis and depression, are known as non-communicable diseases (or NCDs). However, a few NCDs also have an infectious component, for example:

- in most cases of cervical cancer there is evidence of infection with a specific virus (the human papilloma virus, or HPV)
- hepatitis viruses cause liver disease and cancer of the liver
- a bacterium (*Helicobacter pylori*) causes stomach ulcers.

These examples illustrate the point that there is some overlap between some infectious and non-communicable diseases. The biology of bacteria and viruses is the subject of Session 3 Pathogens and infectious diseases.

For completeness, we should mention here that the third major category of diseases, disorders and disabilities is termed injuries, i.e. physical damage to the body caused by accidents or violence.

1.2 Symptoms and signs of infection

Symptoms are sensations in the body that only the person who is unwell can experience; for example, a headache, pain in the abdomen, blurred vision and nausea are all symptoms, because no one but the sufferer can experience them. Lay people, including children, can usually describe their symptoms accurately or report them if asked the right questions, but symptoms are subjective experiences that others cannot observe or verify.

By contrast, the signs of a disease are indicators of illness that other people *can* observe (e.g. a runny nose and frequent sneezing). Considering the symptoms and signs together may give enough information for a trained health worker to make a diagnosis, i.e. identify the underlying cause of the illness and give it a definite name. An example will illustrate this point.

You probably agree that the children in Figure 2 look ill, but how did you decide this?



(a)



(b)

Figure 2 What tells you that these children are unwell?

- What signs of disease can you identify from their photographs? Did the name of any infectious diseases spring to mind when you looked at these children?

We expect that you noted the numerous tiny red spots on the children's faces and shoulders and that their eyes look sore. Some of you (especially if you have children or much younger siblings) may have wondered if the cause could be roseola, or perhaps chickenpox or measles?

A trained health worker would first note the rash and sore eyes and ask the caregivers about other observable signs of disease, for example 'Does the child have a cough or a fever?' However, these signs alone are not enough to make a diagnosis. In this example, the health worker would look for clusters of tiny white spots inside the mouth (so-called Koplik spots), which

are not always present, but if visible are a definite sign of measles. Combining all the information leads to the diagnosis that the children in Figure 2 do in fact have measles – an infectious disease caused by a virus.

However, it should not be assumed that only trained health workers can diagnose an illness. Most adults and parents at some stage make a ‘good enough’ diagnosis of what ails them or their children. Lay people very often decide on the basis of their own symptoms or the signs of disease they observe in family members whether to treat an illness at home with simple remedies, or seek advice from a trained health worker.

1.3 Acute or chronic conditions

Two useful terms that are equally relevant to infectious and non-communicable diseases (NCDs) refer to the *time course* of the illness. Knowing how long the symptoms of a disease have persisted and how quickly they are worsening or improving can help in making a diagnosis.

An *acute* condition is characterised by symptoms that develop rapidly and reach their peak within a few days or weeks. The patient either recovers relatively quickly or dies! Note that acute means ‘fast’ and ‘short-term’ – it does not necessarily mean ‘serious’. Some acute infections are mild and resolve in a short time without any treatment.

- Can you identify an acute infectious disease that you or someone you know has suffered from in the past year, resulting in complete recovery within a week or two?

You may have suggested the common cold, or perhaps a stomach upset with an episode of diarrhoea. There are other possible examples.

By contrast, a *chronic* condition develops slowly and may take many months or years to reach its most severe extent. The term ‘chronic’ comes from *Cronos*, the Greek god of time. People with a chronic condition may cope well with its effects, but they may not fully recover the health they previously enjoyed. If left untreated, chronic diseases usually progress (get worse) and some conditions may result in permanent disability or loss of life. Tuberculosis (TB) is an example of a chronic infectious disease caused by bacteria that most often affect the lungs, but can also invade other parts of the body. TB progresses slowly but inevitably unless specific drugs are taken consistently every day for three-to-six months (Figure 3).



Figure 3 Tuberculosis requires consistent long-term drug treatment.

Most NCDs are chronic conditions, but some can have an acute episode – for example, people with cardiovascular disease (a chronic disease of the heart or blood vessels) can have a heart attack (an acute event).

1.4 What causes infectious diseases?

Infectious diseases are transmitted between individuals by infectious agents, known as pathogens [path-oh-jens], from the Greek word *pathos* (to suffer) and *genès* (to produce). Pathogens produce a lot of human suffering and disability across the world, including in relatively wealthy nations like the United Kingdom (UK). Most people have heard of at least some types of pathogen, for example bacteria or viruses.

The wider causes of infectious diseases range from insanitary living conditions in impoverished communities, to inadequate hygiene in the high-tech environments of modern hospitals (Figure 4). The impact of infectious diseases is therefore unequally distributed around the world, not only between countries, but also between individuals and groups within the same population.



(a)



(b)

Figure 4 Infectious diseases are a threat everywhere: (a) A shanty settlement without piped water or sanitation in Indonesia. (b) Testing for pathogens in a hospital laboratory in England.

Human biology is another factor to consider in explaining the cause of infectious diseases. Infancy and old age, inadequate nourishment, other illnesses and some types of medication can all create conditions in the body in which infection is more easily established.

In addition, there are individual human behaviours, habits and traditional practices that contribute to the causes of infectious diseases by spreading pathogens from one person to another.

■ Can you suggest any behaviours that can cause pathogens to spread?

There are many possible answers, but we thought of:

- not washing hands after using the toilet or before preparing food
- not covering the nose and mouth when sneezing or coughing
- spitting in the street
- leaving food uncovered where flies can settle on it

- not cooking raw meat thoroughly or inadequate reheating of cooked food.

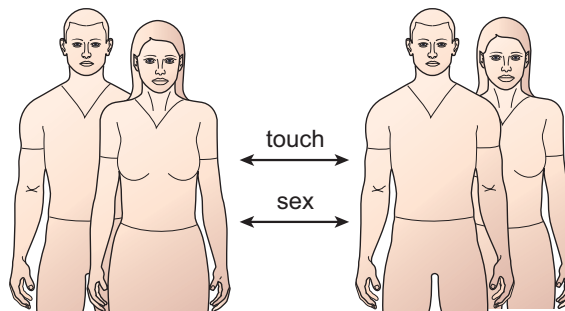
These behaviours give some clues about the routes by which pathogens can be transmitted, as the next section describes.

1.5 Direct person-to-person transmission of pathogens

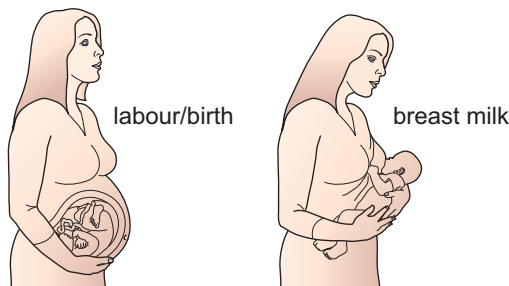
A new infection begins when pathogens leave the body of their host – the infected individual in which the pathogens are multiplying – and enter a new host. They may be repelled by defence mechanisms in the new host as discussed in Section 4 ‘Immune defences against infectious diseases’, or they may survive and reproduce in sufficient numbers to cause an infectious disease.

Transmission of pathogens can occur directly between people, or indirectly in the air, water or food, or via other animals to humans, or from sources in the environment. In this section we explore direct transmission.

Figure 5 represents the three ways in which pathogens can be transmitted by direct person-to-person contact.



(a) contagious and sexually transmitted infections



(b) mother-to-child transmission

Figure 5 Direct person-to-person transmission of infection. (a) Contagion and sexual transmission. (b) Mother-to-child transmission.

They are:

- Contagious infection, when touch, such as a handshake, transfers pathogens to a susceptible person; they may enter the new host through a cut or graze, or be transferred from hand to mouth.
- Sexually transmitted infection (or STI) involving infected semen, vaginal secretions, saliva or blood transmitting pathogens to the infected

individual's partner during unprotected sex. This is the most common route for the worldwide spread of HIV (the human immunodeficiency virus), which causes AIDS (acquired immune deficiency syndrome). Sexual transmission is more likely if the partner's genitals, mouth or rectum are inflamed, for example, by another STI such as gonorrhoea [gonn-or-ree-ah] or syphilis [siff-ill-iss].

- Mother-to-child transmission, when pathogens pass from mother to baby during labour and delivery, or via breast milk.

1.6 Indirect person-to-person transmission of pathogens

Indirect person-to-person transmission occurs when the original host sheds pathogens into the air, water, food or objects in the environment, which then infect someone else (Figure 6).

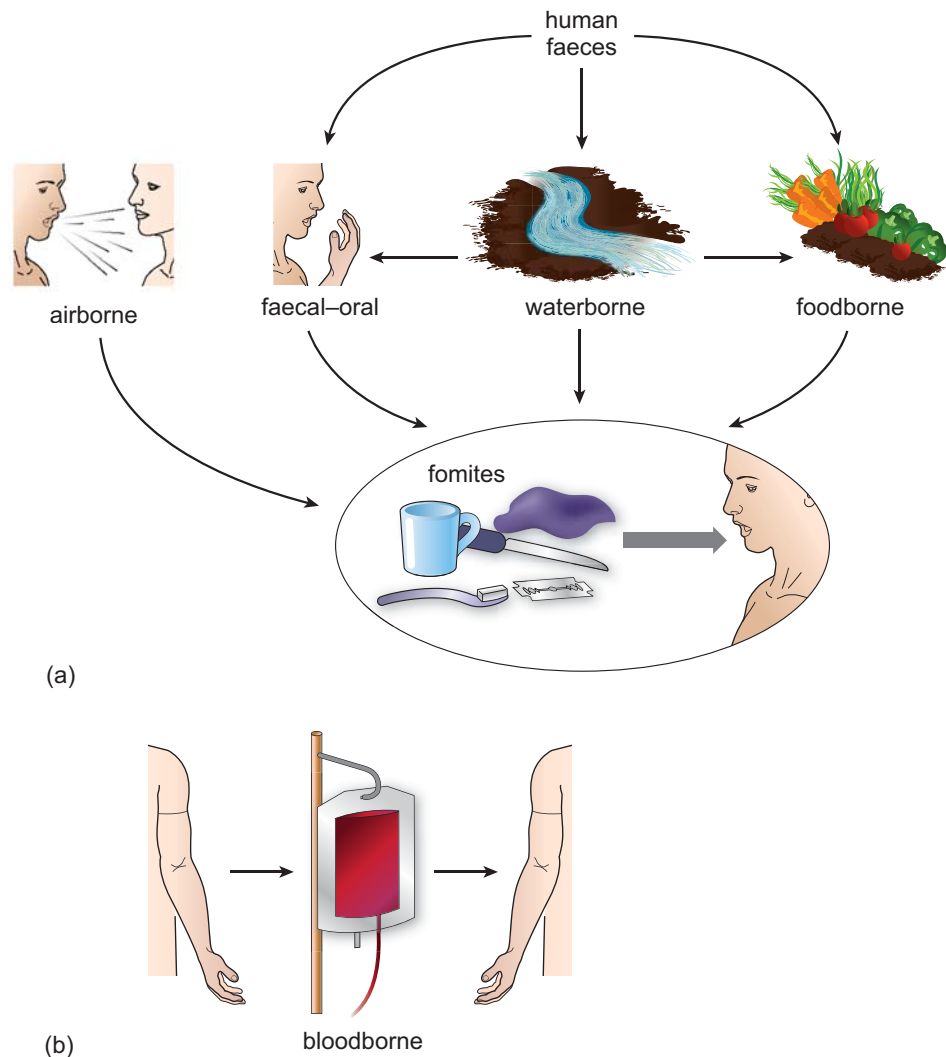


Figure 6 There are many routes for indirect person-to-person transmission of infection.

Most airborne infections are transmitted when a cough or sneeze expels fine droplets of water (known as an aerosol) containing millions of bacteria or viruses (Figure 7). The aerosol droplets may be inhaled by a susceptible person, or settle on surfaces where the pathogens contaminate hands, utensils, clothing, water or food, which are then touched or consumed by someone else.

Waterborne infections are particularly common in parts of the world where large numbers of people don't have access to clean drinking water or safe disposal of sewage. Infected urine and faeces from humans and animals can



Figure 7 Coughs and sneezes spread diseases!

wash into lakes and streams, where the pathogens multiply and reinfect people when they drink or bathe in contaminated water. Some pathogens (including the bacteria that cause cholera [koll-err-ah], a serious diarrhoeal disease) live naturally in environmental water sources, so they will always pose a threat to health.

Faecal–oral infections (‘faecal’ [fee-kal] and ‘faeces’ [fee-seez] refer to solid waste, or excrement) occur when pathogens from faeces enter the mouth (‘oral’ [orr-ahl]) and multiply in the gut. Transmission occurs when unclean hands, dirty cooking utensils or food contaminated by faeces enters the mouth. Flies can transfer pathogens from faeces to food via their feet. Contact with faeces is unavoidable when people are forced to defecate in the open because there is no sanitation. In these cases, people can get contaminated soil on their hands and the pathogens are easily transmitted from hand to mouth if there is no clean water or soap for handwashing.

Diarrhoeal diseases are often transmitted via the faecal–oral route, and some (e.g. cholera) are mainly waterborne. But they may also be due to foodborne infections caused by pathogens that originated in food components, for example, pathogenic bacteria in raw meat, eggs and on salad leaves.

Non-living objects in the environment, such as cups, spoons and door handles that people routinely touch, can also transmit infection and are known collectively as fomites [foh-mytz]. Clothing can also act as a fomite, which is why hospital doctors in the UK now rarely wear neckties that could drape across a patient during a medical examination and pick up infection that the next patient might acquire (Figure 8).

- Can you identify the fomites in Figure 8 that could undermine infection prevention and control in this hospital?

In addition to the neckties worn by the two male doctors, all three doctors have stethoscopes, long-sleeved clothing, staff badges worn at waist height where they could brush against a patient, and the nurse is wearing a wristwatch. (If you go into a hospital in the UK nowadays, all staff must have their arms bare below the elbows, and wristwatches, rings and neckties are banned. Stethoscopes still touch a lot of patients on ward rounds and can’t be sterilised.)



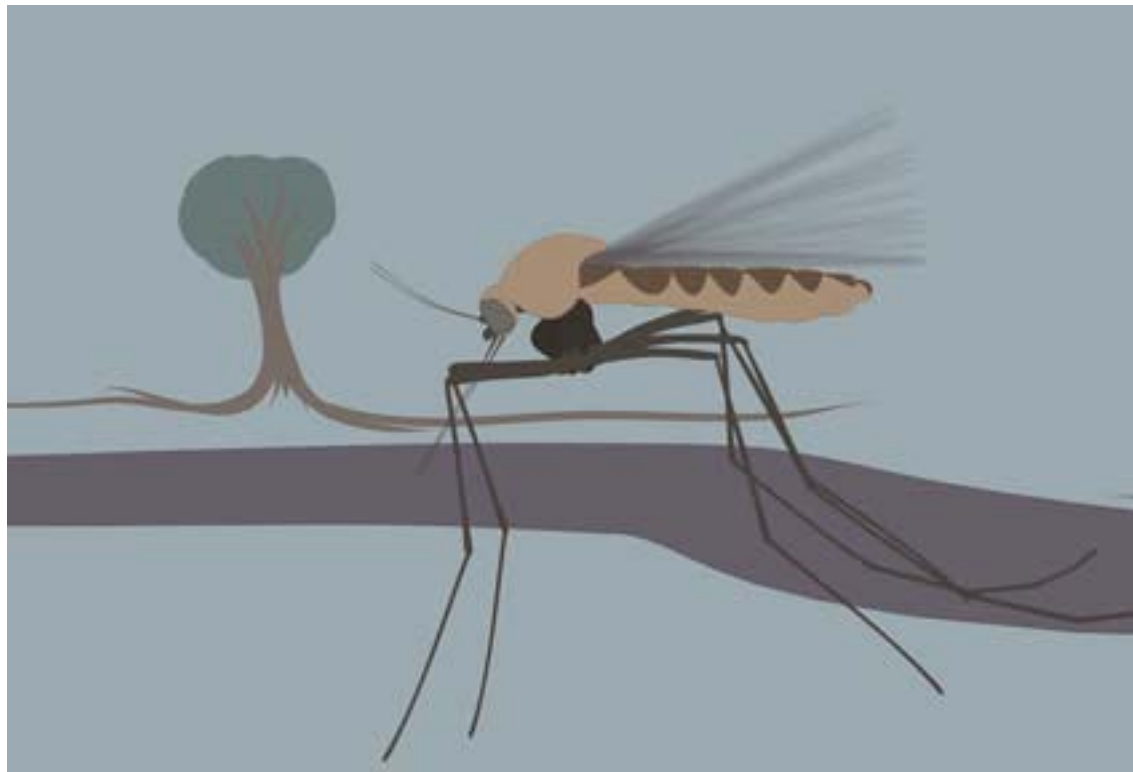
Figure 8 Hospital staff photographed in 2001.

Medical procedures can also transmit bloodborne infections; for example, before the transmission of HIV was understood, thousands of infections occurred from HIV-contaminated blood transfusions. Bloodborne pathogens can also spread via shared needles and syringes among people who inject illegal drugs, such as heroin.

1.7 Animal-to-human transmission of pathogens

Pathogens are often transmitted from animals to humans ‘accidentally’, for example via infected meat or water contaminated with animal faeces. But there are two transmission routes in which the animal is an essential agent in the transfer of pathogens to humans.

You can learn more about these in the following animation which focuses on malaria. Note that for simplicity in this animation we have referred to the pathogen that causes malaria as the ‘malaria pathogen’ or ‘malaria parasite’ but it should be remembered that the name ‘malaria’ refers to the disease and not the pathogen. The correct name for the parasite pathogen is *Plasmodium* and it has several different species including *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae*.



An example zoonosis that may be familiar is influenza originating in pigs (swine flu) or poultry (bird flu). The influenza viruses that cause these diseases can sometimes be transmitted from animals to humans during the slaughter or handling of livestock. Some zoonotic [zoo-not-tik] influenza viruses pose a much greater health risk than the airborne seasonal influenza viruses that commonly circulate in human populations every winter.

- Can you think of any other zoonoses that have made news headlines, at least in the UK?

You may recall that cattle can be infected with the bacteria that cause tuberculosis (TB), which can then be transmitted to humans. Badgers can also host TB bacteria, although there are no known cases of badger-to-

human transmission. The mosquito borne Zika virus has also made news headlines because of its increasing incidence and the effects that have been observed on babies whose mothers have been infected. This virus may have originally been transmitted to the human population from monkeys.

A zoonosis that is well known in India and some other parts of the world is rabies [ray-beez]. The rabies virus can infect many warm-blooded vertebrates including squirrels, raccoons and bats, but the main route of transmission to humans is via dogs. Every year, over 3000 people in India die from rabies transmitted by a dog bite (Figure 9). The majority of these deaths are among children because they are more likely to try to play with unfamiliar dogs (Chatterjee, 2009).



Figure 9 Dogs are the main source of rabies transmission to humans.

Another route of transmission from animals to humans results in vector-borne infections. They differ from zoonoses in that they are transmitted by an invertebrate animal (without a backbone), mainly biting insects and ticks. The term ‘vector’ [vek-torr] comes from the Latin word for ‘carrier’, so in this context it means a carrier of an infectious disease. The pathogen must complete part of its life cycle in the vector, so transmission to humans may be prevented if the vectors can be killed. For example, Lyme disease is caused by a bacteria transmitted from birds or small mammals (such as deer) to humans by a type of tick.

- Can you suggest why aeroplane cabins are sprayed with insecticide before take-off from a country where malaria is common?

The spray is to kill any mosquitoes that may have got onto the plane in the clothing or luggage of passengers. Mosquitoes are the vectors of malaria and transmit the pathogen when they bite humans to take a blood meal.

There are many other vector-borne infections, including bubonic plague [byoo-bon-nik playgg] transmitted by rat fleas, typhus [ty-fuss] transmitted by ticks, and yellow fever transmitted by mosquitoes. In 2014, the World Health Organization (WHO, pronounced ‘double-you-haitch-oh’ rather than ‘who’) – the branch of the United Nations responsible for coordinating and directing international policy and actions on health – devoted its annual

‘World Health Day’ to publicise the risk from vector-borne infections (Figure 10).



Figure 10 The WHO's poster publicising the threat in 2014 from vector-borne infections transmitted by biting invertebrates.

1.8 The end of infectious diseases?

In 1967, William H. Stewart (1921–2008), the Surgeon General of the United States of America (USA) – a role equivalent to the Chief Medical Officer in the UK – is alleged to have announced:

It is time to close the book on infectious diseases and declare the war against pestilence won.

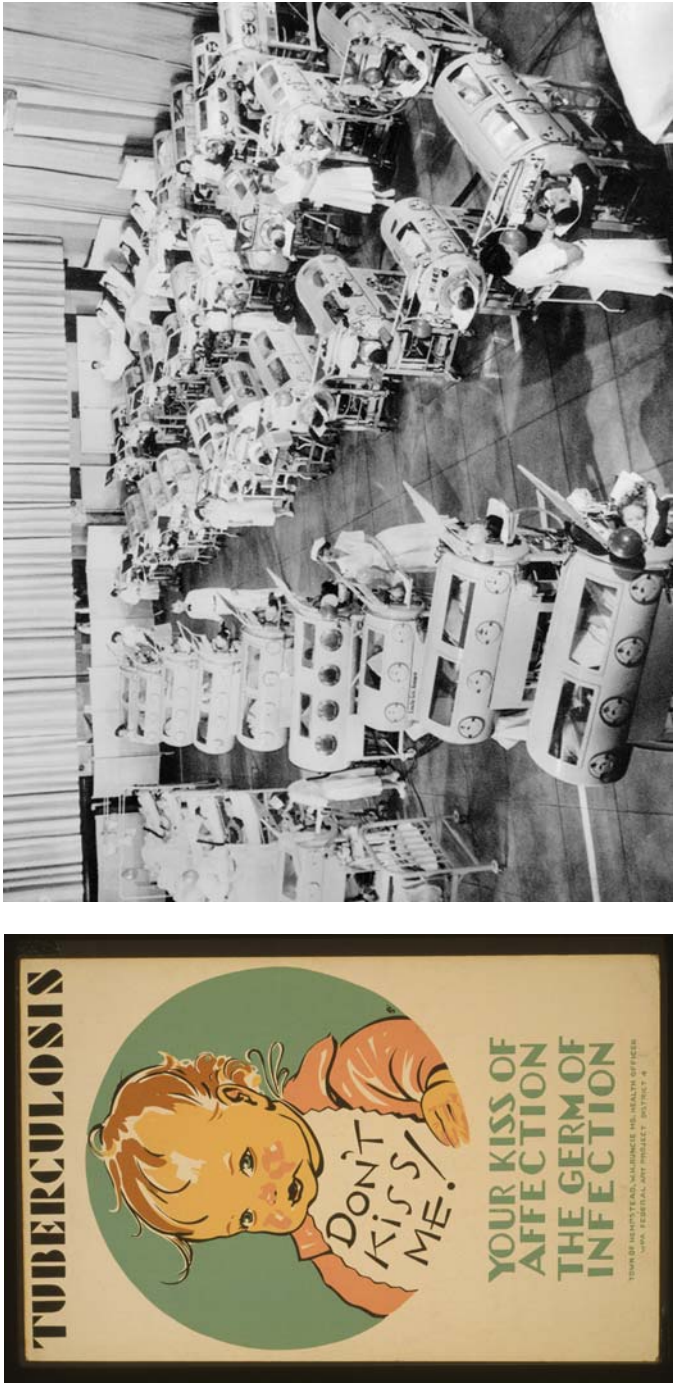
(quoted in Spellberg et al., 2008; note that ‘et al.’ indicates that there were several other authors)

Less than 40 years before this woefully optimistic claim, at least 20 million people had died in 1918–19 from influenza, most of them young adults in the UK, USA and Europe. Public health officials in the USA in the 1940s were actively campaigning to halt the spread of tuberculosis (TB) in ways that may surprise you (Figure 11a), and in the decade ending in 1960 more than 102 000 people in the USA – many of them children (Figure 11b) – were paralysed by polio (data from Post-Polio Health International, n.d.; note that ‘n.d.’ indicates that no date was given).

So what gave public health officials like Stewart such confidence that the threat from infectious diseases was really over in 1967? The belief that infection had been vanquished in the USA and would ultimately be conquered in the rest of the world was based on the success of two innovations in medical science in the early 20th century:

- The development of new and more powerful antibiotics – a type of drug that kills bacteria, which dramatically cut the death rates in the 1950s and 1960s from bacterial infections such as pneumonia.
- Mass vaccination programmes after World War 2, where new vaccines containing substances derived from pathogens were given to children in injections or by mouth. In the 1950s and early 1960s, new vaccines gave effective protection for the first time against polio, diphtheria [dipp-thear-ree-ah], whooping cough (pertussis [purr-tuss-is]) and tetanus [tett-ann-us].

Unfortunately, Stewart was fundamentally wrong in predicting that infectious diseases would disappear as a cause of human suffering. They are still very much with us in the 21st century. New infectious diseases are emerging at an accelerating rate and pathogenic bacteria are developing resistance to antibiotics, so in some ways the threat is increasing, not decreasing as the next section briefly explains.



(a)

(b)

Figure 11 (a) Public health poster on TB prevention in the USA in 1941. (b) Children paralysed by polio in 'iron lungs' to help them breathe, USA in the 1950s.

1.- 9 E- mer- ging in- fec- tious dis- ea- ses

Emerging infectious diseases (EIDs) is the collective term for a group of conditions that pose new threats to human health. EIDs can be distinguished into three types:

- 1 New infectious diseases caused by pre-

viously unknown pathogens:

Many of the diseases in this category are caused by zoonotic viruses, i.e. the viruses originated in other vertebrate animals, but at some point in the past they changed in ways that made them infectious to people. The best known ‘new’ infectious disease is AIDS but the virus that causes AIDS (HIV) may have originated in monkeys. Since HIV was identified in 1984, several other new infectious diseases caused by potentially fatal viruses have been identified. They include SARS (Severe Acute Respiratory Syndrome, Figure 12), which may have originated in poultry, MERS (Middle East Respiratory Syndrome), which may have originated in camels, and zoonotic strains of influenza (swine flu and bird flu).



Figure 12 Doctors in Toronto struggled to contain SARS in 2002; the highly infectious virus was spread to Canada by a passenger on a flight from Hong Kong.

- 2 Infectious diseases that have spread far outside their original range:
One example is Ebola virus disease (EVD), a ‘haemorrhagic’ [hemm-orr-adj-ik] fever, which means it causes severe internal bleeding, among other symptoms. Cases have occurred from time to time in remote villages in West Africa, but the first urban cases were detected in the capital of Guinea in February 2014 and from there Ebola quickly spread to neighbouring Liberia and Sierra Leone. A few travellers or health workers caring for Ebola patients developed the disease in other countries, including Nigeria, Mali, Senegal and the USA. By October 2015, over 11 000 deaths had occurred from over 28 000 suspected, probable and confirmed cases (Centers for Disease Control and Prevention, 2015). Many of these cases have not been confirmed in a laboratory, so the ‘case fatality rate’ (the proportion of confirmed infected people who die) is unknown; however, it is likely to fall within the range of 30 to 60 per cent.
- 3 Previously declining infectious diseases that have resurged:
Tuberculosis and some other infections caused by bacteria are a growing health concern because the causative pathogens are becoming increasingly resistant to antibiotics, which previously treated them successfully. So-called ‘hospital super-bugs’ are bacteria that have developed resistance to antibiotics in health care facilities, where

antibiotics are heavily prescribed. An additional factor in countries where HIV/AIDS is common is that infection with HIV suppresses the body's immune defences, so people with AIDS are more susceptible to other infections, including TB.

Session 1 quiz

This quiz allows you to test and apply your knowledge of the material in Session 1.

Session 1 quiz

Open the quiz in a new window or tab then come back here when you're done.

Summary to Session 1

In this first session of the course you have learned about infections, which along with non-communicable diseases and injuries, are one of the three types of diseases, disorders and disabilities suffered by humans. You have learned that infections are diagnosed by health workers on the basis of signs and symptoms. Signs are consequences of the infection that are readily observable by other people, like raised temperature; symptoms are consequences of infection that can only be reported by the patient, like a headache.

You have also been introduced to pathogens. Pathogens are the biological agents that cause infectious disease and can be passed between people directly or indirectly, and can also come from animals and the environment. Importantly, however, you should now be aware that pathogens are *everywhere*, although if sensible measures are taken their transmission can be minimised and the incidence of the diseases they cause can be reduced considerably. Indeed, as we have outlined, the success of some early prevention strategies led scientists in the 1960s to predict that all infectious diseases would soon be defeated. As you are aware, this prophecy has not come true.

The shortage of clean water, sanitation and adequate health care in some parts of the world, the continual emergence of new infectious diseases and the capacity of some pathogens to adapt and become resistant to disease prevention measures, means the study of infectious disease is as critical to human health as it has ever been.

You can now go to Session 2.

Session 2

Introduction

In Session 2 you'll look at the conditions in England in the 18th and 19th centuries which help to explain the high rates of death and sickness in the past from infectious diseases, such as cholera and smallpox. Similar living conditions still exist in parts of the world where infectious diseases remain the principal threat to health. Evidence for the impact of infectious diseases on populations comes partly from statistical studies of data on deaths from infection, which began in England in the 19th century.

You will analyse two classic experiments from the history of infectious diseases to identify the key features of the scientific method of investigation. These are significant because the origins of public health and mass vaccination programmes can be traced back to these two experiments. One of these classic experiments eventually contributed to the eradication of smallpox.

In the video, Dr Claire Rostron, Senior Lecturer in Health Sciences at The Open University, describes this in more detail.



2.1 Origins of the scientific method

There are two reasons for looking at ‘lessons from the history of infectious diseases’ when discussing the origins of the scientific method.

The first is to describe the conditions in which infectious diseases flourished in the relatively recent past of a major western industrialised nation, and underline similarities with present-day locations where infections still cause millions of deaths.

The second reason is to describe two classic experiments that form the basis of modern day strategies for preventing infectious diseases. In different ways they each illustrate the fundamental features of what has become known as the ‘scientific method’.

The *Oxford English Dictionary* defines the scientific method as:

A method of observation or procedure based on scientific ideas or methods ... that has underlain the development of natural science since the 17th century.

It is now commonly represented as ideally comprising some or all of (a) *systematic observation, measurement, and experimentation*, (b) induction and the *formulation of hypotheses*, (c) the making of deductions from the hypotheses, (d) the experimental *testing* of the deductions, and (if necessary) (e) the *modification* of the hypotheses.

(Our italics added.)

The key words in this definition are shown in italics.

Systematic refers to any procedure conducted according to a fixed, pre-determined plan. All scientific experiments are ‘systematic’ in that the methods, materials, conditions and the sequence of actions involved are clearly and precisely described, so that other scientists can exactly follow the ‘system’ used in the original experiment.

A hypothesis is a statement proposing an explanation for an observation, made on the basis of limited evidence, as a starting point for further investigation. It has sometimes been described as ‘an informed guess’ about what the explanation for the observation might turn out to be. A fundamental principle of every hypothesis is that it must be *testable*, i.e. capable of being strengthened or ruled out as a result of further investigation. Of course if it is ruled out, then *modifications* must be made.

The first step on this investigative journey takes you back to the industrial cities of England in the early 19th century (Figure 1).
Figure 2.1



Figure 1 Stockport viaduct about 1850, lithograph by A. F. Tait.

2.2 Infant deaths in 19th-century England

More than 50% of all deaths in England and Wales in the mid-19th century were due to infections, with infants and children at greatest risk, as they still are in many parts of the world today. But in the 19th century, the death rates were far higher than they are currently anywhere in the world. A lot of progress has been made in reducing child deaths from infection, which can be tracked using two internationally recognised measures:

- the infant mortality rate (or IMR), the number of deaths occurring under one year of age per 1000 live births in a population ('per' means 'out of every', so the IMR tells you how many out of every 1000 live-born babies died in infancy)
- the under-five child mortality rate, the number of deaths before the fifth birthday per 1000 live births in a population.

Note that babies who died before birth ('stillbirths') are excluded from both of these mortality rates. In a moment we will look at some infant mortality data from the 19th century, but before we do that it is worth unpacking the term mortality rate.

'Mortality' simply means 'death', but what does 'rate' mean in this context? Just counting the total number of infants or children who died in a particular year or location doesn't allow you to compare changes over time or between places, because the total number of people in the population fluctuates. If infant deaths go up or down between two years this might simply be because more (or fewer) babies were born in those years, so more (or fewer) babies died. Expressing the number of deaths as a 'rate per 1000 individuals' (or per 10 000, per 100 000 or per million – it doesn't matter as long as you say what the rate refers to) allows meaningful comparisons to be made between different times or places. For example, we can compare the IMR in the 19th century and the IMR today and see how it has changed without having to allow for any difference in the total number of live births in the past and the present.

Figure 2 shows how infant deaths rose and fell between 1855 and 1880 in Stoke-upon-Trent (an English industrial town famous for its pottery factories in the 19th century) and in England and Wales as a whole.

Figure 2 is a line graph – a method of presenting numerical data plotted on a grid between vertical and horizontal axes, each marked with a scale; the data points are joined by lines that makes it easy to see 'at a glance' how the pattern of values changes from left to right across the graph.

Line graphs are particularly suited to showing time trends (often abbreviated simply to 'trends'), i.e. changes in a sequence of data during a period of time. There is a convention in graph plotting that if one of the variables is 'time', the time scale is plotted on the *horizontal* axis, as it is in Figure 15. We mentioned that infant mortality rates were much higher in the past than they are today. For comparison, the infant mortality rate has not exceeded

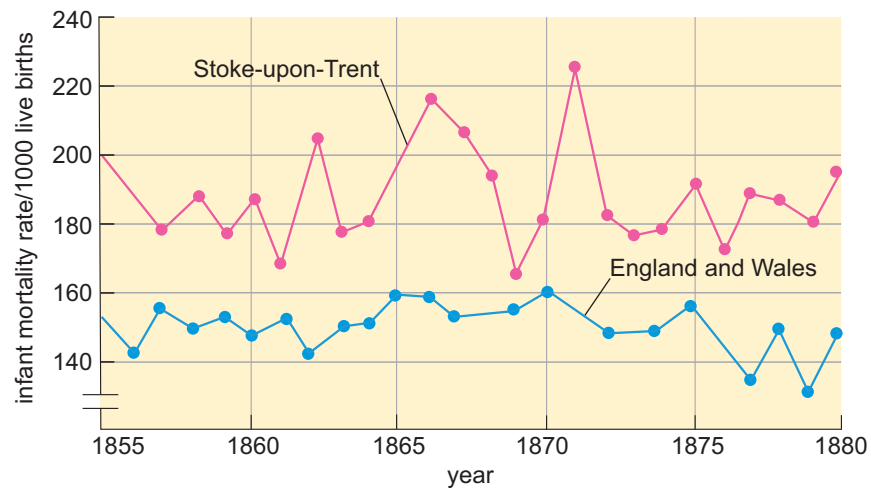


Figure 2 Infant mortality rates (deaths under 1 year of age) per 1000 live births in England and Wales and Stoke-upon-Trent between 1855 and 1880.

100 infant deaths per 1000 live births anywhere in the world at any time in the 21st century and is falling steadily, as Figure 3 shows.

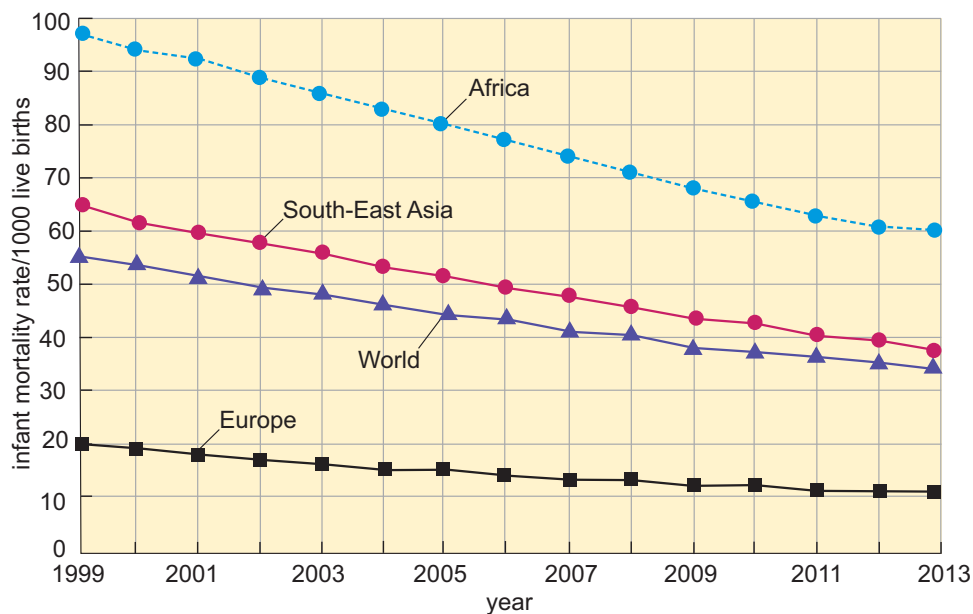


Figure 3 Time trends in the infant mortality rates (IMRs) per 1000 live births in Africa, Europe, South-East Asia and the World between 1999 and 2013.

Although we are rightly appalled by the modern-day loss of infant lives represented in Figure 16, it is hard to imagine that in communities like Stoke-upon-Trent in the 19th century almost a quarter of all babies died before their first birthday. Mortality among older children and adults was also much higher in the 19th century than it is today. We know this because the process of collecting population statistics began in the 19th century, demonstrating that infectious diseases were the major cause of death in England and the rest of the so-called ‘developed’ world until the 1950s, and they remain the major cause in poorer countries today.

2.3 Waterborne infection in 19th-century England

Water contaminated with pathogens is still a major source of infection, despite significant improvements in the provision of filtered drinking water and treatment of sewage in many parts of the World. The present truly resembles the past!

Until well into the 19th century, most Londoners obtained their water from the polluted rivers and streams that flowed through the capital. London's domestic and industrial waste was discharged directly into the rivers or found its way there from over 200 000 cesspits. Several major causes of death in the period were waterborne diarrhoeal diseases and fevers – principally cholera, dysentery and typhoid.

The cartoon shown in Figure 4 was published during a period known popularly as 'The Great Stink' when the Houses of Parliament had to be closed for several weeks due to the foul smell from the Thames River. The cartoon is subtitled 'A Design for a Fresco in the New Houses of Parliament' because of a rumoured plan to move parliament upstream to Hampton Court in Middlesex and it shows how politically important it had become to deal with the health hazards caused by polluted rivers.



FATHER THAMES INTRODUCING HIS OFFSPRING TO THE FAIR CITY OF LONDON.
(A Design for a Fresco in the New Houses of Parliament.)

Figure 4 'Father Thames introducing his Offspring to the Fair City of London', cartoon by Sir John Tenniel, published in *Punch* magazine, 3 July 1858. The 'offspring' are labelled Diphtheria, Scrofula and Cholera (scrofula meant tuberculosis).

The vicious cycle of river pollution and waterborne infection was repeated in other industrial cities of the period, as Frederick Engels (1820–1895), the son of a German textile manufacturer, found when he came to work in his father's factory in Manchester. His outraged account, written in 1844, of what he saw there gives an unparalleled insight into the causes of infectious diseases at that time:

The manner in which the great multitude of the poor is treated by society today is revolting. They are drawn into large cities where they breathe a poorer atmosphere than in the country; they are relegated to districts which, by reason of the method of construction, are worse ventilated than any others; they are deprived of all means of cleanliness, of water itself, since pipes are laid only when paid for, and the rivers so polluted that they are useless for such purposes; they are obliged to throw all offal and garbage, all dirty water, often all disgusting drainage and excrement into the streets, being without other means of disposing of them; they are thus compelled to infect the region of their own dwellings.

(Engels, F. 1969 [1845])

There are striking similarities between Engels' description of the conditions of life for the poor of 19th century English cities, and communities who live in shanty settlements, refugee camps and disaster zones in the modern world (Figure 5). In 2012, around 2.5 billion (or 2500 million) people had no access to sanitation and around 750 million had no access to safe drinking water.

It was well understood by city dwellers in 19th-century England that the water they drank was filthy and a major source of disease (Figure 6).

The caption at the top of this 1828 etching reads: 'MICROCOSM dedicated to the London Water Companies. Brought forth all monstrous, all prodigious things, hydras and gorgons, and chimeras dire.' The caption underneath reads: 'MONSTER SOUP commonly called THAMES WATER, being a correct representation of that precious stuff doled out to us!'

As Figure 6 demonstrates, examination of microscopic animal and plant life in water was well established by the early 19th century, but the existence of cells as small as bacteria was not proven until the 1890s, when dyes to stain individual cells and render them visible under new and more powerful microscopes enabled 'microbes' to be directly observed.

In the early-to-mid-19th century, the lack of scientific knowledge that bacteria were the root cause of many major diseases of the period did not deter pioneers (like John Snow who you will learn about in the next section) who tackled the death toll from infections, such as cholera, through application of the scientific method.



(a)



(b)

Figure 5 The Kibera shanty settlement near Nairobi, Kenya, is home to at least half a million people who have no sanitation and collect all their water from standpipes.

2.4 John Snow, cholera and the Broad Street pump

Cholera is a diarrhoeal disease caused by a specific type of bacteria (their Latin name is *Vibrio cholerae*) that occur naturally in environmental sources of water, such as rivers, lakes and estuaries. Cholera was endemic (always present) in 19th-century England, as it is in many parts of the world today. People infected with cholera bacteria suffer from diarrhoea, which results in rapid dehydration and loss of essential salts from the body. Unless the fluids and salts are rapidly replaced, death follows in about one-third of cases within a few days. In 19th-century London, and in impoverished communities all over the modern world, contamination of drinking water, food, hands and clothes by cholera bacteria shed in the diarrhoea of sufferers is almost impossible to prevent and the disease quickly spreads.



Figure 6 'Monster soup' by William Heath, published in 1828, shows a woman dropping her teacup in horror after seeing a magnified view of a droplet of London water.

Cholera was first recorded in London in 1831 and numerous outbreaks followed. In 1854 the numbers of cholera cases rose sharply across the city, causing over 850 deaths. No one knew what caused cholera at the time and the health authorities were powerless to halt the epidemic – until Dr John Snow (1813–1858), a London doctor, conducted an experiment that has become not only a classic illustration of the scientific method but also of epidemiology. Epidemiology [eppy-deem-ee-yoll-odjee] is the statistical study of data on the occurrence, distribution, potential causes, prevention and control of diseases, disorders and disabilities (the three Ds) in human populations. Epidemiologists (experts in this discipline) collect and analyse population data to discover 'Who gets ill and why?'

Snow plotted the deaths from cholera on a map of all the households in the district of London roughly corresponding to modern-day Soho (Figure 7a). He observed that most of the cholera households in this district obtained their water from the pump in Broad Street (Figure 7b). Snow took the simple step of removing the handle from the pump and the local cholera outbreak rapidly subsided. The origins of 'public health' as a discipline can be traced back to this experiment. Public health is defined as:

The science and art of promoting and protecting health and well-being, preventing ill-health and prolonging life through the organised efforts of society.

(The UK's Faculty of Public Health, n.d.)

In the next section, you will conduct an activity where you will analyse John Snow's experiment to identify the features that characterise the 'scientific method' of investigation.



(a)

(b)

Figure 7 (a) A redrawn portion of John Snow's map of the spread of cholera in Soho, London, in 1854. The blue bars represent the number of fatal cases in each household. (b) A replica of the Broad Street pump in modern-day Broadwick Street, with the *John Snow* public house in the background.

2.5 John Snow's experiment

In 1854 Snow did not know what was in the water from the Broad Street pump, or if the water was indeed the source of cholera. *Vibrio cholerae* bacteria were not identified until almost 30 years later in India in 1883, by the pioneering German physician and scientist Dr Robert Koch (1843–1910; Figure 8).

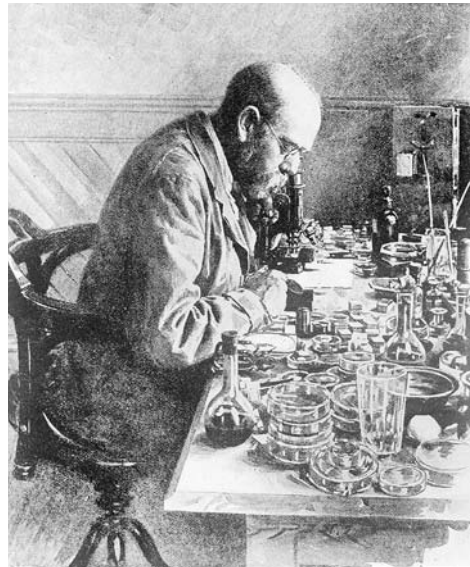


Figure 8 Robert Koch, photographed in 1896 or 1897 at work in his laboratory.

Activity 1 What does Snow's experiment tell us about the scientific method?

Allow about 30 minutes to work through this activity and answer all the questions.

Despite his ignorance of bacteria, Snow's approach to identifying and eliminating the source of the 1854 outbreak elegantly illustrates the main features of the scientific method. Take a moment to look back at the definitions in Section 2.1 and then answer the following questions:

Question 1

How does Snow's starting point for tackling the outbreak illustrate the scientific principles of *systematic observation* and *measurement*?

Answer

He made an accurate map of the households in his district and recorded the number and location of every death from cholera. He had a fixed, pre-determined 'system' for making observations and measurements of the scale and geography of the outbreak.

Question 2

When Snow looked at his completed map, what pattern did he *observe* in the data and what *hypothesis* did the data suggest to him?

Answer

He *observed* that most of the affected households took their water from the same pump and he formed the *hypothesis* that something in the water had caused them to develop cholera.

Question 3

Snow's *experiment* was to remove the handle from the pump, so the local population had to get their water from elsewhere. Why is it crucial to the scientific method that Snow continued to measure the number and location of cholera deaths *after* the pump handle was removed?

Answer

A scientific hypothesis must be *testable* in order to rule it in or out as a valid explanation. Snow's hypothesis that water from the Broad Street pump was the source of cholera would have remained just a 'guess' unless he put it to the test by cutting off this water supply and measuring the subsequent decline in the number of cholera deaths.

Snow's experiment demonstrates the two essential components of what scientists call a causal association (sometimes referred to as a causal 'correlation'), i.e. he found evidence that a specific event is the cause of a specific outcome. In Snow's case, the two components of his evidence can be expressed simply as:

- intact pump is associated with many cases of cholera, and
- removing the pump is associated with declining cases of cholera.

We can illustrate the problems in proving a causal association and some other aspects of the scientific method with an even earlier experiment to prevent an infectious disease, this time involving smallpox.

2.6 Edward Jenner, smallpox and vaccination

Smallpox begins with a high fever, fatigue, muscle pain and headaches, followed by the eruption of characteristic sores all over the body, which become filled with pus – a thick, yellowish fluid containing infected and dead cells.

Smallpox is caused by a virus, but it was not until the late 19th century that ‘infective agents’ much smaller than bacteria were shown to remain in filtered extracts from diseased animals and plants. Viruses were not ‘seen’ until the electron microscope was invented in the 1930s.

Edward Jenner (1749–1823) was a doctor in the small English country town of Berkeley (Figure 9). Smallpox was then endemic in England, causing deaths in about one-third of cases, but those who recovered were protected from smallpox for the rest of their lives. This fact was well known in India and Turkey long before this time. The practice of ‘inoculation’ (intentional exposure of children to mild cases of smallpox) became fashionable among wealthier parents in the 18th century, who hoped to protect their children from a subsequent fatal outbreak. The risk of dying from such intentional exposure was less than the risk in a smallpox epidemic, and Jenner himself had been inoculated as a child.



Figure 9 Edward Jenner, painted in about 1800 by John Raphael Smith. Note the cow and milkmaid in the background.

2.7 Edward Jenner's experiment

Jenner was aware of the country folklore that people who caught cowpox were also somehow protected from smallpox. Cowpox was a mild disease in cows and humans, characterised by the development of a small number of pustules on the skin that resembled smallpox pustules, but resolved without causing much concern.

In 1796, Jenner put the folklore to the test in an astonishingly risky and entirely unethical experiment by modern standards (Box 1). Jenner took pus from cowpox pustules on the hand of a dairymaid and rubbed it into scratches he made on the arm of an eight-year-old boy, James Phipps, the son of his gardener (Figure 10). James developed mild cowpox, from which he quickly recovered. Some weeks later, Jenner scratched James's arm again and introduced pus from smallpox pustules – a procedure that he repeated on several occasions. Thankfully, Jenner's experiment was successful and James did not develop smallpox.



Figure 10 Edward Jenner vaccinating James Phipps in 1796, painted by Ernest Board in the 1920s.

Jenner had no knowledge of what caused smallpox or why exposure to cowpox was protective, but he spent the rest of his life promoting his method and supplying dried cowpox matter to people all over the world. The term vaccination is derived from *vacca*, the Latin for cow, reflecting its origins in Jenner's experiments. Nowadays, vaccination and the modern term immunisation are used interchangeably to refer to exposure of an uninfected person to a vaccine, i.e. material derived from an infectious organism, which provokes a protective response from the recipient's immune system if the recipient is subsequently exposed to the live organism from which the vaccine was derived.

Box 1 Ethics in medical and scientific experiments

We've said that Jenner's experiment on James Phipps was 'unethical' by modern standards, but what does this mean? Medical ethics is a set of principles that govern the way that doctors and other health professionals conduct their interactions with patients. These principles began with the Hippocratic Oath, which is still sworn in one version or another in many countries when doctors graduate from medical training. The portion of the oath that relates most closely to Jenner's experiment translates roughly as:

I will prescribe treatments for the good of my patients according to my ability and my judgement and never do harm to anyone.

Jenner certainly intended to 'do good' to James Phipps by protecting him from smallpox, but he could also have caused great 'harm' if James had died from the disease. If he had carried out his experiment today, Jenner would have been struck off the Medical Register, meaning that he could no longer practice as a doctor.

The modern-day principles of medical ethics are summarised as follows:

- respecting the patient's autonomy – the right to be involved in all aspects of their treatment and to have their wishes respected
- acting in the patient's best interests (known as the principle of 'beneficence')
- doing no harm to the patient (the principle of 'non-maleficence')
- maintaining justice, fairness and equality of treatment for all patients
- communicating clearly and truthfully to ensure informed consent to treatment and other interventions
- maintaining confidentiality about the patient's medical condition, which should not be discussed with anyone except health professionals involved in their care without the patient's consent.

If a medical or scientific experiment involving humans or other animals as subjects is conducted today, the researchers must first obtain permission from the relevant Research Ethics Committee governing the proposed research.

2.8 Edward Jenner and the scientific method

Now you know what Jenner did, the following activity prompts you to analyse how this action illustrates the scientific method and identify how it departs from accepted practice in modern day experiments.

Activity 2 What does Jenner's experiment tell us about the scientific method?

Allow about 20 minutes to work through this activity and answer all the questions.

Question 1

Summarise the hypothesis on which Jenner based his experiment on James Phipps and write your hypothesis in your notes. (Hint: remember that a hypothesis is a statement (not a question) proposing an explanation for an observation as a starting point for further investigation.) Then compare your hypothesis with ours below.

Answer

Your wording may be a little different to ours but it should capture the same point: 'Exposure to cowpox infection will result in lasting protection against smallpox infection.'

Question 2

Fortunately for James, Jenner's hypothesis proved to be correct. However – unlike John Snow when he removed the handle from the Broad Street pump – Jenner could not *prove* that exposure to cowpox *caused* the protection against smallpox that he observed when he exposed James to the potentially fatal infection.

Can you explain why Jenner's experiment on James does not prove a *causal association* (also known as a causal correlation) between recovery from cowpox and protection against smallpox?

Answer

There is an alternative explanation – James might have been exposed to mild smallpox earlier in his life, which protected him from reinfection when Jenner exposed him to smallpox in 1796.

Question 3

Suggest an even more unethical experiment that Jenner would have had to conduct in order to demonstrate a causal association between cowpox recovery and smallpox protection?

Answer

As far as we know Jenner never attempted this, but he would have had to find another 8-year-old boy and expose him to smallpox at the same time as James, but without previously exposing the second child to cowpox. If Jenner's hypothesis was correct, this (imaginary) second child would develop smallpox and James would remain well.

The 'second child' in this imaginary experiment is what modern day investigators call a control, that is, an individual – or more usually a significant number of individuals – who resemble the 'experimental' individual or group in as many ways as possible, *except* that they are not exposed to the experimental condition.

Over time, the large number of cases recorded by Jenner and others who copied his method established that cowpox successfully protected most (but not all) of those exposed to it against smallpox. They applied the scientific method by counting and comparing numbers of smallpox cases in cowpox vaccinated and unvaccinated individuals during smallpox outbreaks. The effectiveness of vaccination was demonstrated by the lower percentage of smallpox cases in the people they had vaccinated with cowpox, compared with the rest of the population who had not received the vaccine. Although the discipline of epidemiology was not established until the mid-to-late 19th century, Jenner and his followers were (in effect) collecting and analysing epidemiological data to establish proof that cowpox vaccination worked.

2.9 The eradication of smallpox

Jenner's discovery had relatively little impact on smallpox outbreaks in his lifetime, partly because it proved difficult to generate sufficient quantities of cowpox vaccine in order to vaccinate large numbers of people. Moreover, the method of producing the vaccine in cattle was unreliable and the extracts were often contaminated with other pathogens. Some feared the 'unnatural' consequences of a vaccine extracted from cows, as a famous cartoon of the early 19th century illustrates (Figure 11).



Figure 11 Cartoon by James Gillray, published in 1802, depicting Edward Jenner vaccinating against smallpox. The caption reads 'The Cow-Pock — or — the Wonderful Effects of the New Inoculation!' — Note... the Publications of J. and A. Vaccines Society.

Yet despite many setbacks in the intervening years, the last case of naturally transmitted smallpox anywhere in the world occurred in 1977 and in 1980 the World Health Organization (WHO) announced that smallpox had been eradicated globally. Eradication refers to the total elimination of all the infectious agents causing a particular disease in all populations throughout the World. The smallpox virus now only exists in small quantities in secure laboratories and there is controversy about whether even these samples should be destroyed. Smallpox is the first, and so far only, infectious disease to be globally eradicated.

Worldwide success against smallpox so soon after the WHO began its global eradication programme in 1966 raised hopes that mass vaccination would soon 'win the war' against other infectious diseases. There are several reasons why it took almost 200 years from Jenner's first successful vaccination in 1796 to eradicate smallpox. It was not until the 1950s that an effective, stable vaccine derived from a modified pox virus — named *vaccinia* in honour of Jenner's discovery — was produced in sufficient quantities for mass vaccination against smallpox. Optimistic predictions

about the potential impact of other vaccines failed to take into account the unusual biological conditions that made smallpox uniquely susceptible to eradication.

The special features of the smallpox vaccination campaign that made it so successful can be summarised as follows:

- A single vaccination with vaccinia provokes such a strong protective response that the individual develops lifelong 'immunity' to smallpox; most other vaccines require repeated 'booster' doses to achieve this level of protection.
- Smallpox viruses survive only in humans – there are no non-human hosts, so there is no 'reservoir' of pathogens in other animals that can be transmitted to people; several other major pathogens (e.g. influenza viruses and TB bacteria) are zoonoses, i.e. they can be transmitted from animals to humans.
- Smallpox has such unique, easily recognisable diagnostic signs (Figure 12) that medical expertise is not needed to identify suspected cases, and fear of smallpox strongly motivates community members to report them immediately to the health authorities.
- The characteristic pustules (Figure 12) appear very soon after someone is infected, so they can often be quarantined (isolated) before the infection spreads and their contacts can be identified, vaccinated and kept under surveillance.



Figure 12 This child with smallpox was photographed in Bangladesh in 1973 – four years before the country was declared free from the disease.

Session 2 quiz

This quiz allows you to test and apply your knowledge of the material in Session 2.

Session 2 quiz

Open the quiz in a new window or tab then come back here when you're done.

Summary to Section 2

In Session 2 you have been introduced to the concept of the scientific method and should now appreciate how useful it has been in combating infectious disease. The power of using systematic observation to identify correlations and develop testable hypotheses is well illustrated by the story of John Snow and the 1854 cholera outbreak in London. This example also underlines the terrible effect of pollution on human health – in particular as a cause of water-borne infectious diseases – and the utility of concerted public health campaigns.

Through a second historical tale, the example of Edward Jenner and smallpox, you have also learned about vaccination and its capacity to fight infectious disease. As we have described, the success of vaccination against smallpox has been absolute and the WHO have declared smallpox to be globally eradicated.

However, the war against infectious disease is far from over. Although effective vaccines now exist against diphtheria, measles, polio and several other infectious diseases, current vaccines against some others, including cholera, are only weakly effective or short-lasting. In 2015, there were still no effective vaccines against several life-threatening infections, including HIV/AIDS, but a vaccine against malaria was looking promising and the first Ebola vaccine proved highly effective in initial trials (Henao-Restrepo et al., 2015). Another problem is illustrated by influenza viruses, which change their structural features so rapidly that this year's flu vaccine may not give protection against the viruses in circulation next year. And as you have learned, although entirely preventable, pollution remains a major source of water-borne infectious diseases in much of the developing world today. Thus, effective strategies to combat infectious disease remain as relevant today as in Jenner's era.

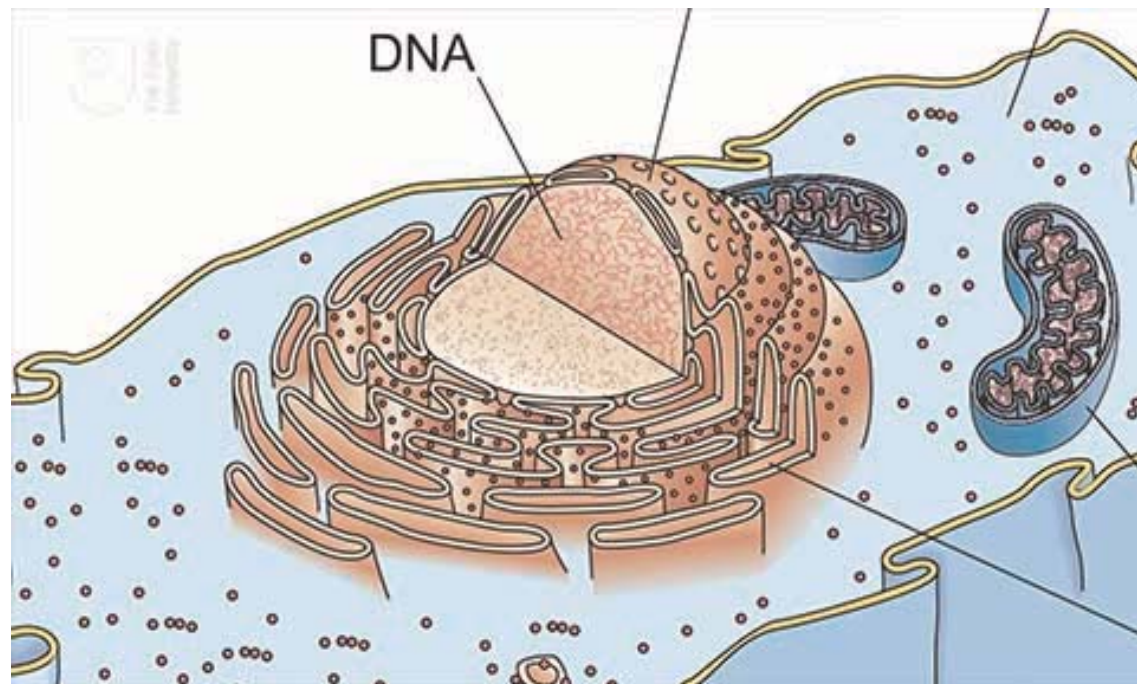
You can now go to Session 3.

Session 3

Introduction

Session 3 provides a brief overview of the many different infectious agents, also known as pathogens [path-oh-jens], that cause infectious diseases in humans and the ways in which these pathogens are transmitted between people, the environment and other animals. The most numerous pathogens are bacteria, as you will discover. In fact, there are more than twice as many different types of bacteria that cause human disease compared to the number of infection causing viruses.

In the video you'll learn more about these two different types of pathogens and how they are different from one another.



3.1 How many pathogens cause human disease?

Human infectious diseases are caused by over 1400 different pathogens (Table 1). Some of the diseases they cause are never or rarely fatal, but nevertheless result in millions of acute illness episodes and chronic disabling conditions. Only about 20 pathogens have high mortality rates, causing around two-thirds of the estimated 10 million human deaths due to infection every year. In this section we will focus on some of the most important pathogens, which affect huge numbers of people across the world.

Table 1 Pathogen types and the number that cause infectious diseases in humans, estimated in 2005.

Pathogen type	Number causing human disease
Parasites: multicellular	287
Protists: single-celled	57
Fungi: e.g. yeasts	317
Bacteria	538
Viruses	206
Prions	2
Total	1407

(Data from Woolhouse and Gowtage-Sequeria, 2005)

Examine the data in Table 1. We have listed the pathogens in size order: from the largest – the multicellular (which means many celled) parasites – in the top row, to the smallest – prions [pry-onz] – in the row second from bottom, above the column total. The distinctive biology of each of the six pathogen types is described in later sections, along with the most important diseases they cause.

The table also shows how many pathogens *other than* the more familiar bacteria and viruses infect us. You may have been surprised that 287 different multicellular parasites and over 300 types of fungi [fung-guy] are human pathogens.

Bacteria are the most numerous human pathogens and their impact on human health is likely to increase as many become resistant to antibiotics – the drugs specifically used to control them.

Humans are also infected by over 200 viruses, but only two prions are currently known to cause human disease. Unlike the other four pathogen types, viruses and prions are not composed of living cells. It will help you to understand their biology if we take a short detour to describe the

structure of cells. When you get to viruses and prions you will see how different they are from cell-based life forms.

3.2 Cells and their relationship to pathogens

Parasites, protists, fungi and bacteria are composed of cells – the basic unit from which the bodies of living organisms are constructed. Parasites and other animals (including humans) and plants are multicellular, i.e. their bodies consist of many cells. Pathogenic protists and bacteria are single-celled organisms. Fungi can exist in single-celled and multicellular forms, and some fungal cells can merge to form long filaments.

Bacterial cells are different in several respects from the cells of all other organisms. Figure 1a is a highly simplified diagram of an animal cell and Figure 1b represents a typical bacterium.

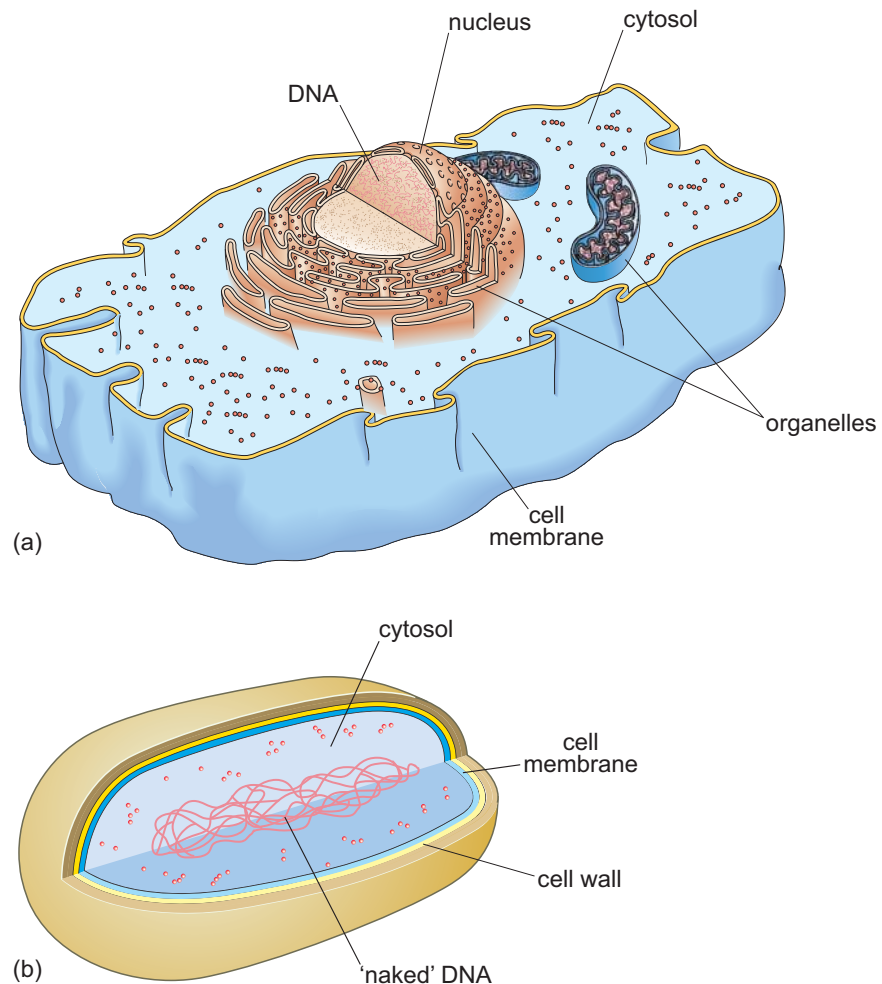


Figure 1 Simplified diagrams of (a) an animal cell; (b) a bacterium (not drawn to scale – a typical animal cell is about 10 times larger on average than a typical bacterium).

There are many similarities between animal and bacterial cells: for example, they both have a cell membrane, a complex structure that controls the passage of substances into and out of the cell. Around 70% of the internal

contents of both cell types is a watery fluid called cytosol [sigh-toh-soll], in which many chemical reactions take place.

The cytosol of animal, plant, protist and fungal cells contains many different structures, collectively called organelles [or-gan-ellz]. The largest single organelle is the nucleus [nyook-lee-uss] enclosing the genetic material (DNA) that governs the functioning of the cell.

- How does the description of an animal cell that you have just read differ from what you can see of the bacterium from the diagram in Figure 1b?

The bacterial cell doesn't contain any organelles and its DNA is 'naked' in the cytosol, not enclosed in a nucleus. Note that bacteria also have an additional protective layer (the cell wall) outside the cell membrane, surrounded by a slimy coating.

Next, we briefly explain how all living organisms, including bacteria, are distinguished from each other by unique scientific names.

3.3 Organisms and their scientific names

Organisms are classified by scientists into hierarchies that reveal how they have evolved from common ancestors. We are not concerned with this evolutionary hierarchy in this course, but you should understand how the unique two-part Latin names that distinguish different organisms unambiguously to scientists have been derived.

The first part of the Latin name indicates the *genus* [jee-nus] of the organism (the genus is a subdivision of the much larger *family* to which the organism belongs). Organisms in the same genus are very closely related. The second part of the Latin name indicates the *species* [spee-sheez] of the organism, which tells you that it has certain unique characteristics that distinguish it from all other species in the same genus. The individual members of a species are not identical; for example, there are obvious differences between individual humans, but we all belong to the species *Homo sapiens* [homm-oh sapp-ee-yenz].

Scientific publications give an organism's two-part Latin name in full the first time it is used, but generally abbreviate the genus to its first letter thereafter, as in *H. sapiens*. Note that the genus always begins with a capital letter, the species begins with a lower case letter, and both parts of the name are printed in *italics* (or you can underline them in handwritten notes).

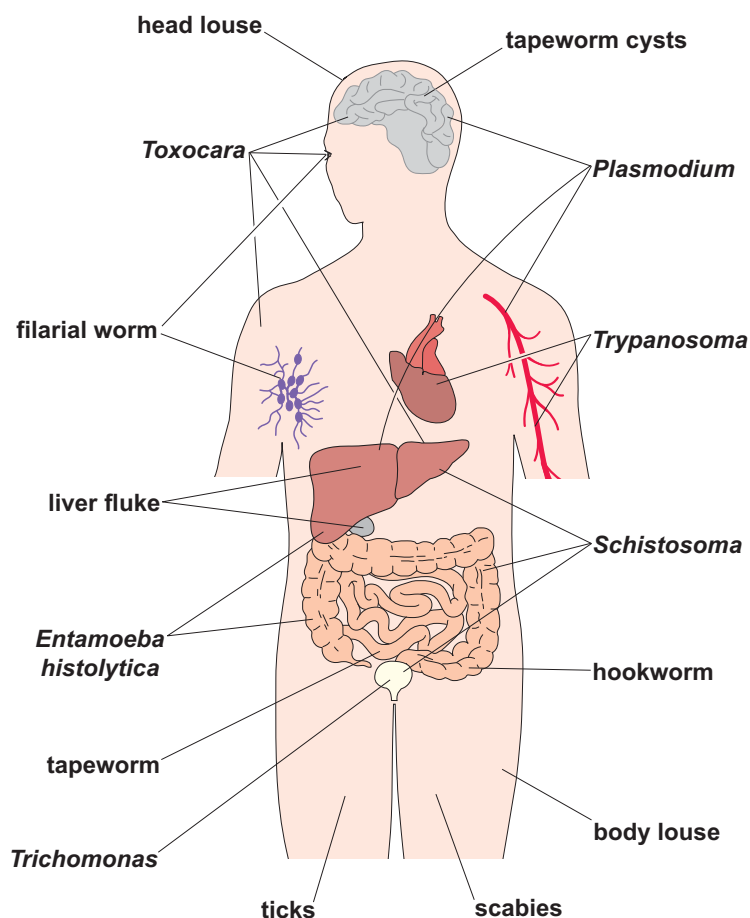
Viruses and prions are not organisms, so they don't have Latin scientific names. With these points in mind, we can describe the biology of each of the pathogen types that were listed in Table 1.

3.4 Introducing parasites and protists

The term parasite refers to an organism that lives in or on the body of another organism (its host) and benefits at the host's expense, so strictly speaking all pathogens are 'parasites'. However, in discussions of human infectious diseases, the term is restricted to:

- multicellular parasitic worms
- pathogenic protists: single-celled organisms with similar cells to those of animals (multicellular protists exist, but none are human pathogens).

In 2013, the World Health Assembly identified 17 so-called 'Neglected Tropical Diseases' affecting over one billion people; it is notable that eight are caused by parasites and three by protists. Figure 2 shows sites on the surface or inside the human body that parasites and protists can infect. Click or tap on each of the labels in Figure 2 to reveal a brief description in a box below the diagram of the disease states the pathogen causes and the site(s) it occupies in the body.



(This is a static version of interactive Figure 3. Please view Figure 3 on the website to access the additional details.)

Figure 2 Some parasites and pathogenic protists, the diseases they cause, and the sites they infect in the human body.

3.5 Ectoparasites and endoparasites

The 287 species of multicellular parasites in Table 1 all live inside the human body. They are the major category of multicellular parasite and are known as endoparasites (*endon* is Greek for ‘within’). Endoparasites can invade vital organs or live in the gut, bloodstream or tissues. The endoparasites of humans belong to four types of worms:

- roundworms
- tapeworms
- filarial (thread) worms
- flukes (or flatworms).

The examples that follow illustrate the often forgotten impact of multicellular endoparasites on human health and the variation in their life cycles and transmission routes. However, before we go on, it is worth observing that there exists an additional category of multicellular parasites: ectoparasites.

Ectoparasites are invertebrates (animals without backbones) that live on the surface (*ektos* is Greek for ‘outside’) of the human body, such as head lice, body lice and ticks. Their bites can cause intense irritation and they also transmit some potentially life-threatening pathogens to humans, such as the bacteria that cause typhus [tye-fuss]. People with typhus develop a very high fever (body temperature well above the normal 37 °C), severe headaches, muscle pain and a dark rash. It can spread rapidly in overcrowded communities, where lice and ticks proliferate because people cannot easily wash themselves or their clothes (Figure 4).

3.5.1 Roundworms, hookworms and anaemia

Pathogenic soil-transmitted roundworms (or nematodes) are transmitted harmlessly from person to person via worm eggs shed into the soil in human faeces. At least 1700 million (or 1.7 billion) people worldwide have these worms in their intestines. Children in heavily infected communities may harbour more than 1000 worms, causing diarrhoea, discomfort and restricting the child’s growth.

- Can you suggest how children get worm eggs onto their hands and transfer them from hand to mouth?

Particles of dirt contaminated with worm eggs stick to the hands when children play or work on soil; if hands aren’t washed before eating, the eggs can easily transfer to the child’s mouth.



Figure 4 Infectious diseases are easily transmitted in the overcrowded conditions of refugee camps, like this one on the Burma (Myanmar)–Thailand border.

Lack of water and soap for handwashing, as well as lack of sanitation, are major contributory factors in hand-to-mouth transmission of all pathogens, not only worms.

Hookworms (Figure 5) are soil-transmitted roundworms measuring 5–10 mm (millimetres), which hook onto the inner wall of the human gut and suck blood from the surrounding blood vessels. Over 400 million people are infected with hookworms and as a result suffer a type of anaemia [an-ee-mee-ah] due to loss of red blood cells. Anaemia caused by hookworms contributes to *stunting* in children (being short for their age) and *wasting* (being underweight for their height). Hookworms also present a risk to pregnant women and their unborn or newborn babies due to the adverse effects of maternal anaemia.

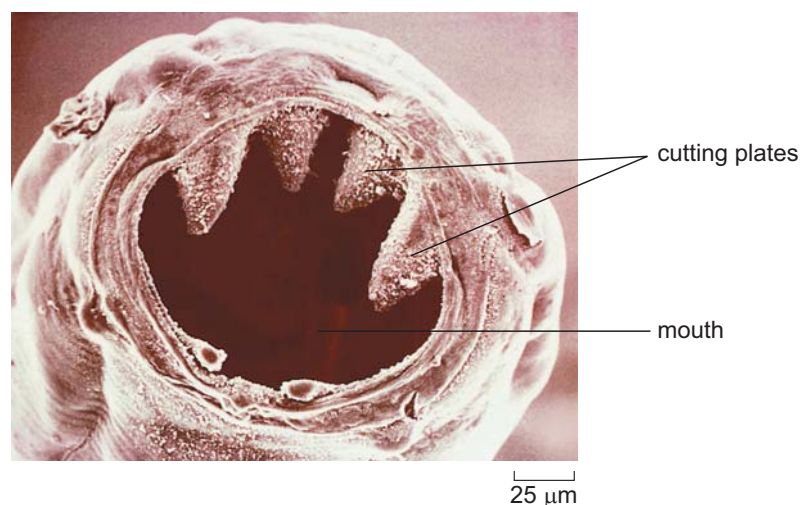


Figure 5 The magnified head of a hookworm (*Ancylostoma duodenale*), photographed with a specialised (scanning electron) microscope.

The scale bar in the bottom right corner of Figure 5 gives a measurement in micrometres (μm); one micrometre is one-thousandth of a millimetre (mm) and one-millionth of a metre (m).

3.5.2 Tapeworms and epilepsy

Tapeworms are easily distinguished from roundworms because they have long flattened bodies (resembling a tape, hence their name). They are the largest of the worms that infect people; some species can grow up to 10 metres in length. Different species of tapeworms are parasites of cattle, pigs, dogs and even fish, but they can also infect humans.

Although deaths due to tapeworms are rare, they cause pain in the abdomen and reduce the nutrients available to their human host. However, the main health risk is from epilepsy, i.e. brain seizures or fits. Figure 6 shows the life cycle of the pork tapeworm (*Taenia solium*), the species associated with acquired epilepsy. Contrary to popular belief, people are rarely infected through eating undercooked pork.

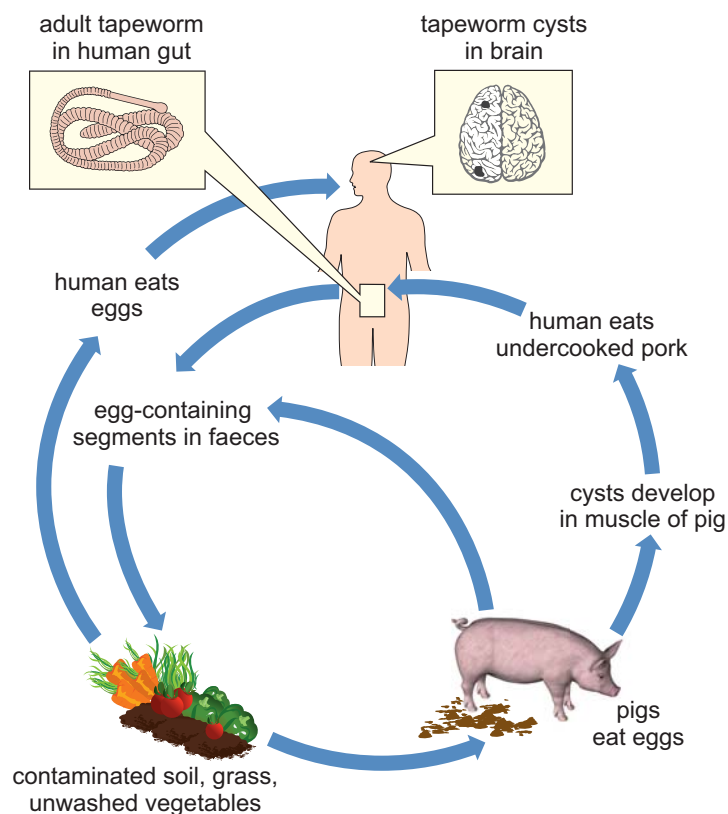


Figure 6 The life cycle of the pork tapeworm, *Taenia solium*.

Tapeworm eggs in pig faeces contaminate land around human settlements where pigs graze. Soil is also contaminated with worm eggs from human faeces if people are forced to defaecate in the open because there is no sanitation. People are infected when they swallow the eggs in soil on unwashed vegetables or when eating with unwashed hands. The eggs hatch

into larvae [lar-vee] in the human gut; larvae (singular, larva) are an immature stage of development in many invertebrates. Worm larvae may develop into adult tapeworms in the human gut, but some burrow into the person's muscles, eyes and brain, where they 'encyst', i.e. become encased in a tough outer covering. Cysts in the brain (Figure 7) can trigger epileptic seizures. Around 30% of people with epilepsy in Latin America, Sub-Saharan Africa and South-East Asia have pork tapeworm cysts in their brain (Ndimubanzi et al., 2010).

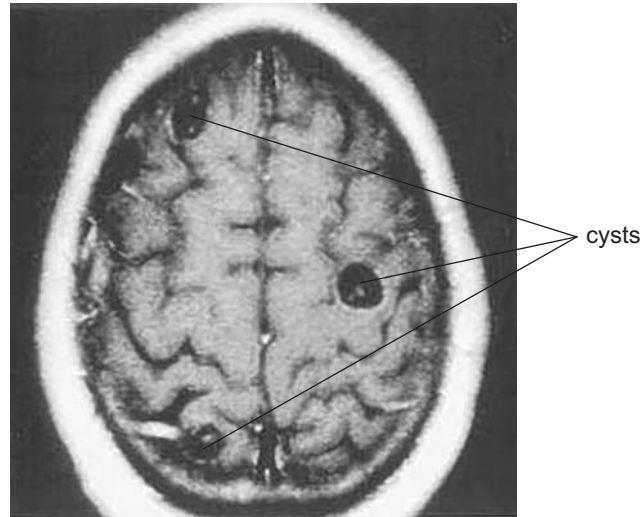


Figure 7 Pork tapeworm cysts in a human brain revealed by medical imaging.

3.5.3 Filarial worms, elephantiasis and river blindness

Adult filarial worms are thread-like parasites measuring 40–100 millimetres in length, whose description 'filarial' [fill-air-ee-uhl] comes from the Latin for filament. The diseases they cause are all vector-borne, transmitted when a biting invertebrate transfers microscopic worm larvae (around 300 micrometres long) to a human host as it takes a blood meal.

The disease once known as elephantiasis because of the appearance of infected limbs (Figure 8) is properly called lymphatic filariasis [lim-fatt-ik fill-arr-eye-ass-iss]. Most cases are due to one species, *Wuchereria bancrofti*, transmitted to humans by mosquitoes. The filarial worm larvae block the fine lymphatic tubules that collect tissue fluid from all over the body and return it to the blood stream. The blockages cause painful inflammation and swelling, as fluid collects in the lower limbs and genitals. More than 120 million people are infected with filarial worms in 73 countries, including Bangladesh, India, Indonesia, Ethiopia, Nigeria and the Philippines, and 40 million people are severely disabled by them.

The microscopic larvae of another species of filarial worm (*Onchocerca volvulus*) are transmitted by blackflies that bite humans. The larvae cause skin lesions that itch relentlessly, but the larvae also invade the eyes and



Figure 8 Swelling and inflammation caused by filarial worms blocking the drainage of tissue fluid from the scrotum and right leg.

cause ‘river blindness’, so-called because blackflies breed in fast-flowing rivers, so this disabling condition only occurs in riverside communities.

3.5.4 Flukes, freshwater snails and schistosomiasis

Rivers, lakes and streams are also essential to the transmission of some species of flukes [flookz] or flatworms, which have flattened ‘leaf-shaped’ bodies. Around 250 million people every year are infected with blood or liver flukes from the genus *Schistosoma* [shist-oh-soh-mah], so the diseases they cause are called schistosomiasis [shist-oh-soh-myah-siss].

Schistosoma flukes must complete part of their life cycle in freshwater snails, which shed microscopic larvae into the water. When people enter infected water to fish or wash themselves or their clothes (Figure 9), the larvae penetrate the person’s skin along the track of hairs, usually on the legs. The larvae mature into adult flukes (10–16 millimetres long) in the person’s body. Male and female flukes mate and produce eggs with sharp spines that damage blood vessels, mainly in the liver, gut and bladder. Fluke eggs excreted in the faeces and urine of infected people are flushed into water sources in the environment, where they hatch into larvae, which reinfect aquatic snails and the cycle begins all over again.

Figure 3.9



Figure 9 The larvae of *Schistosoma* flukes may penetrate the skin of people who use this Ethiopian lake as their only water source.

3.6 Malaria and other protist diseases

The pathogenic protists that infect humans are all single-celled organisms, formerly called ‘protozoa’. They are responsible for a range of diseases, including:

- dysentery (bloody diarrhoea) caused by waterborne protists similar to the amoebae [amm-ee-bee] commonly found in freshwater ponds
- sleeping sickness, caused by protists transmitted via the bite of tsetse flies
- leishmaniasis [leesh-man-eye-ah-sis] transmitted by biting sandflies; *Leishmania* protists cause painful lesions in the skin, affecting around one million people (Figure 10a), or potentially fatal enlargement of the liver and spleen with up to 400 000 cases annually (Figure 10b).



(a)



(b)

Figure 10 Signs of infection with *Leishmania* protists: (a) the skin lesion on this woman's cheek; and (b) this boy's enlarged abdomen and wasted upper body.

The following activity describes the life cycle, impact and prevention strategies against the most widespread infectious disease caused by a protist – malaria.

Activity 3 Malaria: a vector-borne protist infection

Allow about 10 minutes for this activity.

The protists that cause malaria belong to the genus *Plasmodium* [plazz-moh-dee-umm]. Study their life cycle in Figure 35 and then answer the questions below the diagram.

Figure 3.11

Question 1

How are the protists that cause malaria transmitted to a new human host?

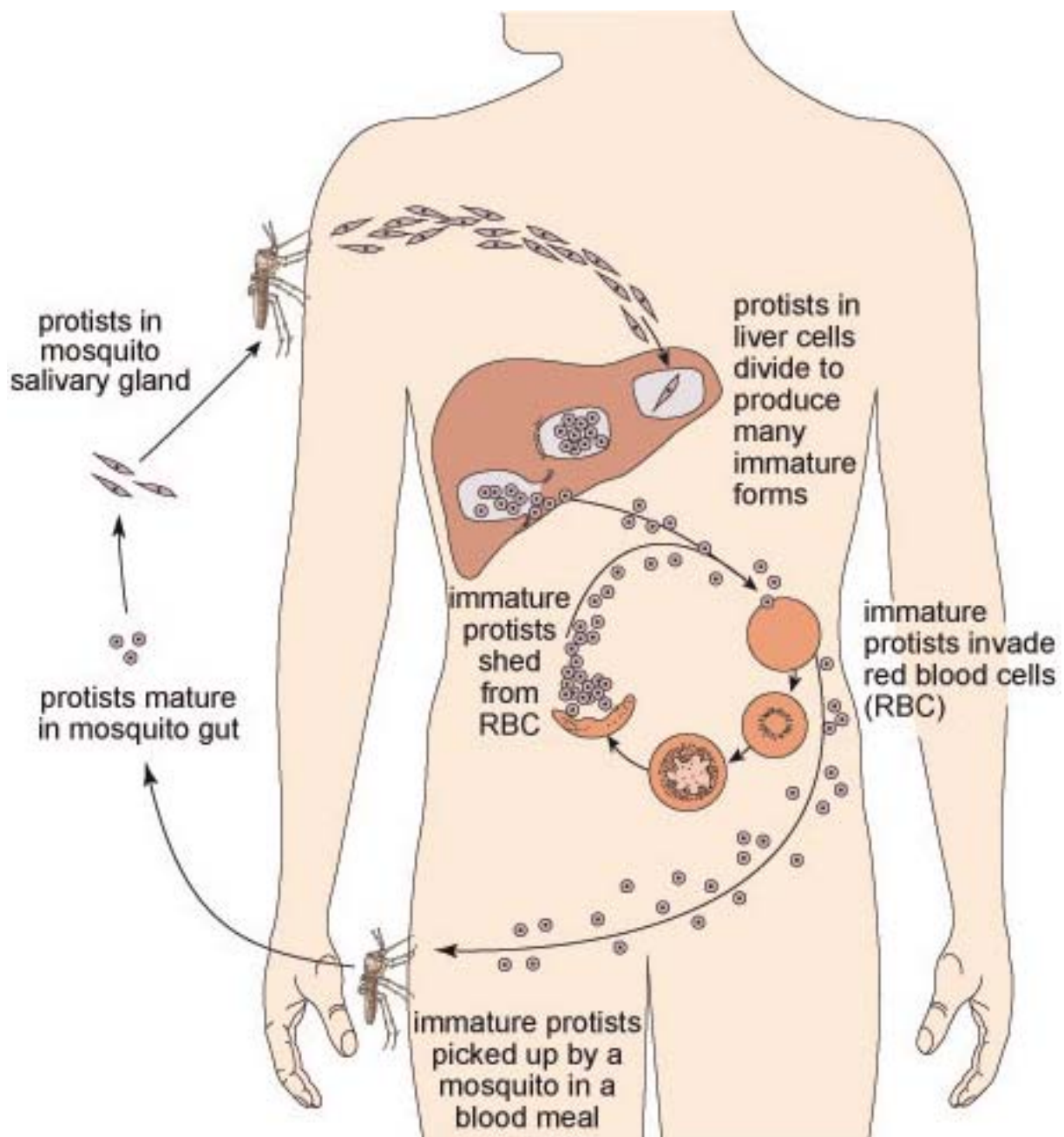


Figure 11 Life cycle of the protists that cause malaria. Details of the developmental stages in humans and mosquitoes have been simplified.

Answer

When an infected mosquito bites someone to take a blood meal, protists in the mosquito's saliva get into the person's bloodstream.

Question 2

How do the protists get into the mosquito's saliva?

Answer

When the mosquito sucks blood from an infected person or animal, the protists are drawn into the mosquito's gut from there they migrate to its salivary glands.

Question 3

Which human cells are routinely invaded by malaria protists?

Answer

Liver cells and red blood cells. (The protists are less than 5 micrometres (μm) in diameter at this stage – small enough to get into a red blood cell.)

3.7 Fungal pathogens

You are probably most familiar with large edible fungi (mushrooms) and the single-celled yeasts used in making bread and beer, but over 300 fungal pathogens cause infectious diseases in humans. They are rarely fatal, except in people whose immune system cannot protect them from infection. Fungal cells in the soil can infect humans through breaks in the skin, but they can also form ‘spores’ encased in a rigid capsule, which can easily become airborne and cause respiratory diseases if inhaled.

Among the most common fungal infections in humans are ringworm, athlete’s foot and thrush. *Candida albicans*, which causes thrush, exists in two forms – as single-celled yeasts (measuring 3–5 micrometres) and as multicellular filaments which can be several millimetres in length (Figure 12). Thrush is characterised by inflammation, especially in the mouth, and also in the vagina where the infection causes intense itching.



Figure 12 *Candida albicans*, the fungus that causes thrush in humans.

3.8 Bacterial pathogens

Bacteria are the Earth's most ancient organisms, evolving over 3000 million years ago. They are also the most numerous: the mass of all the bacteria in the world may exceed the combined mass of all the plants and animals. Each bacterium is a single cell that can multiply very rapidly – in as little as 20 minutes in some species.

Most of the bacteria that live in or on the human body are beneficial. The number of 'friendly' bacteria living in your gut is around 10 times the number of human cells in your whole body! These beneficial organisms are called commensal bacteria. Commensal [coh-mens-uhl] means 'sharing the same table' – a name that reflects the fact that some bacteria in the gut enable us to digest plant-based foods.

Commensal bacteria also have a role in protecting us from some infectious diseases. They occupy habitats in the body that could otherwise be colonised by pathogens such as *Candida albicans*, the fungus that causes thrush. Fungal cells that occur naturally in the mouth and vagina are kept in check as long as commensal bacteria occupy the available space and prevent the fungi from acquiring enough nutrients for growth. However, thrush often develops after treatment with antibiotics to control a bacterial infection.

- Can you suggest why thrush is more common after taking antibiotics?

The antibiotics kill commensal bacteria as well as harmful ones; in the absence of commensal bacteria, fungal pathogens can obtain enough resources to multiply and cause the symptoms of thrush.

Over 500 species of pathogenic bacteria cause a diverse range of human infectious diseases. Some of the most important in terms of numbers of people affected are named in the 'word cloud' in Figure 13.

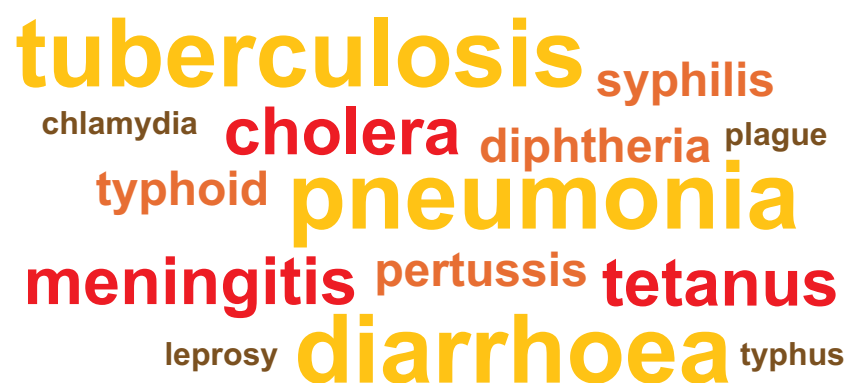


Figure 13 A 'word cloud' of some infectious diseases in humans caused by bacteria.

Here we will focus on just two categories:

- diarrhoeal diseases caused by bacteria transmitted via the faecal–oral route (i.e. transmitted from faeces to the mouth, usually on contaminated hands), and in food and water
- respiratory infections transmitted primarily by airborne bacteria.

3.8.1 Diarrhoeal diseases

Cholera, caused by the presence of *Vibrio cholerae* bacteria in drinking water, is a potentially life-threatening diarrhoeal disease. The disease is widespread in many parts of the developing world, but cholera was also a major cause of death in industrialised Western countries in the 19th century as discussed in Section 2.4.

However, many other pathogenic bacteria also cause diarrhoea, particularly those transmitted in contaminated food and water. They include *Salmonella* in raw eggs and undercooked poultry, and pathogenic varieties of *Escherichia coli* [esh-err-ish-ee-ah koh-lye], mainly in red meat or raw (unpasteurised) milk, but also in unwashed fruits and vegetables contaminated with faeces. Diarrhoeal diseases are also caused by some viruses and protists.

Around 1.5 million (1 500 000) people die from diarrhoeal diseases every year, most of them young children (Figure 14). If untreated, the loss of tissue fluids and essential salts in diarrhoea rapidly results in dehydration, disruption of body chemistry, and malfunction of the nervous system and vital organs. The loss can be replaced by drinking a simple oral rehydration solution (ORS) of sugar and salt dissolved in clean water until the diarrhoea subsides. Distribution of millions of sachets of ORS powder and teaching parents how to administer it is slowly reducing the mortality from diarrhoea in childhood. In severe cases, the solution may have to be given intravenously (directly into a vein).

Figure 3.14

3.8.2 Lower respiratory infections

Lower respiratory infections (LRIs) result in over 3 million deaths worldwide every year – more than any other category of infectious disease. Around one million of these deaths are due to pneumonia [nyoo-moh-nee-ah] caused by several species of bacteria and some viruses. The infection triggers inflammation in the lungs, which become clogged with infected fluid, resulting in severe breathing difficulties and strain on the heart.

Tuberculosis is counted separately from all other respiratory infections because the TB bacteria (*Mycobacteria tuberculosis*) that infect the lungs (Figure 15) can also invade other vital organs, muscles and bones. About one-third of the world's population (over 2 billion people, i.e. two thousand million) is infected with TB bacteria, but most are unaware of it because the body's defence mechanisms keep the bacteria in check. However, they can multiply if the body's defences are weakened, and TB can quickly develop in undernourished people, especially if they have another illness.



Figure 14 Diarrhoeal diseases are easily transmitted wherever people lack sanitation and are a major cause of death among children aged under five years.



Figure 15 Lung damage caused by TB can often be seen on chest X-rays.

Between 8 and 9 million people around the world develop TB for the first time every year, almost 9000 of them in the UK. Worldwide, this chronic infection killed 1.3 million (1 300 000) people in 2012 – a death toll that has been slowly increasing in the 21st century. The resurgence of TB and its increasing resistance to antibiotics means that it has been classified as a ‘re-emerging infectious disease’.

3.9 Viral pathogens

Remember that viruses are not regarded as ‘living’ organisms because they don’t consist of cells. You could think of them as minute containers for one or more short strands of genetic material and a few other chemicals. Most viruses are about 10 times smaller than typical bacterial cells, and 100 times smaller than typical animal cells. They are so small that they can only be photographed with the huge magnification made possible by an electron microscope (Figure 16).

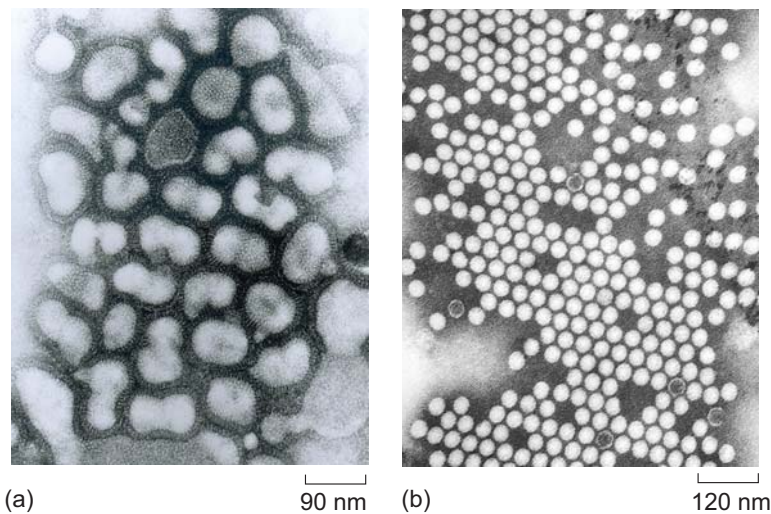


Figure 16 Electron microscope photos of (a) influenza viruses and (b) polio viruses, in both cases magnified approximately 100 000 times. (The scale bars refer to measurements in nanometres (nm); one nanometre is one-billionth of a metre)

Viruses can only reproduce new virus particles or *virions* [vih-ree-onz] by invading a living cell. The genetic material of the virus redirects the genetic material of the host cell and causes it to assemble thousands of new virus particles from the naturally occurring chemicals within the cell. Once assembled, each virus particle remains the same size (i.e. it does not grow). Many viruses eventually kill the host cell they infect, for example when the new virus particles disrupt the cell membrane as they are shed into the surrounding environment, where they can infect new cells and begin the cycle of reproduction all over again (Figure 17).

Viruses don’t have Latin species names but are named after the disease they cause: for example, measles virus, polio virus, and so on. Figure 18 is a ‘word cloud’ of some diseases caused by a few of the 206 different viruses known to be human pathogens. Around 37% of these viruses cause emerging infectious diseases (EIDs) – a much higher percentage than for any other pathogen type (Woolhouse and Gowtage-Sequeria, 2005). Their routes of transmission are highly varied and include:

- airborne viruses causing respiratory diseases, e.g. influenza
- faecal–oral transmission of rotaviruses, which cause more cases of diarrhoea than any other pathogen

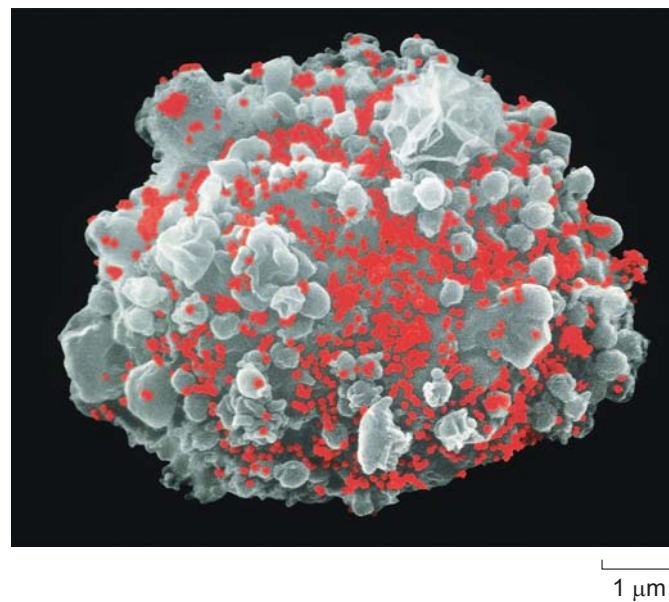


Figure 17 A human leukocyte (white cell) magnified 5600 times; the red colouring has been computer-generated to reveal thousands of HIV particles budding from the cell's surface.

- vector-borne transmission, e.g. of yellow fever viruses by mosquitoes
- transmission via contact with infected body fluids, e.g. HIV/AIDS and Ebola virus disease.



Figure 18 A 'word cloud' of some human infectious diseases caused by viruses.

We now conclude this tour of pathogen biology with a brief mention of the least understood category – the prions.

3.10 Prions

Prions are a very unusual form of infectious agent, consisting of a misfolded version of an otherwise harmless brain protein called prion related protein (PrP). Remarkably, prions are able to turn molecules of normal PrP into more prions, which leads to a chain reaction causing the accumulation of more and more prions. Prions then aggregate into clumps or *plaques* [plahks] in the brain, causing surrounding brain cells to die, so the brain develops a spongy appearance. This, in turn, causes muscle wasting and loss of muscle control. This resulting inability to coordinate breathing ultimately leads to death.

Some cases of prion disease are inherited (passed on from parents to their offspring), but prions are also considered to be infectious agents because they can be transmitted between humans, or between humans and animals. People can become infected by eating the brains or nervous tissue of animals or other people with prion disease.

The best known examples of prion diseases are BSE (bovine spongiform encephalopathy, popularly known as ‘mad cow disease’) in cattle, and vCJD (variant Creutzfeldt–Jakob disease) in humans. BSE is caused by cattle-to-cattle transmission, vCJD is caused by humans eating products derived from cattle with BSE. The transmission of prions between humans is of course very rare, but has been documented in certain Papua New Guinean tribes that practice funerary cannibalism – the eating of dead family members – where it causes a disease known as Kuru. Understandably, funerary cannibalism is now strongly discouraged.

Session 3 quiz

This quiz allows you to test and apply your knowledge of the material in Session 3.

Session 3 quiz

Open the quiz in a new window or tab then come back here when you're done.

Summary to Session 3

Now that you have completed Session 3 you should be aware of the incredible range and diversity of pathogens that infect humans and cause disease. This gives you some idea of the challenge faced by scientists and health care professionals in treating and preventing infectious diseases.

We have introduced you to the multicellular endoparasites; four categories of worm (roundworms and hookworms, tapeworms, filarial worms, and flatworms or flukes) that cause a variety of diseases by invading vital organs or living in the gut, bloodstream or tissues. Smaller in size are protists – unicellular pathogens that cause conditions such as sleeping sickness, leishmaniasis and malaria). Next you learned about fungal pathogens and bacteria. Pathogenic bacteria cause a wide range of diseases (e.g. cholera and tuberculosis) while ‘friendly’ commensal bacteria can be protective against pathogens. You should be aware that the antibiotics used to treat pathogenic bacteria also kill commensal bacteria, which can increase the risk of fungal and other infections. Finally, you have been introduced to the two smallest types of pathogen – viruses and prions – which are not formed from cells so are not considered to be alive. Diseases caused by infectious prions are relatively rare but the same cannot be said about viruses, which cause some of the most common infectious diseases such as influenza. Viruses also cause a considerable proportion of emerging infectious diseases and exhibit a remarkable range in their modes of transmission.

Taking all this together, it should be clear to you that there is no such thing as a generalised pathogen – even within the same category of pathogen they tend to behave differently! It is therefore unsurprising that the challenge to human health posed by infectious diseases shows little sign of abating.

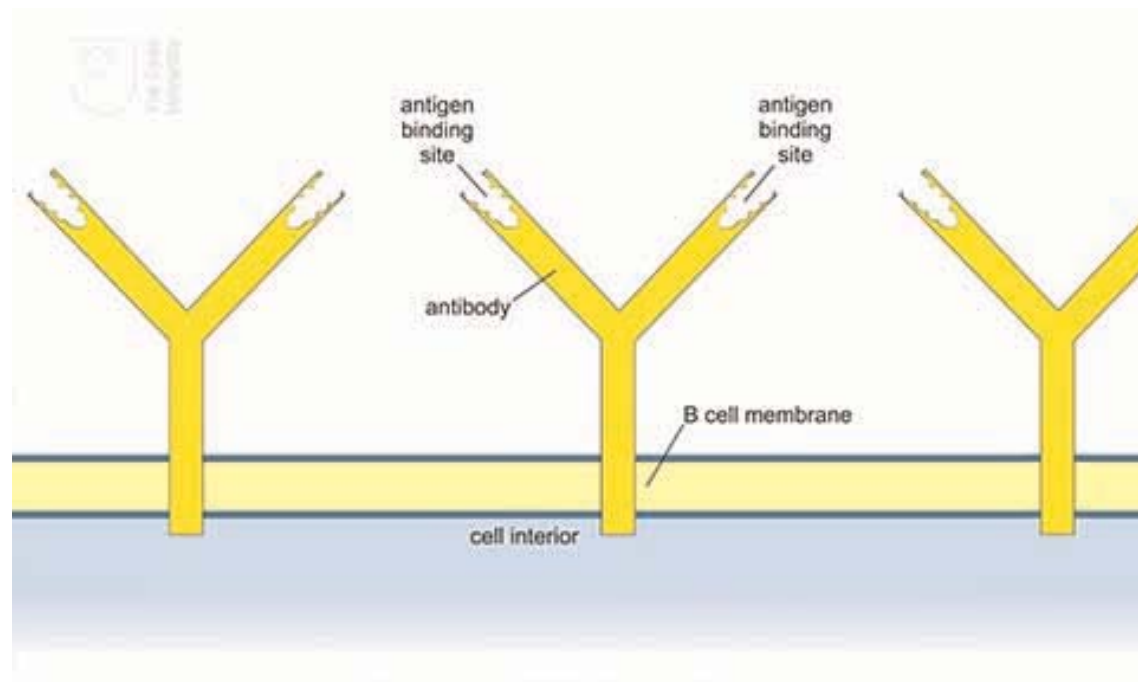
You can now go to Session 4.

Session 4

Introduction

In this part of the course you'll look at the body's natural defences against pathogens – the infectious agents that cause disease. We describe how physical and chemical barriers keep pathogens from entering the body and how the immune system uses a range of specially adapted cells and molecules to attack pathogens that get past these barriers. One of these cell types is known as a B cell and it plays a vital role in producing antibodies to fight infection.

Watch the following video to learn more about this process and the role of B cells in producing an immune response to vaccination.



4.1 Natural barriers against pathogens

The physical and chemical barriers that prevent pathogens from getting into our body tissues in the first place are often overlooked. As Figure 1 shows, the most comprehensive barrier is the waterproof layer of skin that covers the body's surface. Human skin keeps most pathogens out as long as it remains intact. The speed with which a cut or graze can become infected is a reminder of the protection we normally get from our skin.

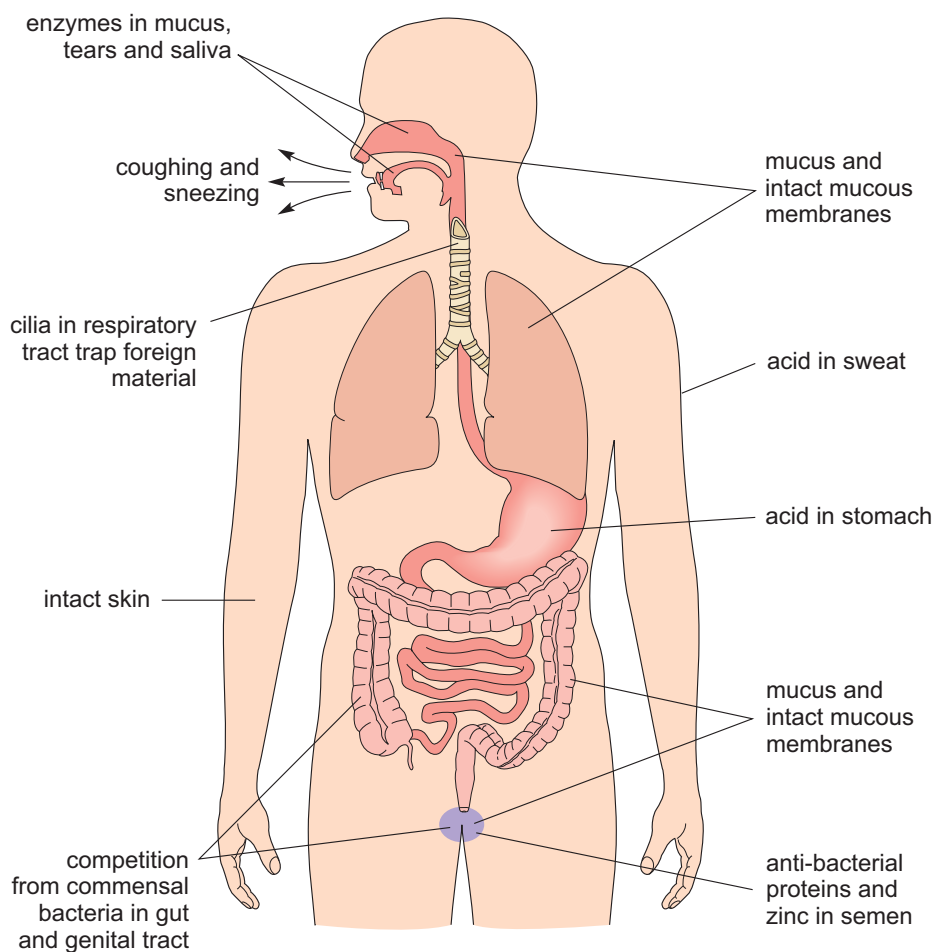


Figure 1 Physical and chemical barriers against infection.

Vector-borne infections (e.g. malaria) are transmitted by biting invertebrates (e.g. mosquitoes) penetrating the skin when taking a blood meal. Humans are also vulnerable to invasion by pathogens in the air, food, water and soil, or during physical contact with infected people, some animals (e.g. pigs, dogs, poultry) or their faeces. As Figure 1 illustrates, the inner surface of the respiratory system (nose, throat, airways and lungs), stomach, intestines, bladder and reproductive tract are lined with membranes that secrete jelly-like mucus, presenting a barrier against pathogens entering our tissues via these routes. Microscopic hairs called cilia [sill-ee-ah] line the respiratory

system and ‘beat’ in unison to shunt mucus containing trapped pathogens towards the nose and mouth, where they can be expelled by coughing and sneezing, or swallowed into the stomach where acid destroys them.

Figure 1 refers to competition from *commensal* bacteria (sometimes referred to as ‘friendly bacteria’) in the gut and reproductive system. Commensal bacteria are non-pathogenic inhabitants of the gut and the reproductive system. They occupy space that could otherwise be colonised by pathogenic species, and they use nutrients for their own growth, thereby reducing the resources available for pathogens to multiply and cause disease.

Chemical barriers against infection include enzymes in tears, saliva and mucus that break down the surface of bacteria. The acid in sweat and in the stomach kills cellular pathogens and there are anti-bacterial proteins in semen (the fluid that contains male sperm).

The more complex mechanisms of the immune system are only needed if pathogens breach these physical and chemical barriers.

4.2 The immune response to infection

The human immune system is an extremely complex network of interacting cells and biological molecules. Our aim here is simply to give you an overview of how an immune response to infection develops, without going into too much detail. It occurs in three overlapping stages, the first of which is triggered when body cells are damaged.

When tissues are injured, the damaged cells release chemicals that trigger the sequence of events described as inflammation. It occurs in response to any type of injury, such as a blow or a cut, an insect bite, or damage caused by pathogens multiplying in body tissues. Inflammation has four characteristic effects at the site of an injury, the first two of which are visible around the splinter shown in Figure 2:

- swelling
- redness
- heat
- pain.



Figure 2 Inflammation of the tissues around a splinter.

The inflamed area shows these signs because the local blood vessels dilate (get wider), increasing blood flow into the injury site, so it looks red as well as feeling warmer than the surrounding tissue. The walls of the blood vessels near the injury become leaky, allowing fluid, defensive proteins and immune system cells (described shortly) to flood into the area, which becomes swollen as a result. One of the proteins released during the inflammatory response also makes the area more sensitive to painful stimuli, so inflamed tissue is sore to touch.

Sites of tissue injury are vulnerable to invasion by pathogens so the benefits of inflammation generally outweigh the discomfort it causes. Flooding the area with fluid dilutes any pathogens that are already present, and the local concentration of immune system cells and defensive proteins enables an immune response to begin more quickly.

4.3 Leukocytes: the cells of the immune system

Once the barriers to infection have been breached and inflammation has begun, the active agents of the immune system, the *leukocytes* [loo-koh-sites], get to work. Leukocytes are often described as ‘white blood cells’ to distinguish them from the red blood cells that transport oxygen around the body; however, calling them ‘blood’ cells is misleading because leukocytes roam throughout the body tissues and only spend part of their lives in the bloodstream. In fact, they spend more time in the lymphatic system (Figure 3), the network of fine tubules that collect tissue fluid from all over the body and return it to the bloodstream.

Figure 7.3

The lymphatic system includes specialised organs and tissues where leukocytes develop. During an immune response to pathogens, we may become aware of swollen lymph nodes (popularly called ‘glands’) in the neck, armpits or groin, which enlarge when the leukocytes they contain are multiplying near a site of infection.

Leukocytes can distinguish between ‘self’, the cells and proteins generated by the organism whose body they patrol, and ‘non-self’ (or ‘foreign’) material such as pathogens that originated outside the host’s body.

Leukocytes are *self-tolerant*, i.e. they do not normally attack the host’s own cells or body proteins, but direct their actions only against non-self material that may pose a threat.

Although we have referred to ‘the’ immune response, as if it was just one thing, in fact, there are two types of immune response, distinguished as *innate* and *adaptive* immunity.

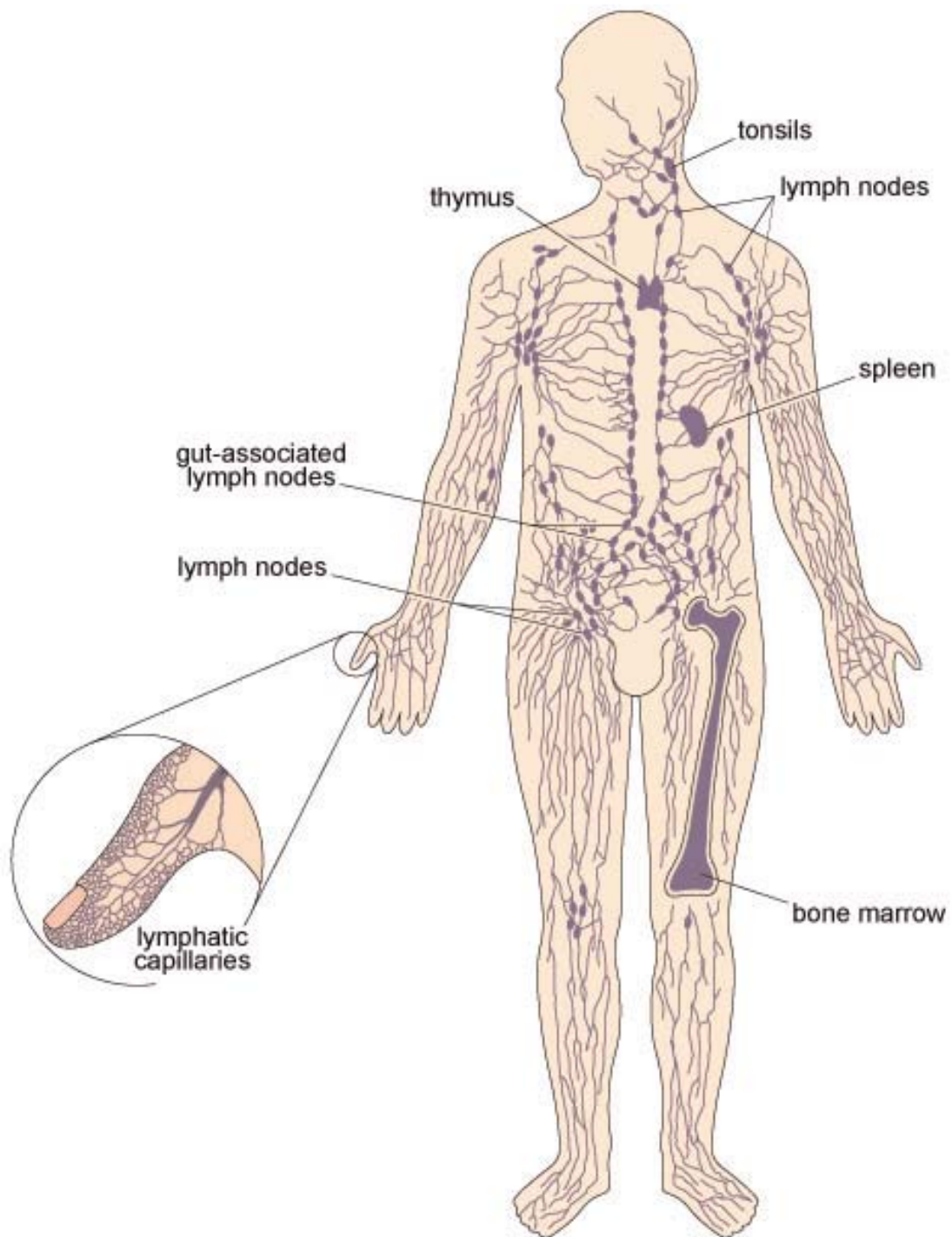


Figure 3 The human lymphatic system.

4.4 Innate immunity

All animals, even those with much simpler bodies than our own (e.g. parasitic worms) respond to tissue damage in ways that resemble inflammation in humans. They have cells similar to leukocytes and defensive proteins that flood into areas of tissue damage or infection. These leukocytes and proteins can defend the organism from pathogens because they recognise common patterns of molecules that occur in the structures of many different types of pathogens. These pathogen ‘signature’ molecules are known as PAMPs, or *pathogen-associated molecular patterns*.

The fact that PAMPs are commonly found in unrelated pathogens means that the leukocytes that recognise them cannot tell one type of pathogen from another. This *non-specific* immune response against pathogens is so widespread among animals that it is described as innate immunity (‘innate’ means ‘inborn’). Some texts use the alternative term ‘natural’ immunity.

The leukocytes involved in innate immunity are of two general types, each with a different action against pathogens:

- Cytotoxic [sigh-toh-tox-ik] leukocytes, which simply means ‘cell poisoning’ (the prefix ‘cyto’ denotes a cell). These leukocytes have various methods of attaching to the outside of a pathogen and releasing destructive chemicals onto its surface. Worm larvae, bacteria and protists can all be killed this way.
- Phagocytic [fag-oh-sit-ik] leukocytes (the prefix ‘phago’ comes from a Greek word meaning ‘to eat’), often abbreviated to phagocytes [fag-oh-sigh-tz]. These leukocytes engulf small pathogens such as bacteria, drawing them into the cytosol where destructive chemicals break them down. This action is termed phagocytosis [fag-oh-sigh-toh-siss].

Figure 4 identifies a phagocyte, red blood cells and two tiny spherical bacteria (*Staphylococcus aureus*) joined together – this species is often found in ‘strings’ of two or more linked cells. Red blood cells are fragile and some have begun to disintegrate in these culture conditions. Note that red blood cells are also known as *erythrocytes* [air-rith-roh-sigh-tz].

- Viruses are small enough for a leukocyte to engulf if the viruses are floating ‘free’ in the bloodstream or tissue fluids, but once in the body, viruses rapidly become hidden from phagocytic leukocytes because they must infect the host’s own cells in order to make new virus particles. Can you suggest how this protects the virus from the innate immune response?

Once inside the host’s cells, they are hidden from the self-tolerant phagocytic leukocytes, which can only recognise and engulf material that originated outside the host’s body. (As you will see later, adaptive immunity has a solution to this problem.)

The anti-pathogen activities of certain specialised proteins are important contributors to the innate immune response. They include proteins that accelerate inflammation, target leukocytes onto pathogens or make host cells

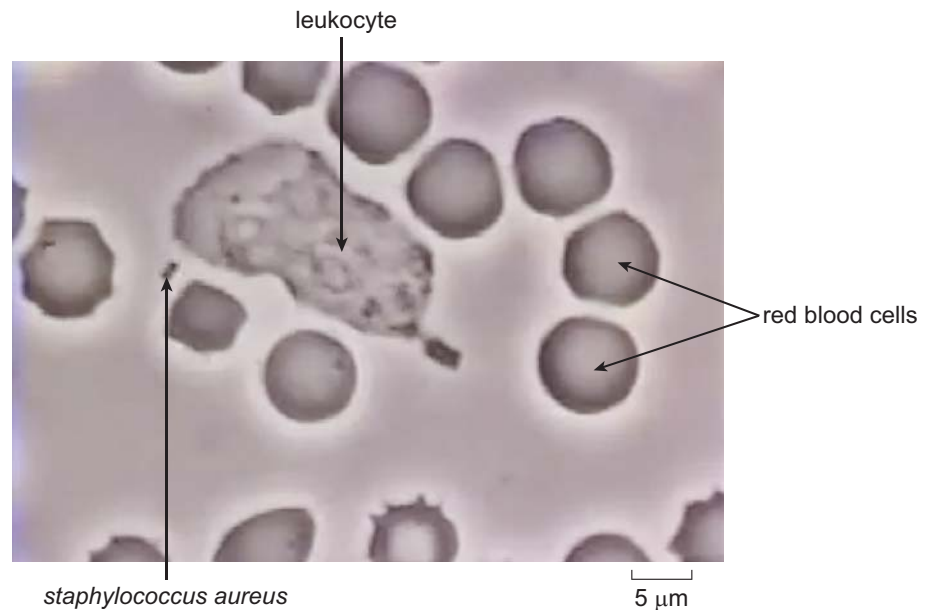


Figure 4 Red blood cells surround a phagocyte following the chemical trail left by two *Staphylococcus aureus* bacteria.

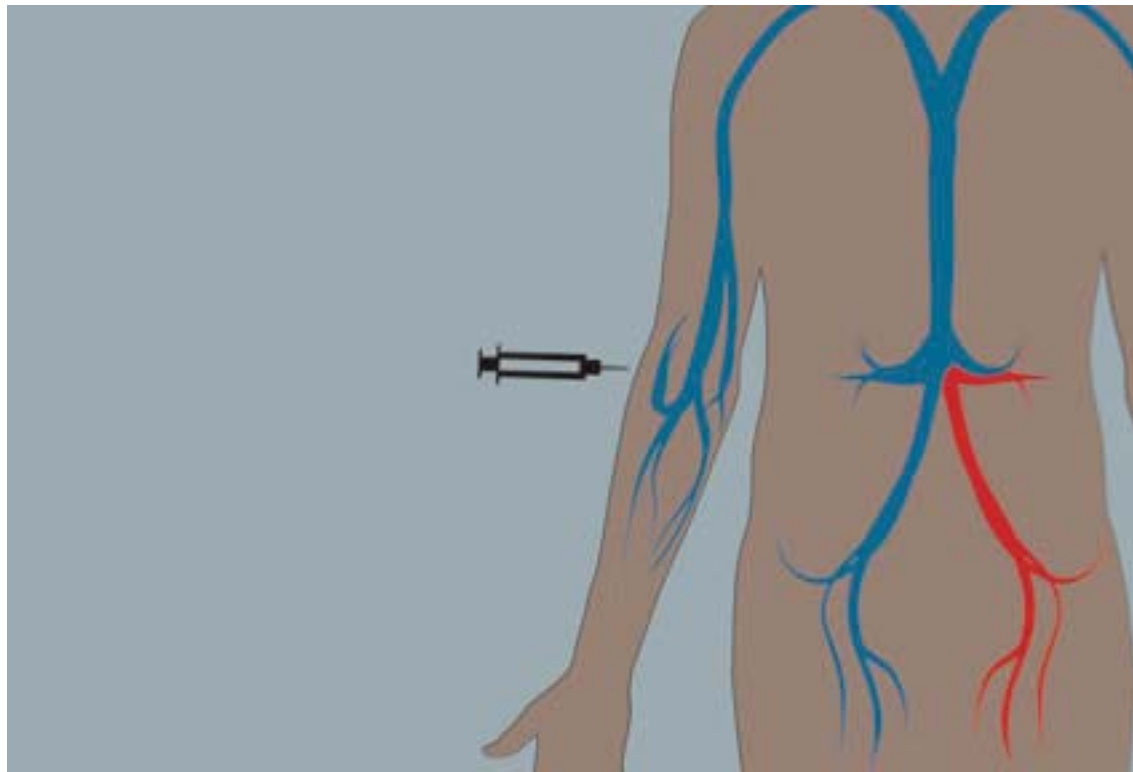
resistant to invasion by viruses. Their concentration increases rapidly in the bloodstream during an infection and this rise can be detected in blood tests as a diagnostic sign of infection.

In summary, all animals have innate immunity based on cells similar to human leukocytes and defensive proteins that defend the organism against pathogens ‘in general’ in a non-specific way, i.e. these defences cannot distinguish between one type of pathogen and another. Humans and other warm-blooded animals have an additional defensive capability called *adaptive* immunity, which differentiates specifically between pathogens, as the next section describes.

4.5 Adaptive immunity

Adaptive immunity is due to the actions of two types of specialised leukocytes, known as T cells and B cells. (If you are interested, the letters denote 'thymus' and 'bone marrow', the tissues where each of these leukocytes mature.) We will describe their individual contributions to the adaptive immune response shortly, but first we focus on the most striking difference between innate and adaptive immunity. The clue lies in the word 'adaptive'.

T cells and B cells have recognition methods that distinguish between different pathogens (e.g. different species of bacteria), and they *adapt* during their first encounter with a particular pathogen. The second time they meet it in the body, the adaptive response begins earlier, lasts longer and is more effective than it was on the first occasion. You can learn more about this by watching the following animation. (If you do not wish to see closed captions, use the 'CC' (captions) button to remove or reveal the subtitles.)



So, there is a much faster and increased response to a subsequent encounter with a pathogen and this demonstrates the adaptability of the immune system. This response is due to the production of long-lived memory cells that circulate in the body after the primary adaptive immune response subsides. These memory cells are specifically programmed to recognise the *same* pathogens that triggered the primary response if they ever get into the body again. You will learn much more about these later in this session.

Overall then it is to be expected that one of the appropriate immune system responses to infection is an increase the concentration of leukocytes in the blood circulation. This expected response can actually be tested in a laboratory by taking a blood sample from an individual who is suspected to be suffering from an infection. Blood from the sample is then smeared onto

a microscope slide and air dried, and the sample can then be viewed at different magnifications using a light microscope to enable the number of leukocytes to be counted. In the activity in the next section you can test for the presence of the suspected infection by counting leukocytes in blood samples using our digital microscope.

4.6 Counting leukocytes in blood samples

The Digital Microscope Leukocyte Counting Activity is one of a number of interactive, practical science resources that you can access from The OpenScience Laboratory website: a collaborative initiative of The Open University and The Wolfson Foundation. Here you will find investigations, tools and activities covering a broad range of scientific fields, including health science, astronomy and earth science many of which are also built into the learning experience on our modules.

When you first access the tool you will be prompted to either sign in (if you are already an Open University student), or to register with your email address to create an account free of charge. This only takes a few minutes to do and the website will guide you through the process.

Note that the interactive activities on the OpenScience Laboratory website require a modern web browser, such as Mozilla Firefox, Google Chrome, Apple Safari or Microsoft Internet Explorer 9 or later.

The easiest way to look at leukocytes is to take a tiny quantity of blood and smear it onto a glass slide, air dry the cells and then treat them with a dye that stains leukocytes blue/purple. Figure 5 shows several leukocytes that have been prepared in this way, with some red blood cells around them, which appear grey. Not all leukocytes look exactly like the ones in Figure 5, but the most numerous type in the bloodstream – the neutrophils [nyoo-troh-fillz] – have this general appearance. The dark blue/purple shapes inside each neutrophil are the connected lobes of its irregularly shaped nucleus.

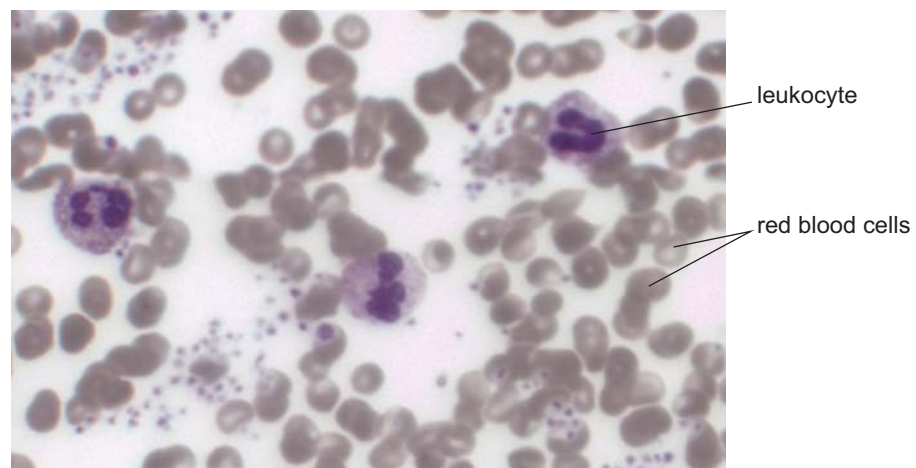


Figure 5 Leukocytes known as neutrophils have a distinctive multi-lobed nucleus; the smaller red blood cells appear grey because they have not absorbed the dye which has stained the leukocytes blue/purple.

4.6.1 The digital microscope

In the following activity, you will use the digital microscope to count leukocytes in microscope slides of blood smears that look like Figure 6. This figure shows a magnified blood sample from a healthy person (termed the 'Normal' sample). A second slide (not shown here) has blood from someone whose immune system was *believed* to be fighting a severe infection when the sample was taken. We have labelled this one 'leukocytosis' [loo-koh-sigh-toh-siss]. Leukocytosis refers to an increase in the total number of leukocytes of all types circulating in the bloodstream.

When you have counted the leukocytes in your two blood samples, you can compare your counts and decide whether there is evidence to suggest that the sample labelled 'leukocytosis' was taken from an individual who was indeed suffering from an infection.

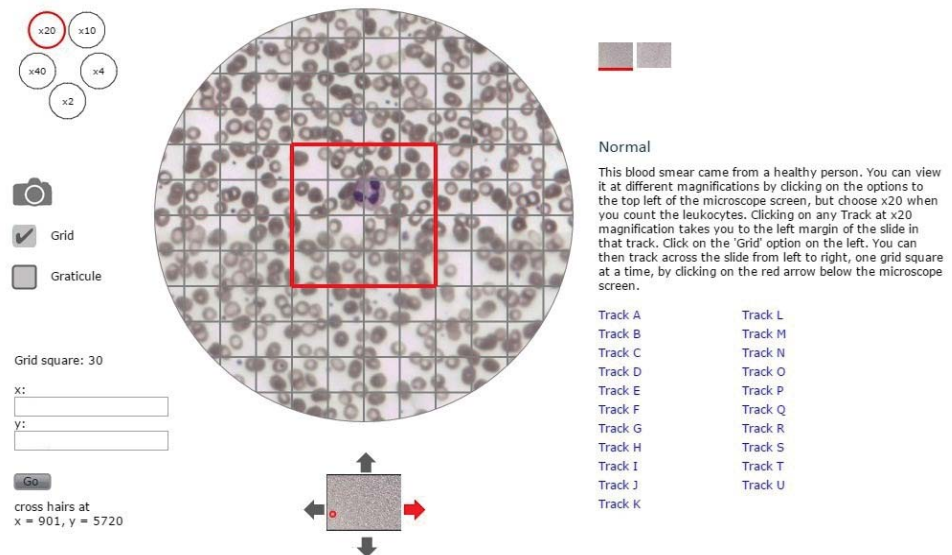


Figure 6 A screenshot of the digital microscope displaying a microscope slide of a 'Normal' blood with the magnification set at times 20 (' $\times 20$ '). The large blue/purple cell in the red square is a leukocyte surrounded by hundreds of red blood cells, which appear grey.

Note the following features in Figure 6, which will help you to navigate the digital microscope when you access it online:

- You can switch between the 'Normal' and the 'Leukocytosis' slides by clicking on the squares to the top right of the microscope screen.
- The small circles to the top left of the microscope screen show the magnification factors you can choose for viewing the blood smears. They range from $\times 2$ (twice the actual size of the cells) to $\times 40$. Click on the circle labelled $\times 20$ to choose the optimum magnification for this activity.
- When you click on the small square labelled 'Grid' on the left of the microscope screen, a matrix of faint grey lines is superimposed on the blood smear with a large red square in the centre of the grid. Your task

is to count any leukocytes in the red square as you move it across the blood smear.

- The slides have been divided into horizontal sections labelled Track A to Track U, which are listed on the right of the microscope screen. It is not necessary to count all tracks on a slide although you can do if you wish. We suggest you just choose one track as a representative sample of the whole slide. When you click on a track (e.g. Track A) with the magnification set at $\times 20$, the microscope screen shifts automatically to the left margin of the slide in that track.
- Notice the up/down/left/right arrows around the small image of the slide below the main microscope screen. If you click on the red arrow, it moves the slide to the right by one red grid square. This enables you to move across the blood smear one red grid square at a time until you reach the other side of the slide.

4.6.2 Testing for the presence of infection

You'll now use the digital microscope to test for the presence of infection.

Activity 1 Using the digital microscope

Allow about 1 hour

Before you access the digital microscope read through the following instructions for the leukocyte counting activity carefully:

- 1 Remember to increase the magnification to help you count leukocytes by clicking on the circle labelled ' $\times 20$ ' in the top left corner of the screen.
- 2 Locate the square button labelled 'Grid' below the camera symbol on the left of the screen and click on it so that the grey counting grid appears to help you count systematically.
- 3 Now choose which track you wish to count (A-U) and click on the appropriate letter. This will take your viewer (a red square) to the far left of the correct track so that you can begin counting.
- 4 Count the number of leukocytes (if any) in the red grid square on the far left of your track noting down the number of leukocytes into the grid square number 1 of Table 1 (see below).
- 5 Return to the digital microscope and click once on the red arrow pointing to the right in the small box below the blood smear. This moves the blood smear an exact distance to the right, so the red square is now around Grid square 2 in your track.
- 6 Count the leukocytes (if any) in Grid square 2 and enter the number into Grid square number 2 in Table 1.
- 7 There are 29 complete red grid squares in every track, plus 'half' a grid square (numbered 30) at the right-hand edge of the track, which you should include in your counts. You can then keep moving the slide one red grid square to the right by clicking once on the red arrow and counting and recording the number of leukocytes in each red square until you finally reach the right-hand margin of the slide.

- 8 Finally, add up the total number of leukocytes in your track of the Normal blood smear and enter the total in Table 1. Once you have completed a table for your one of the slides (e.g. the normal slide), repeat the process for the other slide (e.g. the leukocytosis slide).

Table 1 Table for recording the number of leukocytes in your track of the Normal blood smear.

Track (letter)															
Grid square number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Number of leukocytes															
Grid square number	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Number of leukocytes															
Normal Track total:															

Note that some leukocytes will inevitably sit across the margin of a grid square, as in the example in Figure 7.

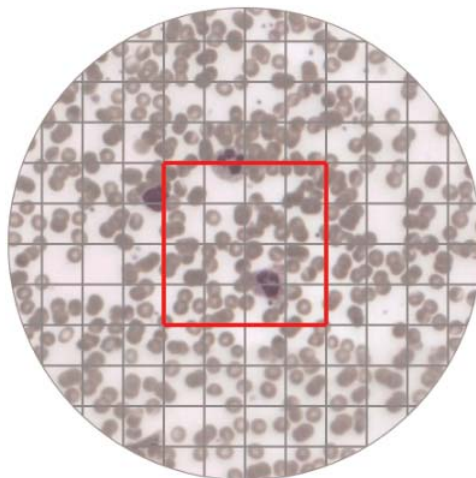


Figure 7 Screenshot showing a leukocyte partly inside and partly outside the left margin of the red square, another sitting across the top margin, and a third entirely inside the red square.

This is a very common occurrence in biological investigations where large numbers of ‘subjects’ (e.g. cells or organisms) are counted systematically using a grid to ensure that every cell or organism is accurately recorded.

If a leukocyte is ‘divided’ by a grid line on the left or the right margin of the red square, it is still in ‘your’ track so it will count towards your track total no matter which grid square you decide to record it in Table 1. But if a leukocyte is partly inside and partly outside the upper or lower margin of a red square (as in Figure 3), you must make a decision about whether to count it in ‘your’ track or exclude it as belonging to the track above or below yours.

Now access the digital microscope leukocyte counting activity on the Open Science Laboratory website. (If you don't already have one, you'll need to sign up for a free Open University account in order to access this. The website will guide you through the process.)

Once you have counted the number of leukocytes for each slide, compare the two values. Do they differ? If so which one is larger? Does this support the suspected infection in the participant whose sample was taken for the 'leukocytosis' slide?

Discussion

You should have found that the leukocytosis slide contained more leukocytes than the normal slide. This supports the suspected infection in the participant whose sample was taken for the leukocytosis slide. Note that if you opted to count more than one track on each slide you would also have reached a more reliable answer to this question about suspected infection. This is because the larger the area you count the more representative this is of the number of leukocytes that are present in the blood as a whole.

You might also wish to reflect on how straightforward you found this counting process. Did you find it easy to decide whether to count a borderline cell or not? Was it easy to spot a leukocyte using the purple staining colour or was there an element of subjectivity involved?

We have designed this microscope activity to make it as close to the reality of cell counting on a microscope as possible. As such the subjectivity you may have applied to the counting process would be representative of the real experience of cell counting. Whatever subjective criteria you applied when deciding whether to count a leukocyte or not should have been applied consistently.

4.7 Chickenpox: adaptive immunity in action

Chickenpox infection demonstrates how effective the adaptive immune response can be in preventing reinfection with the chickenpox virus. Children who have suffered from chickenpox (Figure 8) and recovered are unlikely ever to develop it again, because they have circulating memory cells specifically programmed to recognise chickenpox viruses. These memory cells are unable to recognise any other pathogens, but they react swiftly and effectively if the chickenpox virus gets into the body again. These memory cells direct the more vigorous secondary adaptive immune response, which produces many new T cells and B cells programmed specifically to attack chickenpox viruses.



Figure 8 Chickenpox pustules on a toddler's face.

The secondary adaptive immune response is usually so effective that the person doesn't become ill and may never know that they have been infected by chickenpox viruses for a second time. When the secondary response subsides, even more memory cells that recognise chickenpox viruses as their specific target are left in circulation, providing lifelong protection against this pathogen to almost everyone who suffered this disease as a child.

Chickenpox usually resolves without treatment and because it is extremely rare for someone to develop it a second time, many countries (including the UK) do not routinely vaccinate children against this virus unless they have a deficient immune system. But many other pathogens produce far more serious diseases during their first encounter because the infection develops faster than the primary adaptive immune response can react against it. In a later section, we explain how vaccination can enhance the secondary adaptive immune response and prevent an infection from developing.

But first we have to explain how leukocytes in the adaptive immune system recognise each type of pathogen so specifically.

4.8 Antigens and the specific recognition of pathogens

Every type of pathogen has at least one (often many more) unique molecules known as antigens in their structure. In addition to the PAMPs (pathogen-associated molecular patterns) shared by many different pathogens, each type of pathogen also has its own unique distinctive antigens. Each individual T cell and B cell (the leukocytes responsible for adaptive immunity) is programmed to recognise just one specific antigen, so it follows that each T or B cell can usually recognise only one type of pathogen, or at most two or three closely related pathogens that have very similar antigens. Recognition of an antigen by these adaptive leukocytes triggers an immune response against only those pathogens with that antigen in their structure. The political slogan ‘One person, one vote’ springs to mind as an analogy for ‘One adaptive leukocyte, one target’!

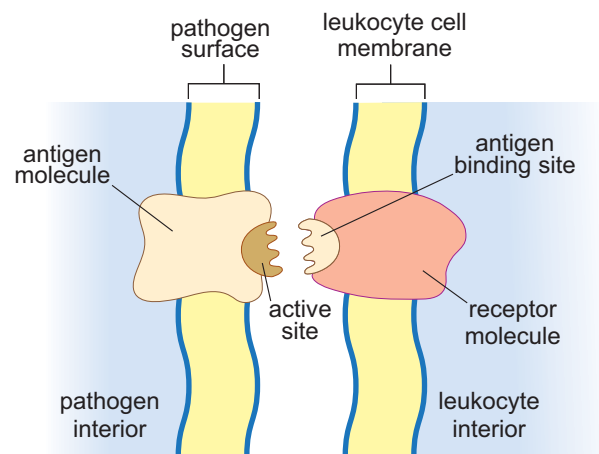
We haven’t yet answered the question of *how* T cells and B cells recognise antigens. Each of these leukocytes carries receptor molecules (often abbreviated to ‘receptors’) on its outer cell membrane. Receptors are very large molecules containing hundreds or even thousands of atoms. As a consequence, they fold up into very complex 3D shapes with many troughs, crevices, humps and hollows, creating a molecular landscape that is unique for each receptor molecule.

A particular type of receptor molecule on the surface of a T cell or B cell can only recognise an antigen that has a 3D shape which is the ‘mirror-image’ of this receptor, so the two molecules can fit together like a key in a lock. In fact, the contact area between the receptor and the antigen involves only a tiny part of each molecule (Figure 9), but this is enough to hold them together long enough to trigger changes in the leukocyte.

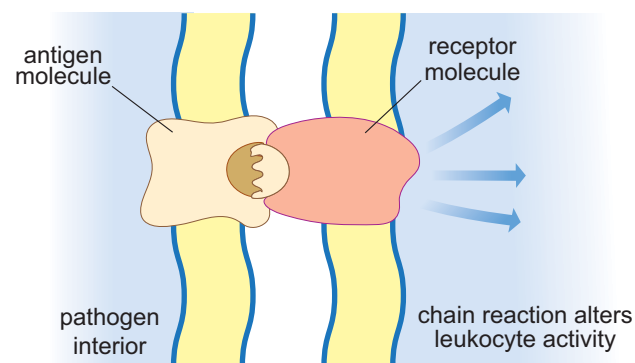
Each T cell and B cell carries many identical copies of a *single* antigen receptor, so an individual T or B cell can only bind to pathogens that display the corresponding antigen. For example, a T or B cell with receptor molecules that fit an antigen found only in the structure of malaria protists is unable to recognise any other pathogen as a target for an adaptive immune response – it cannot bind to the antigens of (for example) TB bacteria or polio viruses.

At least 10 million different antigen receptors, each with a unique 3D shape, are necessary to recognise all the pathogens an individual may encounter in a lifetime. How this vast array of antigen receptors is generated by T and B cells, each of which carry just one antigen receptor shape, is beyond the scope of this course, but our survival depends on this marvellous phenomenon.

By contrast, the leukocytes responsible for innate immunity have receptor molecules that recognise PAMPs, which many different pathogens have in common. This is why innate leukocytes have a non-specific response to infection – in a sense, all pathogens ‘look alike’ to them, so they are incapable of forming a ‘memory’ of having encountered a pathogen before.



(a)



(b)

Figure 9 (a) A receptor molecule on the surface of a leukocyte in the adaptive immune system has a binding site that exactly matches the shape of part of an antigen molecule on a pathogen. (b) Binding between the two is an essential stage in the activation of the leukocyte.

We said earlier that we would explain the different actions of T cells and B cells in the adaptive immune response to infection. We start by considering B cells in the next section, which produce proteins called antibodies.

4.9 Antibodies and B cells

Antibodies are very large proteins that contribute to adaptive immunity. There are several types, but the most abundant antibody molecules in humans each contain about 25 000 atoms. A distinguishing feature of antibodies is that their structure includes at least *two* binding sites for antigens. Most antibodies resemble the simplified representation in Figure 10.

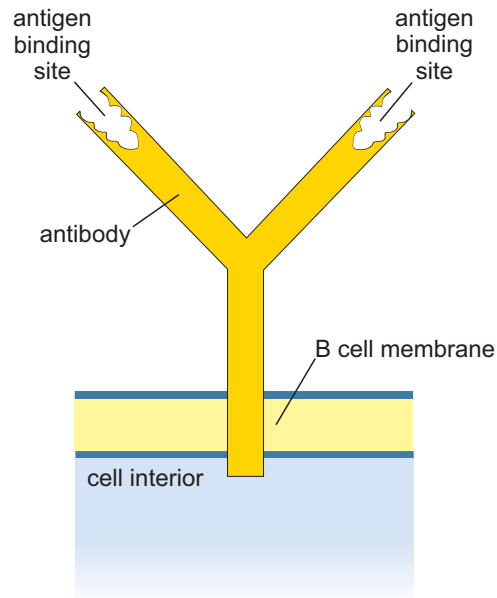


Figure 10 An antibody molecule with two antigen binding sites at the tip of its two ‘arms’ and a single ‘tail’, which is embedded in the outer membrane of a B cell.

B cells produce antibodies and also use them as their antigen receptors. The B cells carry antibodies embedded by the ‘tail’ in their outer cell membrane, with the binding sites facing outwards (Figure 10). This enables the B cell to bind to antigens that fit the binding sites in the antibodies it carries on its surface. This binding event is essential (but not sufficient on its own) to activate B cells into making a lot more antibody molecules that recognise the *same* antigen. These antibodies are released by the B cells and circulate in the bloodstream, tissue fluids and the lymphatic system. Antibodies are also abundant in the mucus membranes lining the respiratory system, the gut and the reproductive system, i.e. the sites in the body in contact with substances such as air, food, drinking water and sexual fluids that could contain pathogens.

Antibodies are often portrayed in the media as if they were ‘magic bullets’ that attack pathogens, but in fact they are more like ‘waving flags’ with a message that reads ‘here is a pathogen – come and destroy it’. When antibodies bind to a pathogen, they simply label it for destruction by leukocytes with the innate ability to phagocytose (engulf) it, or cytotoxic (cell-killing) leukocytes and defensive proteins. You can think of them as

recruiting the cells and defensive proteins of the innate immune system to join the attack.

We conclude this tour of adaptive immunity by describing the T cells.

4.10 T cells in adaptive immunity

There are two types of T cells with different roles in adaptive immunity. The cytotoxic T cells release destructive chemicals onto their target's outer surface in much the same way as the cytotoxic leukocytes do in an innate immune response. But there is one crucial difference. Cytotoxic T cells are programmed to kill the body's *own* cells that have become infected by viruses or by the few types of bacteria and single-celled pathogens that can 'hide' inside the cells of their host (*Mycobacterium tuberculosis*, the bacteria that cause TB, can do this). Without the cytotoxic T cells, we would be particularly susceptible to infectious diseases caused by these pathogens.

The other T cell type is called the **helper T cells**. They send activation signals to all the other leukocytes involved in inflammation, phagocytosis, cytotoxicity or production of antibodies by B cells (Figure 51). Recognition of a pathogen by binding to it is only the first step. The other leukocytes cannot take action against the pathogens they encounter without activation signals from the helper T cells.

If you have seen documentaries or read reports about HIV/AIDS, you have possibly heard that HIV (the human immunodeficiency virus) infects and ultimately destroys the helper T cells.

- Why does the destruction of helper T cells by HIV leave a person susceptible to many other infections?

When the number of helper T cells declines to a low level, they cannot activate the other leukocytes to act effectively against other pathogens, so the person becomes susceptible to infections they could otherwise have overcome. Eventually the person develops AIDS – acquired immune deficiency syndrome – because their immune responses have become so deficient.

Next we explain how our defences against pathogens can be enhanced by vaccination, and consider some of the problems that limit the ability of vaccines to protect us from infection.

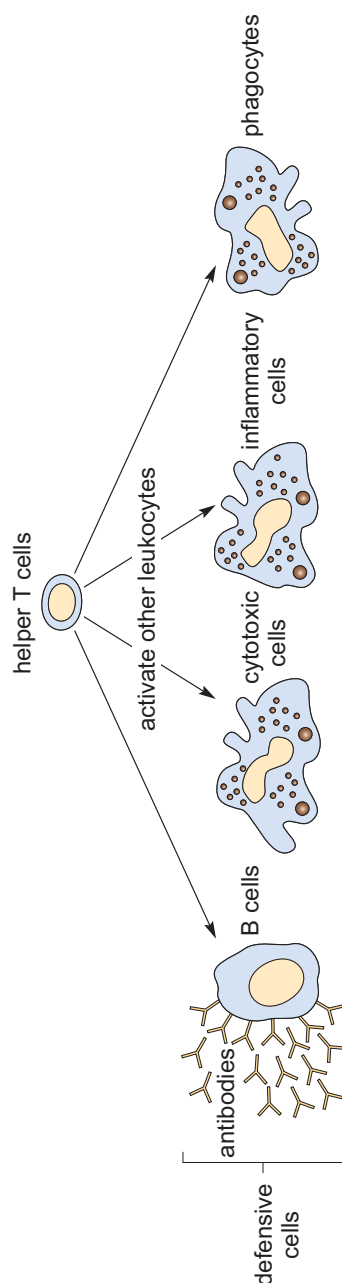


Figure 11 Helper T cells activate all the other leukocytes responsible for innate and adaptive immune responses against pathogens.

4.11 Vaccination

Vaccination relies on the development of immunological memory for its protective effect. Vaccines contain killed pathogens, or extracts from pathogens, or modified strains of pathogens that are no longer harmful. For example, the MMR vaccine contains weakened (the technical term is ‘attenuated’) variants of the three viruses that cause measles, mumps and rubella (Figure 12).

- Why do you think most vaccines are given in two (or more) doses spaced at intervals of weeks or months?

The first dose triggers a primary adaptive immune response, but this doesn’t reach a high level and subsides over time. The second dose triggers a much more vigorous secondary response, generating a lot of memory cells, which remain on patrol to protect the child if he or she is subsequently infected with live pathogens of the same type as used in the vaccine.

Note that each of the memory cells and the T cells and B cells generated in an adaptive immune response are specifically directed against just one type of pathogen or a very closely related strain. Vaccination with MMR vaccine is only protective against measles, mumps and rubella infection.

Despite decades of effort, medical science has so far been unable to produce effective vaccines against a number of important infectious diseases, including HIV/AIDS and other sexually transmitted infections (although trials of several candidate vaccines are underway). Vaccines against malaria have shown some potential, but they only protected about half the vaccinated children in large-

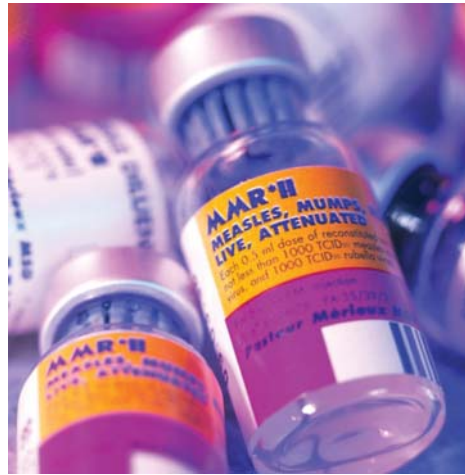


Figure 12 The MMR vaccine contains live attenuated strains of measles, mumps and rubella viruses.

scale African trials (RTS,S Clinical Trials Partnership, 2012). There are no effective vaccines against infections caused by any other single-celled or multicellular parasites.

Some vaccines are effective only for a relatively short time, e.g. cholera vaccines give protection for only around six months. Others, such as the tetanus vaccine, need repeated booster doses. Annual influenza vaccinations are offered to vulnerable groups in the population because influenza viruses alter their antigens over time.

- Why can't vaccines prepared from last year's influenza viruses be guaranteed to give protection against currently circulating flu strains?

Vaccines prepared from earlier strains of influenza viruses will not contain any of the altered antigens that currently circulating strains may have developed; last year's vaccine cannot boost adaptive immunity against viruses with these new antigens.

The second practical challenge is organising and delivering mass vaccination programmes in low- and middle-income countries, especially in remote areas and urban shanty settlements. The terrain may be difficult, transport and communication links are often poor, and communities may not be aware when vaccination teams arrive. Most vaccines have to be kept cold or they lose their potency, but maintaining vaccines at 2–8 °C while vaccinating thousands of children in warm climates without adequate refrigeration requires ingenuity (Figure 13).

Thirdly, education programmes struggle to overcome basic lack of knowledge about vaccination, especially in communities where literacy rates are low and poverty is a daily fact of life. A survey of over 27 000 children in 24 African countries concluded that poor parental education and lack of access to information were critical factors in areas of low vaccine coverage. Only 71% of these children had received the full series of three vaccinations against diphtheria, tetanus and pertussis (whooping cough) by their first birthday, leaving an estimated six million African children unprotected (Wiysonge et al., 2012).



Figure 13 This insulated vaccine carrier is lined with ice packs to keep the vaccines cold during transport to a vaccination session in Ethiopia.

4.12 Opposition to vaccination

Another major challenge is parental opposition to vaccination because of concerns about vaccine safety. Some parents are understandably anxious about taking a healthy child to be given a vaccine derived from infectious agents. Most vaccines are injected, which can be a frightening and painful experience for a child. Of even greater concern is that some children experience a negative reaction to a vaccine, most often inflammation around the injection site and/or a mild fever lasting a day or two, but rare instances of more severe reactions such as convulsions sometimes occur.

Hesitancy about vaccinating a child is increased if parents have no experience of the disease the vaccine prevents, because it has become rare in communities with high vaccine coverage. Some parents conclude that vaccination is unnecessary and might expose their children to an avoidable risk.

Negative rumours about a vaccine are another deterrent. For example, the myth that vaccination is a Western plot to sterilise Muslim children has deterred parents in northern Nigeria, Pakistan and Afghanistan from allowing their children to be vaccinated against polio (Figure 14). Terrorist attacks have occurred against polio vaccination teams in all three countries – the only remaining locations where polio had not been eradicated by the WHO target of 2015.



Figure 14 Negative rumours about the oral polio vaccine did not deter this Nigerian child's parents from bringing her for vaccination.

An inevitable consequence of falling vaccination rates in a community is an increase in infections, sometimes with fatal outcomes. In 2014, the WHO warned that progress on eliminating measles had stalled and the number of deaths had begun to rise – from 122 000 in 2012 to 145 700 in 2013 (WHO News release, 2014). Dr Peter Strebel, from the WHO Department of Immunization, Vaccines and Biologicals warned that:

Countries urgently need to prioritize maintaining and improving immunization coverage. Failure to reverse this alarming trend could jeopardize the momentum generated by a decade of achievements in reducing measles mortality.

(WHO News release, 2014)

Even in countries where over 90% of children are fully vaccinated, uptake rates can plummet under pressure from negative rumours. For example, false claims in 1998 that the MMR vaccine caused autism led to a sustained fall in vaccinations in the UK, followed by a significant rise in measles cases and, to a lesser extent, mumps. The largest outbreak of measles around Swansea in Wales in 2012–13 caused more than 1200 cases and one death (Public Health Wales, 2013). Once parents saw the reality of measles infection and the misery and discomfort it causes, a rapid increase in uptake of the MMR vaccine followed the outbreak. The memory of infection fades in well-protected communities, until an outbreak reminds everyone of how devastating infectious diseases can be.

Session 4 quiz

This quiz allows you to test and apply your knowledge of the material in Session 3.

Session 4 quiz

Open the quiz in a new window or tab then come back here when you're done.

Summary to Session 4

Having completed this final session of the course you should now be familiar with the basic features of a human being's defences against pathogens. The first lines of defence are the physical barriers formed by the skin and secreted mucus, and the initial reaction to a breach of these defences is inflammation. We have introduced you to leukocytes, the key family of cells involved in the two types of immunity: innate and adaptive.

- Innate immunity involves the targeting of non-specific structures, known as PAMPS, on the surface of pathogens, and involves cytotoxic and phagocytic leukocytes.
- Adaptive immunity involves B cells and cytotoxic T cells, two types of leukocyte with receptors that bind to specific molecules on the surface of individual types of pathogen, as well as helper T cells that release signals to boost the immune response.

You have also learned that adaptive immune responses are boosted with repeated exposure to the pathogen due to the remarkable phenomenon of immunological memory. Importantly, immunological memory can be used by health care professionals to prevent disease through the process of vaccination. By exposing a person to an inactive form of a pathogen, that individual acquires an immunological memory of the pathogen. This means that if in future they become infected with the live pathogen they will launch a strong adaptive immune response and the pathogen is quickly destroyed.

As we have outlined, mass vaccination programs represent a key strategy in global health initiatives aimed at eradicating, or at least controlling, infectious diseases. Mass vaccination can be highly effective but, as you will now be aware, vaccine delivery is not straightforward; health workers often have to overcome ignorance and fear, as well as the logistical problems associated with so large a task.

Conclusion

In this free course on *Infection and immunity* you have learned that from prion to protists, via all manner of pathogenic bacteria, viruses and parasites, it is clear that pathogens pose a major threat to human health. Through our immune systems we possess some effective weapons to fight off them off, but these aren't fool proof; infectious diseases remain a major health care challenge.

However, with the careful use of the scientific method we can understand more about the nature of pathogens and use this information to develop new strategies to prevent – and perhaps eradicate – the deadly threat they pose.

- Infectious diseases kill around 10 million people every year worldwide and are caused by pathogens.
- There are more than 1400 different pathogens that cause human diseases, but only about 20 cause two-thirds of human deaths from infection.
- There are many types of pathogen, including multicellular parasites, single-celled protists, yeasts and bacteria, as well as viruses and prions.
- Pathogens can be transmitted directly or indirectly. Direct methods included transmission by touch, sexual transmission and mother-to-child transmission. Indirect methods involve transmission via air, water or food, such as the faecal–oral route and environmental contamination.
- The underlying causes of infectious diseases include biological susceptibility, the social and economic conditions in which people live, and behaviours that influence the spread of infection.
- The symptoms of a disease can only be experienced by the person who suffers from them, whereas the signs of a disease can be observed by others.
- Infectious diseases may be acute, resulting in recovery or death within a few weeks, or chronic and slowly progressing over months or years; a chronic condition may include an acute episode.
- The application of the scientific method has been central in humankind's fight against infectious disease, and is characterised by systematic observation, measurement, experiment, and the formulation, testing and modification of hypotheses.
- Early examples of the use of the scientific method include John Snow's experiment of removing the handle from the Broad Street pump, which demonstrated that cholera was transmitted in contaminated water almost 30 years before bacteria were identified, and Edward Jenner's smallpox inoculation experiment.
- A person's defences against pathogens begin with physical and chemical barriers such as intact skin; when these are breached we rely on our immune system to fight infection.
- The immune system has two distinct branches – innate and adaptive immunity – each of which uses different types of leukocytes.

- The innate immune system is non-specific; the leukocytes involved cannot distinguish between different types of pathogen. By contrast, leukocytes involved in adaptive immunity are specific to different pathogens.
- Some adaptive immune system leukocytes have a 'memory'. This leads to more effective immune responses with each exposure to the pathogen.

Now you've completed the course we would again appreciate a few minutes of your time to tell us a bit about your experience of studying it and what you plan to do next. We will use this information to provide better online experiences for all our learners and to share our findings with others. If you'd like to help, please fill in this optional survey .

If you enjoyed the course and are thinking about studying the module this material was adapted from (SDK100 *Science and health, an evidence based approach*) you can read more about the module and the health sciences qualification. You can also undertake a self-diagnostic quiz to check whether you have the necessary background knowledge and skills to cope with studying SDK100.

Finally, if you have any questions about this course, or about studying health sciences with The Open University, you can discuss these with Claire Rostron on the course forum.

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Session 1

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