Cambridge AS Level Biology

Code (9700)

Chapter 10 and Chapter 11

Infectious diseases and immunity

Infectious diseases are diseases that are caused by organisms known as **pathogens**.

In Chapter 9, we considered **non-infectious diseases** of the gas exchange and cardiovascular systems, such as lung cancer and COPD. These are long-term degenerative diseases.

The word '**disease'** implies something very serious, yet many conditions that make us feel ill, such as the common cold, are not as harmful to health as the diseases discussed in this chapter

A **disease** is an illness or disorder of the body or mind that leads to poor health; each disease is associated with a set of signs and symptoms.

Some people may spread a pathogen even though they do not have the disease themselves. People like this who lack symptoms are called **carriers**, and it can be very difficult to trace them as the source of an infection.

The way in which a pathogen passes from one host to another is called the **transmission** cycle.

Vaccination is a major control measure for many infectious diseases; it works by making us immune so that pathogens do not live and reproduce within us and do not then spread to others

Worldwide importance of infectious diseases

This chapter discusses five significant infectious diseases globally: cholera, malaria, HIV/AIDS, tuberculosis, and measles. Smallpox has been eradicated, but the high number of people infected remains a significant public health issue, especially in areas lacking efficient health services.

Table 10.1 shows the **causative agents** of the six chosen diseases. To control a disease, we must first know what causes it.

A new strain of **cholera** appeared in 1992 but is so far restricted to South-East Asia.

Malaria has been on the increase since the 1970s and constitutes a serious risk to health in many tropical countries.

AIDS was officially recognised in 1981, but the infective agent HIV) was in human populations for many years before it was identified

TB, once thought to be nearly eradicated, has shown an increase since the 1970s and is a considerable health risk in many countries. Thanks to vaccination, **measles** is a disease that is now very rare in developed countries, but remains a serious threat to the health of children who live in poverty in many developing countries.

Diseases that are always in populations are described as **endemic.**

The **incidence** of a disease is the number of people who are diagnosed over a certain period of time, usually a week, month or year.

The **prevalence** of a disease is the number of people who have that disease at any one time. An **epidemic** occurs when there is a sudden increase in the number of people with a disease.

A **pandemic** occurs when there is an increase in the number of cases throughout a continent or across the world. The death rate from different diseases is referred to as **mortality**.

Cholera

Transmission of cholera

The features of cholera are given in Table 10.2. Cholera is caused by the bacterium Vibrio cholerae (Figure 10.2).

Infected people, three-quarters of whom may be symptomless carriers, pass out large numbers of bacteria in their faeces. If these contaminate the water supply, or if infected people handle food or cooking utensils without washing their hands, then bacteria are transmitted to uninfected people.

Pathogen	*Vibrio cholerae*
Methods of transmission	food-borne, water-borne
Global distribution	Asia, Africa, Latin America
Incubation period	two hours to five days
Site of action of pathogen	wall of small intestine
Clinical features	severe diarrhoea ('rice water'), loss of water and salts, dehydration, weakness
Method of diagnosis	microscopical analysis of faeces
Annual incidence worldwide	3–5 million
Annual mortality worldwide	100 000–120 000

Table 10.2 The features of cholera.

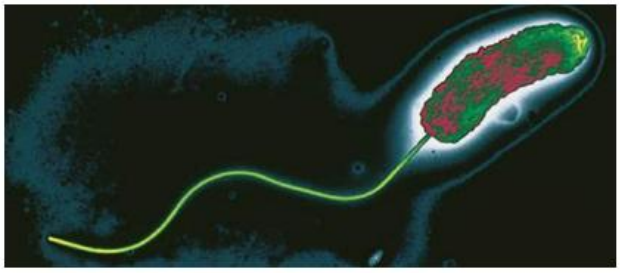


Figure 10.2 An electron micrograph of *Vibrio cholerae*. The faeces of an infected person are full of these bacteria, each with its distinctive flagellum (×13 400).

However, if the bacteria do reach the small intestine, they multiply and secrete a toxin, **choleragen**, which disrupts the functions of the epithelium lining the intestine, so that salts and water leave the blood.

Treating cholera

If people can drink, they are given **oral rehydration therapy**. Glucose is effective, because it is absorbed into the blood and takes ions (for example, sodium and potassium ions) with it.

Preventing cholera

Cholera is a disease that thrives in developing countries due to inadequate sewage treatment and clean water supply. The disease is endemic in West and East Africa and Afghanistan. However, due to sewage treatment and clean piped water, the transmission cycle has been broken. Health authorities fear outbreaks following natural disasters, such as Haiti's 2010 earthquake. Vaccination for travelers from free to endemic areas has been dropped, as the vaccine only provides short-term protection.

Figure 10.3 People being treated in Port-au-Prince in Haiti during the 2010 cholera epidemic. The drips contain a solution of salts to replace those lost through severe diarrhoea. Cholera causes many deaths when normal life is disrupted by war and by natural catastrophes such as earthquakes.

Strains of cholera

Cholera is caused by various strains of V. cholerae, with the most common strain being O1. Between 1817 and 1923, six cholera pandemics occurred in Bangladesh, each originating from the 'classical' strain, O1. In 1961, a new strain, 'El Tor', emerged in Indonesia, spreading to India, Italy, and South America. The virus spread rapidly, with an

average of 2550 cases per day in 1991. In 1992, a new strain, O139, emerged in Chennai and spread to India and Bangladesh, potentially causing an eighth pandemic.

Malaria

Transmission of malaria

Malaria is caused by Plasmodium, a protoctist. Female Anopheles mosquitoes feed on human blood to obtain protein for egg development. Infected individuals take up gametes from the blood meal, fuse in the mosquito's gut, and form infective stages. These stages pass into the blood, where parasites multiply. The female Anopheles mosquito is a vector, transmitting the disease when she passes the infective stages into an uninfected person. Malaria can also be transmitted during blood transfusions and reusing unsterile needles.

Pathogen	*Plasmodium falciparum*, *P. vivax*, *P. ovale*, *P. malariae*
Method of transmission	insect vector: female *Anopheles* mosquito
Global distribution	throughout the tropics and sub-tropics (endemic in 106 countries)
Incubation period	from a week to a year
Site of action of pathogen	liver, red blood cells, brain
Clinical features	fever, anaemia, nausea, headaches, muscle pain, shivering, sweating, enlarged spleen
Method of diagnosis	microscopical examination of blood (Figure 10.5); dip stick test for malaria antigens in blood
Annual incidence worldwide	about 207 million cases of malaria in 2012 (about 80% are in Africa)
Annual mortality worldwide	about 630 000 deaths in 2012 (about 90% are in Africa)

Table 10.3 The features of malaria.

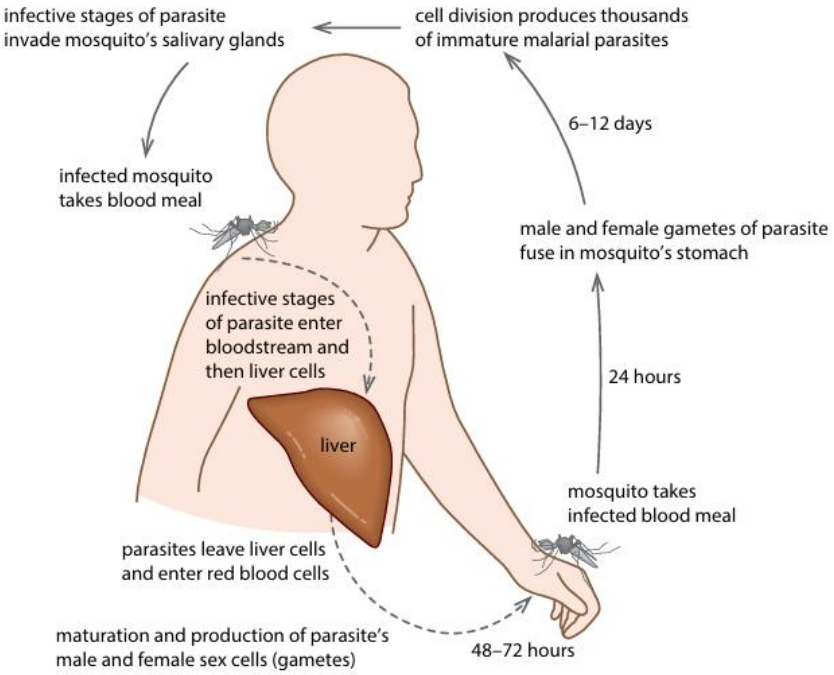


Figure 10.4 The life cycle of *Plasmodium*. The parasite has two hosts: the sexual stage occurs in mosquitoes, the asexual stage in humans. The time between infection and appearance of parasites inside red blood cells is 7–30 days in *P. falciparum*; longer in other species.

Plasmodium increases in both humans and mosquitoes, increasing the chances of infection. Individuals become immune to malaria if they survive the first five years of life, but immunity only lasts as long as they are in contact with the disease. Malaria is more dangerous during and after the rainy season, affecting agriculture and the economy.

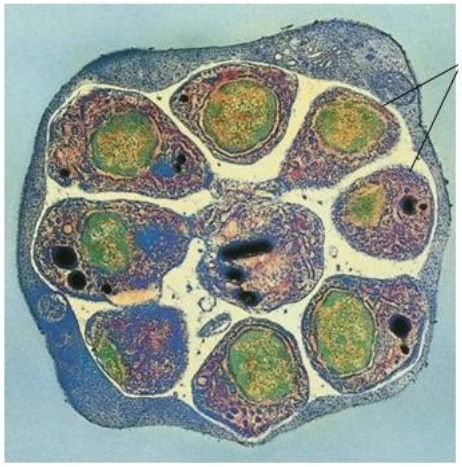


Figure 10.6 A transmission electron micrograph of a section through a red blood cell packed tightly with malarial parasites. *Plasmodium* multiplies inside red blood cells; this cell will soon burst, releasing parasites which will infect other red blood cells.

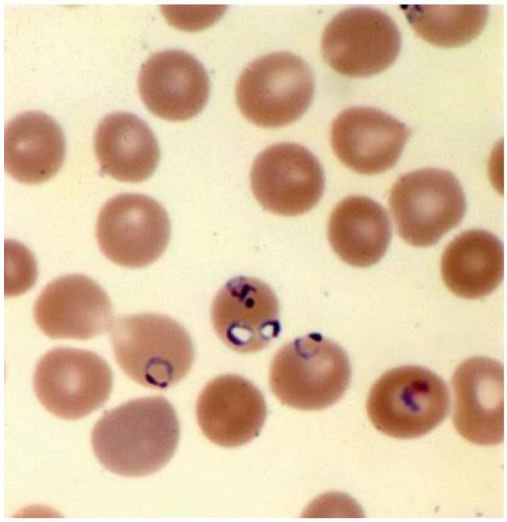


Figure 10.5 Red blood cells infected with *Plasmodium falciparum*. Notice the characteristic 'signet ring' appearance of the parasites inside the red blood cells (× 1300).

Treating malaria

Anti-malarial drugs such as quinine and chloroquine are used to treat infected people. They are also used as prophylactic (preventative) drugs, stopping an infection occurring if a person is bitten by an infected mosquito.

Prophylactic drugs like chloroquine and proguanil are used to prevent malaria in areas with endemic malaria. However, drug-resistant Plasmodium strains have led to the use of newer drugs like mefloquine in some regions. Non-malarial countries visiting tropical areas are at high risk of contracting malaria, with many misdiagnosed as influenza. Settled immigrants visiting relatives in Africa or India often do not take prophylactic drugs, unaware of the loss of immunity.

Preventing malaria

There are three main ways to control malaria:

■ reduce the number of mosquitoes

■ avoid being bitten by mosquitoes

■ use drugs to prevent the parasite infecting people

Marshes can be drained and vegetation cleared. Two biological control measures that can be used are:

■ stocking ponds, irrigation and drainage ditches and other permanent bodies of water with fish which feed on mosquito larvae

■ spraying a preparation containing the bacterium Bacillus thuringiensis, which kills mosquito larvae but is not toxic to other forms of life.

Worldwide control of malaria

In the 1950s, the World Health Organization (WHO) coordinated a worldwide eradication programme. Although malaria was cleared from some countries, the programme was not generally successful. There were two main reasons for this:

■ Plasmodium became resistant to the drugs used to control it

■ mosquitoes became resistant to DDT and the other insecticides that were used at the time, such as dieldrin.

The reasons for the worldwide concern over the spread of malaria are:

■ an increase in drug-resistant forms of Plasmodium

■ an increase in the proportion of cases caused by P. falciparum, the form that causes severe, often fatal malaria

■ difficulties in developing vaccines against malaria

■ an increase in the number of epidemics, because of climatic and environmental changes that favour the spread of mosquitoes

■ the migration of people from areas where malaria is endemic, for economic and political reasons.

Three factors may lead to improvements in the control of malaria:

■ use of modern techniques in gene sequencing and drug design

■ development of vaccines targeted against different stages of the parasite's life cycle

■ a renewed international will to remove the burden of disease from the poorest parts of the world, allied to generous donations from wealthy individuals and foundations.

Acquired immune deficiency syndrome (AIDS)

Features of AIDS and HIV are listed in Table 10.4. AIDS is caused by the human immunodeficiency virus (HIV) (Figure 10.7).

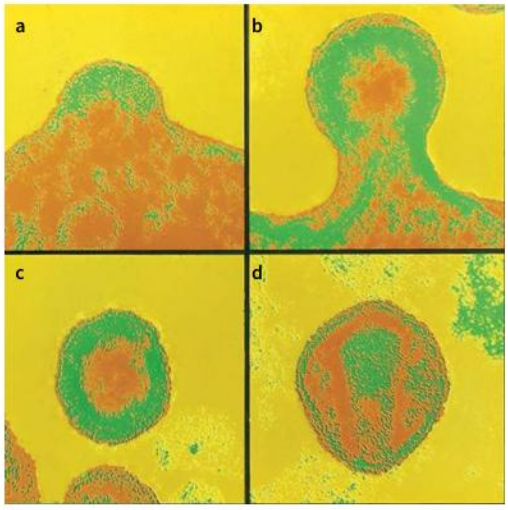


Figure 10.8 A series of transmission electron micrographs showing HIV budding from the surface of an infected lymphocyte and becoming surrounded by a membrane derived from the cell surface membrane of the host cell (×176 000). **a** The viral particle first appears as a bump, **b** which then buds out and **c** is eventually cut off. **d** The outer shell of dense material and the less dense core are visible in the released virus.

Pathogen	human immunodeficiency virus
Methods of transmission	in semen and vaginal fluids during sexual intercourse, infected blood or blood products, contaminated hypodermic syringes, mother to fetus across placenta, at birth, mother to infant in breast milk
Global distribution	worldwide, especially in sub-Saharan Africa and South-East Asia
Incubation period	initial incubation a few weeks, but up to ten years or more before symptoms of AIDS may develop
Site of action of pathogen	T helper lymphocytes, macrophages, brain cells
Clinical features	HIV infection – flu-like symptoms and then symptomless AIDS – opportunistic infections including pneumonia, TB and cancers; weight loss, diarrhoea, fever, sweating, dementia
Method of diagnosis	testing blood, saliva or urine for the presence of antibodies produced against HIV
Estimated total number of people infected with HIV worldwide in 2012	35.5 million (69% of these in sub-Saharan Africa)
Estimated number of new cases of HIV infection worldwide in 2012	2.3 million
Estimated number of deaths from AIDS-related diseases worldwide in 2012	1.6 million (UNAIDS estimate)

Table 10.4 The features of HIV/AIDS.

Figure 10.7 Human immunodeficiency virus (HIV). The outer envelope contains two glycoproteins: gp120 and gp41. The protein core contains genetic material (RNA) and two enzymes: a protease and reverse transcriptase. Reverse transcriptase uses the RNA as a template to produce DNA (page 466) once the virus is inside a host cell.

These cells, known as **helper T cells** (page 230), control the immune system's response to infection.

When the numbers of these cells are low, the body is unable to defend itself against infection, so allowing a range of pathogens to cause a variety of **opportunistic infections**

Transmission of HIV

The HIV/AIDS pandemic began in the early 1980s, with over 25 million deaths by 2010. The virus is spread through intimate human contact, sexual intercourse, blood donation, needle sharing, and mother-to-child transmission. The initial epidemic in North America and Europe was among male homosexuals who practiced anal intercourse and had multiple sex partners, as the rectal lining is less thick and less lubricated.

Figure 10.9 shows the global distribution of HIV/AIDS. The statistics below show how serious the pandemic is in sub-Saharan Africa.

■ 70% of the world's deaths from AIDS occur in Africa.

■ In 2007 it was estimated that 15 million people had died of HIV/AIDS in sub-Saharan Africa since the beginning of the pandemic.

■ 25% of the adult population of Botswana is infected with HIV.

■ Between 15% and 25% of people aged 15–49 in Botswana and Zimbabwe are infected with HIV.

■ Over 16 million children are estimated to have lost one or both parents to AIDS; in some places this is 25% of the population under 15.

■ The prevalence of HIV among women attending antenatal clinics in Zimbabwe was around 20% in 2012.

■ A large proportion of women in Rwanda are HIV positive following the use of rape as a genocidal weapon in the civil war of the early 1990s.

■ The average life expectancy in South Africa dropped from 65 to 55 during 1995–1999.

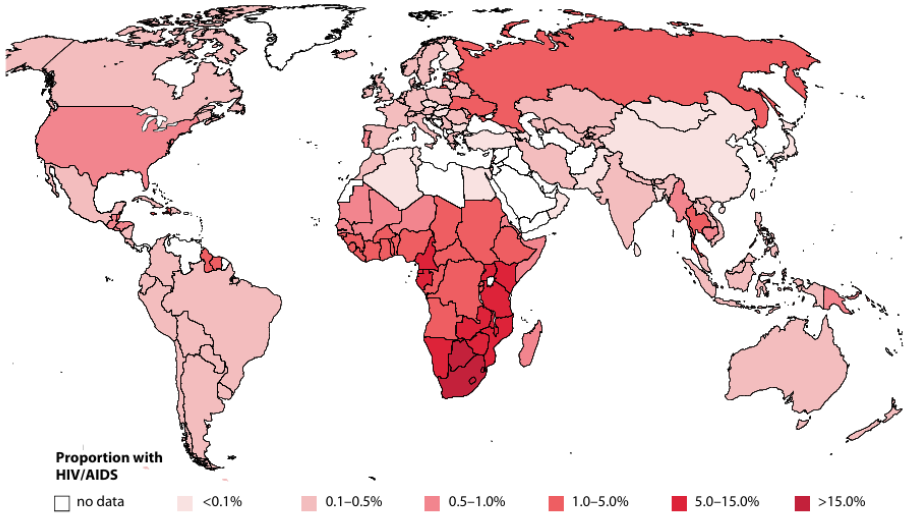


Figure 10.9 The global distribution of HIV/AIDS in 2010.

Treating HIV/AIDS

AIDS has no cure or vaccine, and the number of people with HIV who will progress to full-blown AIDS is unknown. Drug therapy can slow the onset of AIDS, but it is expensive and has side effects. Combination therapy, which involves taking multiple drugs to prevent virus replication, can prolong life but does not offer a cure. It is crucial to follow a strict regimen and avoid strains of HIV that have developed resistance to the drugs.

Preventing HIV/AIDS

HIV/AIDS spread is challenging due to its long latent stage, making it difficult for HIV positive individuals to recognize and develop a vaccine. Public health measures, such as education and the use of condoms, femidoms, and dental dams, are the only effective ways to reduce infection risk. Countries that promote condom use have seen a 25% decrease in HIV infection rates between 2001 and 2009.

Contact tracing is an important part of controlling the spread of HIV. If a person who is diagnosed as HIV positive is willing and able to identify the people whom he or she has put at risk of infection by sexual intercourse or needle sharing, then these people will be offered an HIV test.

Tuberculosis (TB)

Table 10.5 gives the main features of this disease. TB is caused by either of two bacteria, Mycobacterium tuberculosis (Figure 10.10) and Mycobacterium bovis. These are pathogens that live inside human cells, particularly in the lungs. This is the first site of infection, but the bacteria can spread throughout the whole body and even infect the bone tissue.

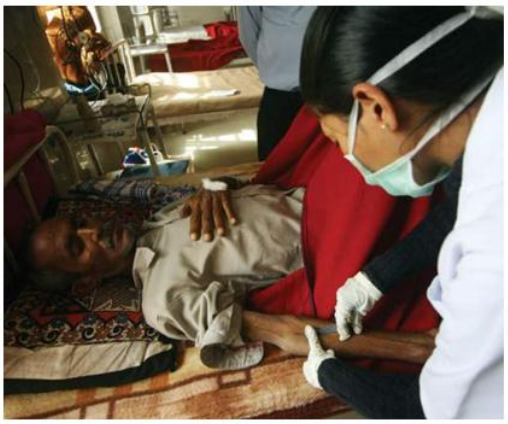


Figure 10.11 A TB patient undergoes treatment in a hospital in India.

Pathogen	*Mycobacterium tuberculosis*; *Mycobacterium bovis*
Methods of transmission	airborne droplets (*M. tuberculosis*); via undercooked meat and unpasteurised milk (*M. bovis*)
Global distribution	worldwide
Incubation period	few weeks or up to several years
Site of action of pathogen	primary infection in lungs; secondary infections in lymph nodes, bones and gut
Clinical features	racking cough, coughing blood, chest pain, shortness of breath, fever, sweating, weight loss
Methods of diagnosis	microscopical examination of sputum for bacteria, chest X-ray
Annual incidence worldwide in 2012	8.6 million
Annual mortality worldwide in 2012	1.3 million (including 320 000 deaths of people who were HIV+)

Table 10.5 The features of TB.

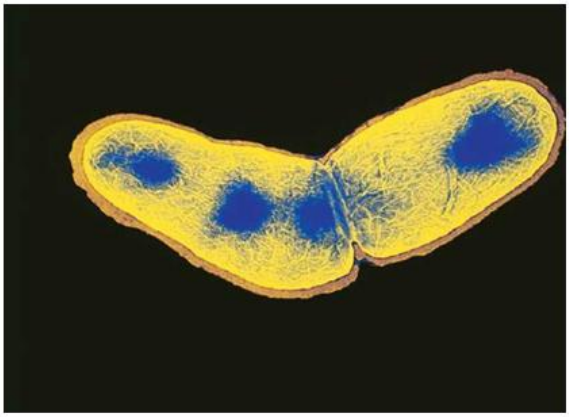


Figure 10.10 False-colour transmission electron micrograph of *Mycobacterium tuberculosis* dividing into two. It may multiply like this inside the lungs and then spread throughout the body or lie dormant, becoming active many years later.

Transmission of TB

TB is spread through coughing or sneezing, with the bacteria carried in droplets of liquid. It is most prevalent in overcrowded conditions, particularly among the homeless and those with low immunity. TB also occurs in cattle and is spread to humans through meat and milk. Between 1850 and 1950, around 800,000 deaths were caused by TB transmitted from cattle in the UK. The incidence of TB decreased before the introduction of a vaccine in the 1950s.

The incidence in such areas is as high as in less economically developed countries. T his increase is due in part to the following factors:

■ some strains of TB bacteria are resistant to drugs

■ the HIV/AIDS pandemic

■ poor housing in inner cities and homelessness

■ the breakdown of TB control programmes; partial treatment for TB increases the chance of drug resistance in Mycobacterium.

Treating TB

Doctors collect sputum samples to identify TB bacteria, which can be quickly identified through microscopy. If confirmed, patients should be isolated during the most infectious stage, especially if infected with drug-resistant strains. Treatment involves multiple drugs to kill bacteria, but it takes six to nine months. Many people do not complete their treatment, potentially harboring drug-resistant bacteria that could spread to others.

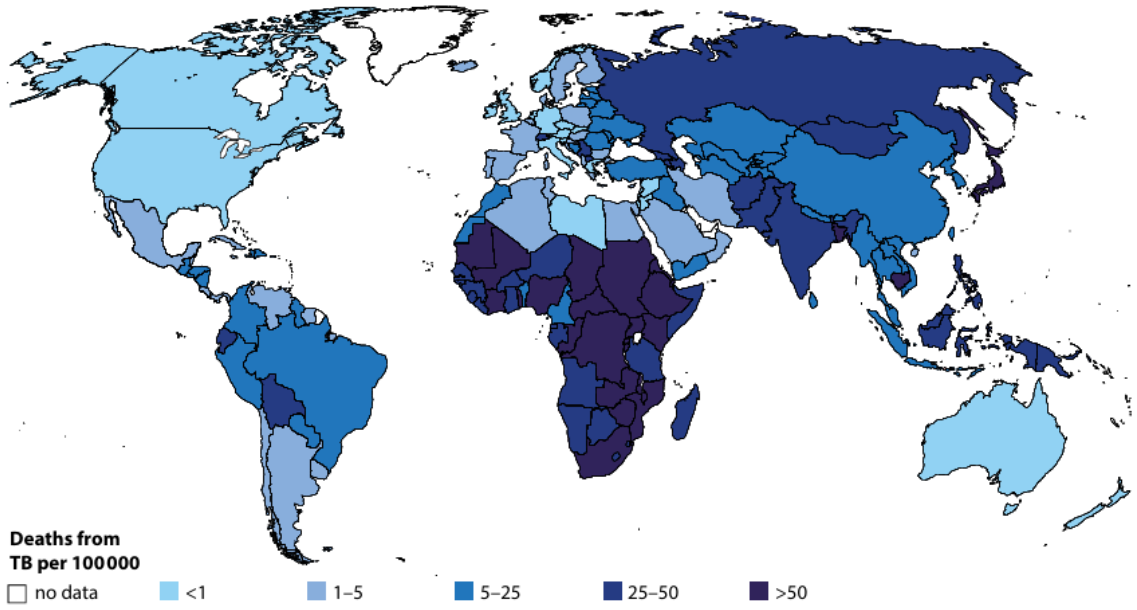


Figure 10.12 The global distribution of TB in 2010 (data from WHO).

Drug-resistant TB

Drug-resistant M. tuberculosis strains were identified in the 1950s, with antibiotic treatment causing mutations in bacterial DNA. If treatment is not completed or the bacteria are not eliminated, mutations can occur, leading to resistance to all drugs. Stopping treatment early can result in drug-resistant forms of TB, with 10 to 15 others infected, especially in overcrowded conditions.

Preventing TB

Controlling TB involves contact tracing and testing for bacterium symptoms, which can take up to two weeks. The BCG vaccine, derived from M. bovis, protects 70-80% of recipients. Countries like the UK and USA do not include BCG vaccination in their immunization programs. TB can be transmitted between cattle and humans, and control methods like cattle testing and pasteurization have reduced the incidence of human TB. In the UK, less than 1% of new TB cases are due to M. bovis.

Measles

Measles is caused by a virus which enters the body and multiplies inside cells in the upper respiratory tract (nasal cavity and trachea). There are no symptoms for 8–14 days after the initial infection and then a rash appears and a fever develops. Other symptoms are a runny nose, a cough, red and watery eyes (conjunctivitis) and small white spots that may develop inside the cheeks.

Antibiotics

An antibiotic is a drug that kills or stops the growth of bacteria, without harming the cells of the infected organism. Antibiotics are derived from living organisms, although they are often made more effective by various chemical processes.

How antibiotics work

Antibiotics interfere with some aspect of growth or metabolism of the target bacterium (Figure 10.13). These include:

- synthesis of bacterial cell walls (Figure 1.30, page 21)
- activity of proteins in the cell surface membrane (Chapter 4)
- enzyme action (Chapter 3)
- DNA synthesis (replication, Chapter 6, pages 113–118)
- protein synthesis (Chapter 6, pages 119–122).

Autolysins in bacterial cells create holes in their cell wall, allowing new peptidoglycan chains to link. Penicillin prevents this, but autolysins continue, weakening the cell wall. Bacteria in watery environments can burst due to this pressure.

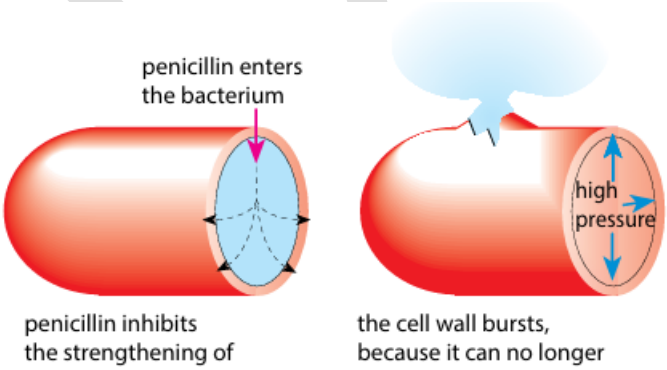


Figure 10.14 How penicillin works.

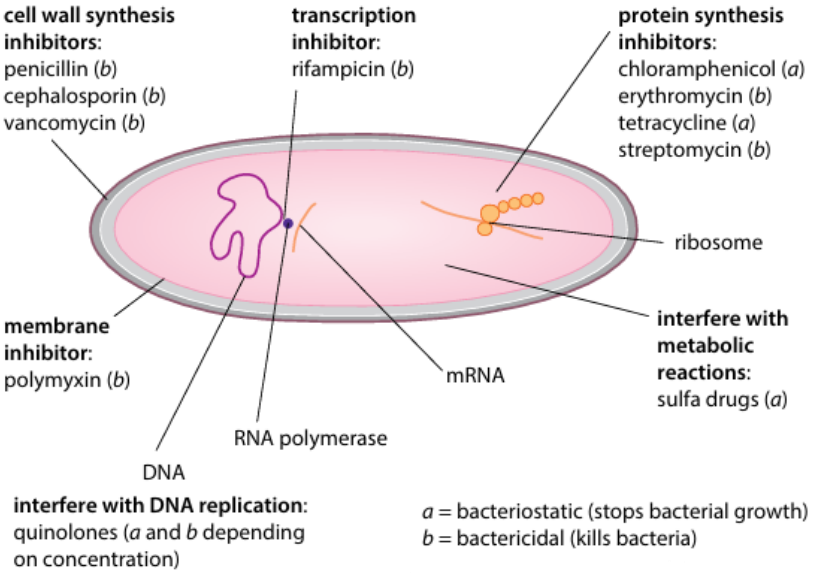


Figure 10.13 The sites of action of antibiotics in bacteria.

Antibiotic resistance

Penicillin doesn't work on M. tuberculosis due to its thick cell wall and enzyme-catalyzing breakdown. Other bacteria's membranes can inactivate antibiotics, and some antibiotics may not bind to the intended site. Strict bacteria may become resistant if they gain a protein-protecting gene. Soil bacteria have resistance mechanisms similar to pathogenic bacteria, and beta-lactamases were not common before antibiotics.

A large population of a penicillin-resistant strain of a bacterium would result. This method of spreading antibiotic resistance in a population of bacteria is called **vertical transmission.**

Transfer of part of the DNA from the bacterial chromosome also occurs in the same way. This method of transmission is **horizontal transmission** (Figure 10.15). Thus it is possible for resistance to a particular antibiotic to arise in one species of bacterium and be passed on to another.

Misuse of antibiotics increases the pressure on bacteria to develop antibiotic-resistant strains, increasing the risk of death and hospital stays. Resistance spreads among different bacteria species, with non-pathogenic bacteriums potentially passing to pathogenic ones. Widespread antibiotic use can lead to multiple resistance genes, posing major problems for doctors, as seen with methicillin-resistant Staphylococcus aureus (MRSA).

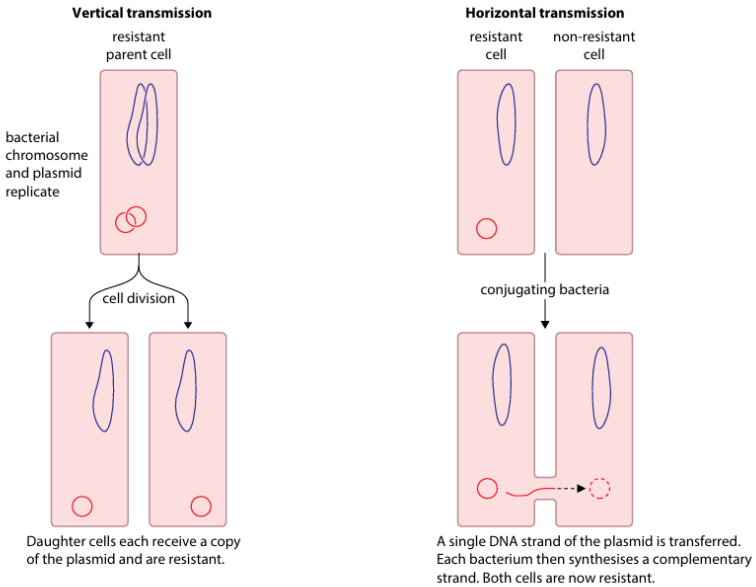


Figure 10.15 Vertical and horizontal transmission of resistance in bacteria.

Choosing effective antibiotics

Antibiotics should be chosen carefully. Testing antibiotics against the strain of the bacterium isolated from people ensures that the most effective antibiotic can be used in treatment. As fast as we develop new antibiotics, bacteria seem to develop resistance to them. It follows from this that there is a constant search for new antibiotics, especially ones that work in a completely different way from those currently in use.

Figure 10.16 The grey areas on the agar jelly in this Petri dish are colonies of the bacterium *Escherichia coli*. The white discs are pieces of card impregnated with different antibiotics. Where there are clear areas around the discs the antibiotic has prevented the bacteria from growing. However, you can see that this strain of *E. coli* is resistant to the antibiotics on the discs at the bottom left and has been able to grow right up to the discs.

Clearly we should try to reduce the number of circumstances in which bacteria develop resistance to antibiotics. Some of the ways in which we can do this include:

■ using antibiotics only when appropriate and necessary; not prescribing them for viral infections

■ reducing the number of countries in which antibiotics are sold without a doctor's prescription

■ avoiding the use of so-called wide-spectrum antibiotics and using instead an antibiotic specific to the infection (known as narrow spectrum)

■ making sure that patients complete their course of medication

■ making sure that patients do not keep unused antibiotics for self-medication in the future

■ changing the type of antibiotics prescribed for certain diseases so that the same antibiotic is not always prescribed for the same disease

■ avoiding using antibiotics in farming to prevent, rather than cure, infections.

Chapter 11 – Immunity

Most people have measles only once. In most cases, it is very unlikely that anyone surviving the disease will have it again. They are **immune.**

Defence against disease

External defence system

We have various defense mechanisms against infectious diseases like measles, including physical, chemical, and cellular defenses. These include airway epithelia, stomach hydrochloric acid, and blood clotting. These mechanisms prevent pathogens from entering our bodies, ensuring their safety and health.

Internal defence system

White blood cells are part of the immune system and they recognise pathogens by the distinctive, large molecules that cover their surfaces, such as proteins, glycoproteins, lipids and polysaccharides, and the waste materials which some pathogens produce. Any molecule which the body recognises as foreign is an **antigen**.

Each of us has molecules on the surfaces of our cells that are not found in other organisms, or even in other humans. These are often called cell **surface antigens.**

Cells of the immune system

The cells of the immune system originate from the bone marrow. There are two groups of these cells involved in defence:

■ phagocytes (neutrophils and macrophages)

■ lymphocytes. All of these cells are visible among red blood cells when a blood smear is stained to show nuclei as shown in Figure 11.2.

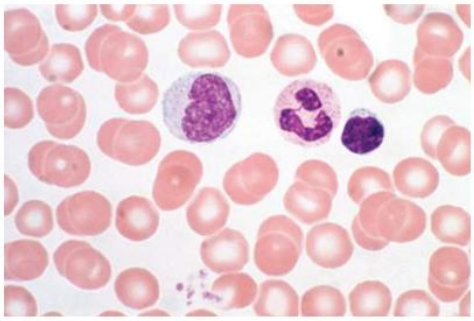


Figure 11.2 A monocyte (left), which will develop into a macrophage, a neutrophil (centre) and a lymphocyte (right), together with red blood cells in a blood smear which has been photographed through a light microscope. The cytoplasm of the neutrophil contains vacuoles full of hydrolytic enzymes (×1000).

Phagocytes

Phagocytes are produced throughout life in the bone marrow.

Macrophages are long-lived cells and play a crucial role in initiating immune responses, since they do not destroy pathogens completely, but cut them up to display antigens that can be recognised by lymphocytes.

Phagocytosis

If pathogens invade the body and cause an infection, some of the cells under attack respond by releasing chemicals such as **histamine**

Neutrophils have a short life: after killing and digesting some pathogens, they die. Dead neutrophils often collect at a site of infection to form pus.

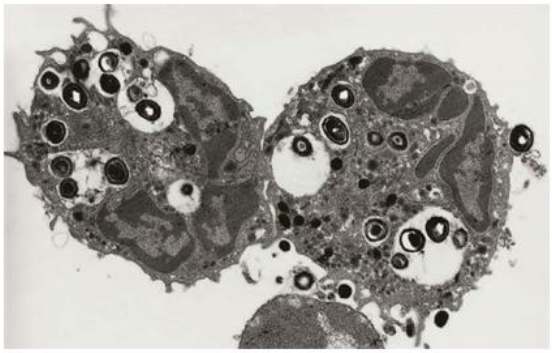


Figure 11.3 A transmission electron micrograph of two neutrophils that have ingested several *Staphylococcus* bacteria (×4000). Notice at the extreme right, one bacterium being engulfed. Compare this photograph with Figure 11.4.

Lymphocytes

Lymphocytes are a second type of white blood cell. They play an important role in the immune response.

here are two types of lymphocyte, both of which are produced before birth in bone marrow.

■ B-lymphocytes (B cells) remain in the bone marrow until they are mature and then spread throughout the body, concentrating in lymph nodes and the spleen.

■ T-lymphocytes (T cells) leave the bone marrow and collect in the thymus where they mature. The thymus is a gland that lies in the chest just beneath the sternum. It doubles in size between birth and puberty, but after puberty it shrinks.

B-lymphocytes

As each B cell matures, it gains the ability to make just one type of antibody molecule. Many different types of B cell develop in each of us, perhaps as many as 10 million. While B cells are maturing, the genes that code for antibodies are changed in a variety of ways to code for different antibodies.

Other B cells become memory cells. These cells remain circulating in the body for a long time. If the same antigen is reintroduced a few weeks or months after the first infection, memory cells divide rapidly and develop into plasma cells and more memory cells.

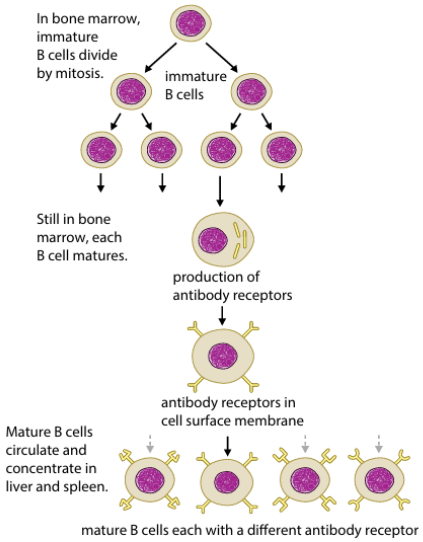
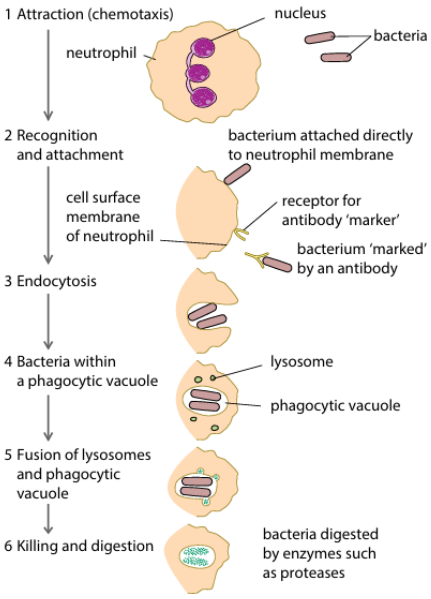


Figure 11.5 Origin and maturation of B-lymphocytes. As they mature in bone marrow, the cells become capable of secreting one type of antibody molecule with a specific shape. Some of these molecules become receptor proteins in the cell surface membrane and act like markers. By the time of a child's birth, there are millions of different B cells, each with a specific antibody receptor.



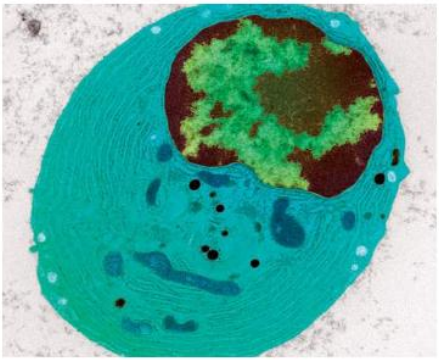


Figure 11.7 Electron micrograph of the contents of a plasma cell (×3500). There is an extensive network of rough endoplasmic reticulum in the cytoplasm (green) for the production of antibody molecules, which plasma cells secrete into blood or lymph by exocytosis (Chapter 4). The mitochondria (blue) provide ATP for protein synthesis and the movement of secretory vesicles.

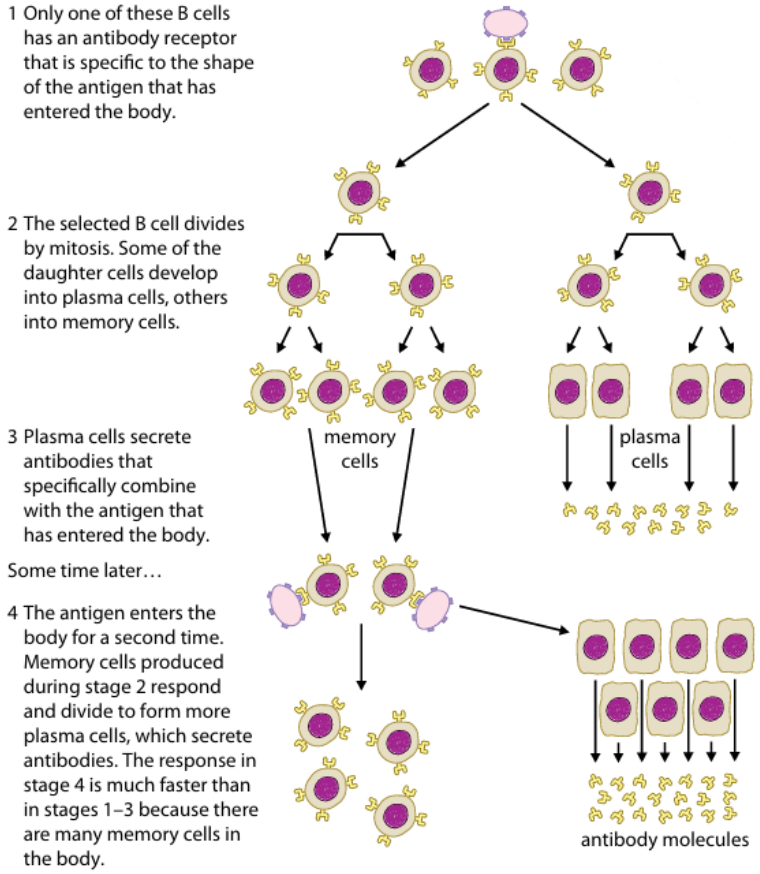


Figure 11.6 The function of B-lymphocytes during an immune response. The resulting changes in antibody concentration are shown in Figure 11.8.

The first or The first or primary response is slow because, at this stage, there are very few B cells that are specific to the antigen. The secondary response is faster because there are now many memory cells, which quickly divide and differentiate into plasma cellsis slow because, at this stage, there are very few B cells that are specific to the antigen. The **secondary response** is faster because there are now many memory cells, which quickly divide and differentiate into plasma cells

However, we do suffer repeated infections of the common cold and influenza, because there are many different and new strains of the viruses that cause these diseases, each one having different antigens. Each time a pathogen with different antigens infects us, the primary response must occur before we become immune, and during that time we often become ill.

Antibodies

Antibodies are all globular glycoproteins with quaternary structure (page 42). They form the group of plasma proteins called immunoglobulins.

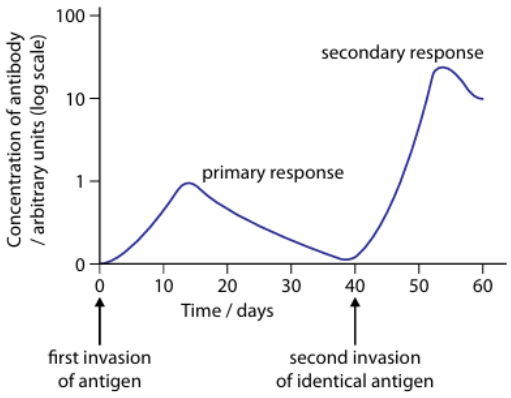


Figure 11.8 The changes in antibody concentration in the blood during a primary and secondary response to the same antigen.

The antigen-binding sites form the **variable region**, which is different on each type of antibody molecule produced. The 'hinge' region gives the flexibility for the antibody molecule to bind around the antigen.

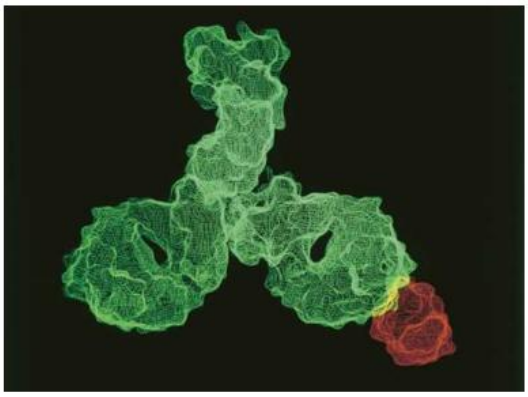


Figure 11.9 A model of an antibody made using computer graphics. The main part (green) is the antibody molecule, and the small part in the bottom right-hand corner (red) is an antigen at one of the two antigen-binding sites. Compare this with Figure 11.10. This type of antibody molecule with four polypeptides is known as immunoglobulin G, IgG for short. Larger types of antibody molecules are IgA with four antigen binding sites and IgM with ten.

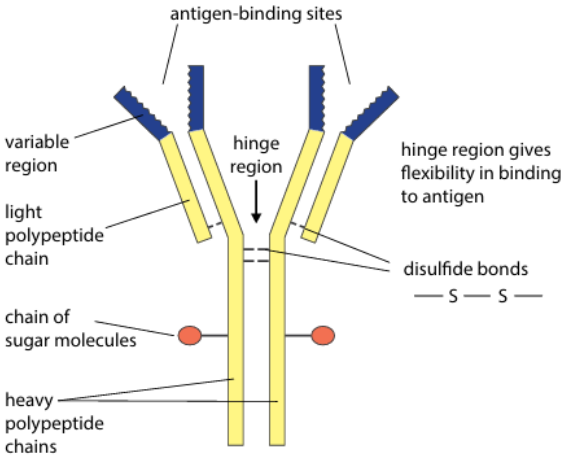


Figure 11.10 A diagram of an antibody molecule. Antigen–antibody binding occurs at the variable regions. An antigen fits into the binding site like a substrate fitting into the active site of an enzyme. The constant region of the molecule is shown in yellow, and it is identical in all antibodies like this that have four polypeptides.

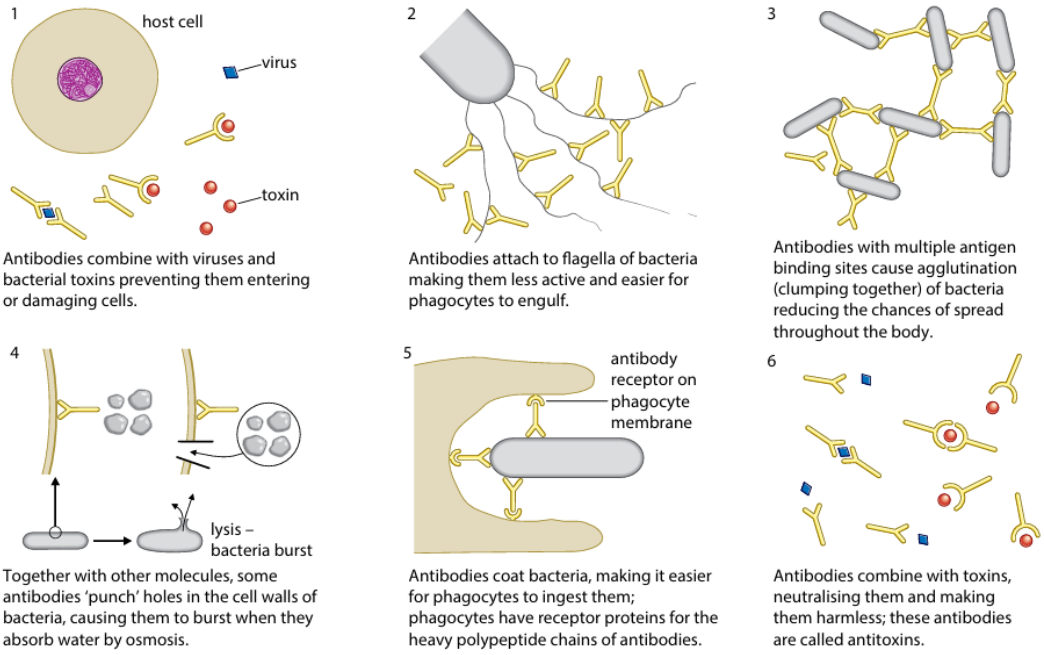


Figure 11.11 The functions of antibodies. Antibodies have different functions according to the type of antigen to which they bind. Note that the diagrams of antibodies are purely symbolic and do not represent their actual shapes, sizes or positions of binding sites.

T-lymphocytes

Mature T cells have specific cell surface receptors called T cell receptors (Figure 11.12). The display of antigens on the surface of cells in this way is known as **antigen presentation.**

There are two main types of T cell:

■ ■ helper T cells

■ ■ killer T cells (or cytotoxic T cells).

When helper T cells are activated, they release hormone like **cytokines** that stimulate appropriate B cells to divide, develop into plasma cells and secrete antibodies.

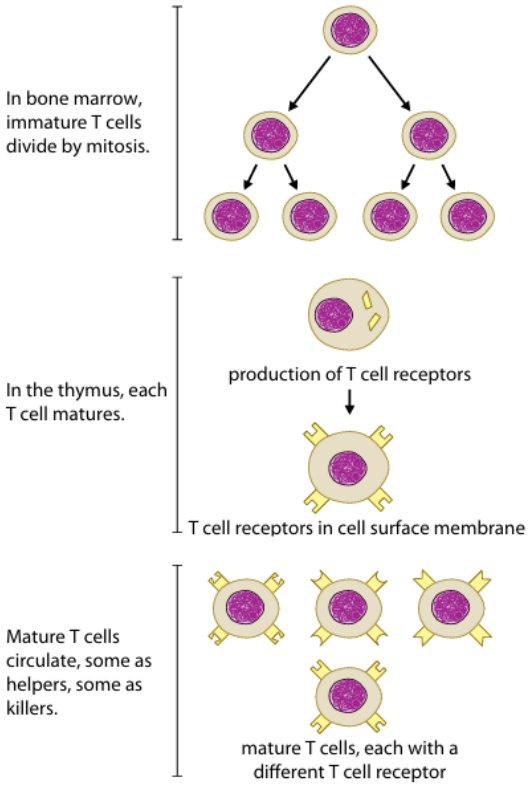


Figure 11.12 Origin and maturation of T-lymphocytes. As T cells mature in the thymus gland they produce T cell receptor proteins. Each cell has a specific receptor. Some cells become helper T cells, others become killer T cells.

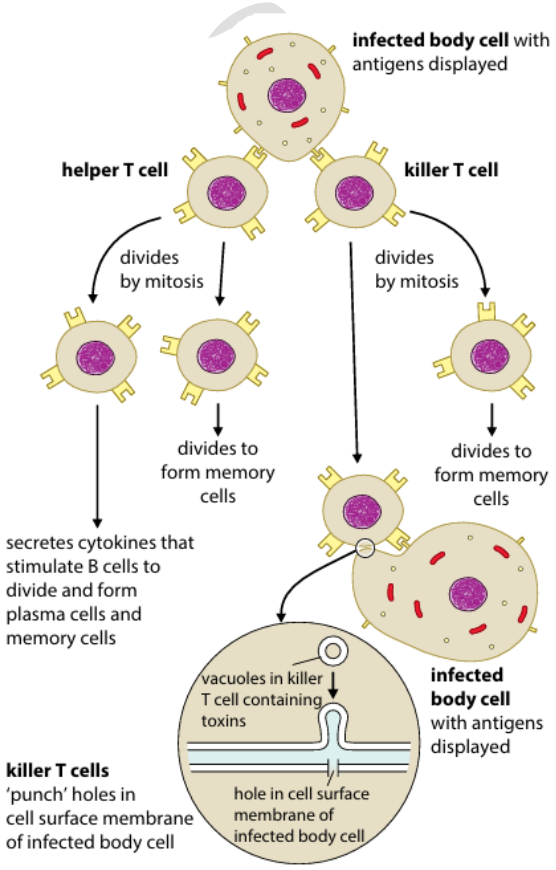


Figure 11.13 The functions of T-lymphocytes during an immune response. Helper T cells and killer T cells with T cell receptor proteins specific to the antigen respond and divide by mitosis. Activated helper T cells stimulate B cells to divide and develop into plasma cells (Figure 11.6, page 227). Killer T cells attach themselves to infected cells and kill them.

Numbers of white blood cells

Blood tests are essential for diagnosing diseases and assessing treatment success. Blood samples are collected from patients and analyzed in automated labs. Results include red and white blood cell numbers and platelets, which stimulate blood clotting. White blood cell results, such as neutrophils and lymphocytes, are given as absolute numbers or percentages, with significant variation between individuals.

Cellular component of blood	Numbers mm^{-3} of blood		Percentage of cellular component within all cellular components
	Typical values	Normal range of values	
red blood cells	5500 000 (males) 4800 000 (females)	4600 000–6200 000	93–96
platelets	300 000	150 000–400 000	4–7
white blood cells	7500	4500–10 000	0.1–0.2
			Percentages of all white blood cells
of which: neutrophils	4500	3000–6000	30–80
B lymphocytes	400	70–600	15–40
T lymphocytes	1500	500–2500	
other white blood cells	1100	800–2000	5–14
Totals	**5807 500 (males)** **5107 500 (females)**		

Table 11.1 The results of blood tests are given as absolute numbers and compared with the normal ranges. They are often given as the numbers in 1 mm^3 which is the same as 1 µl (microlitre) or 1×10^{-9} dm^3 of blood. As numbers of blood cells vary considerably, results are often expressed as percentages, as in the fourth column.

All the white cells in the blood originate from stem cells in the bone marrow. There are two groups of bone marrow stem cells:

- myeloid stem cells that give rise to neutrophils, monocytes and platelets
- lymphoid stem cells that give rise to lymphocytes, both B and T cells.

Active and passive immunity

The type of immunity described so far occurs during the course of an infection. This type of immunity is called active immunity because the person makes their own antibodies. This happens when the lymphocytes are activated by antigens on the surface of pathogens that have invaded the body. As this activation occurs naturally during an infection it is called **natural active immunity.**

This is the basis of **artificial active immunity**, more commonly known as vaccination. The immune response is similar to that following an infection, and the effect is the same – long-term immunity. In both natural and artificial active immunity, antibody concentrations in the blood follow patterns similar to those shown in Figure 11.8 (page 228)

Tetanus kills quickly, before the body's natural primary response can take place. So people who have a wound that may be infected with the bacterium that causes tetanus are given an injection of **antitoxin.**

B and T cells have not been activated, and plasma cells have not produced any antibodies. More specifically, antitoxins provide **artificial passive**

Colostrum, the thick yellowish fluid produced by a mother's breasts for the first four or five days after birth, contains a type of antibody known as IgA

IgA acts in the gut to prevent the growth of bacteria and viruses and also circulates in the blood. This is **natural passive immunity.**

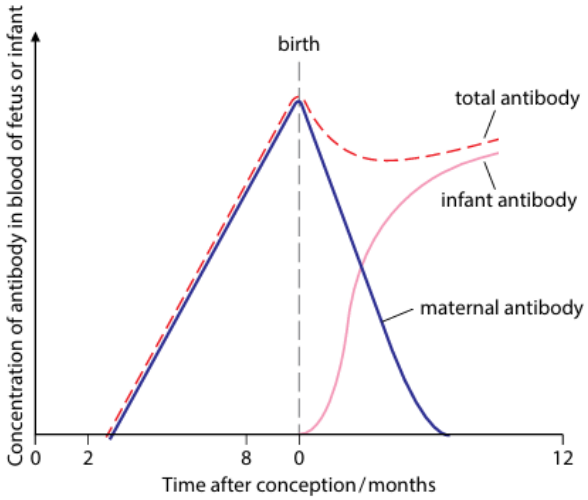


Figure 11.14 The concentrations of antibody in the blood of a fetus and an infant.

Vaccines

A vaccine is a preparation containing antigens which is used to stimulate an immune response artificially.

Immunity	Features				
	Antigen encountered	Immune response	Time before antibodies appear in blood	Production of memory cells	Protection
active	yes	yes	1–2 weeks during an immune response	yes	permanent
passive	no	no	immediate	no	temporary

Table 11.2 Features of active and passive immunity.

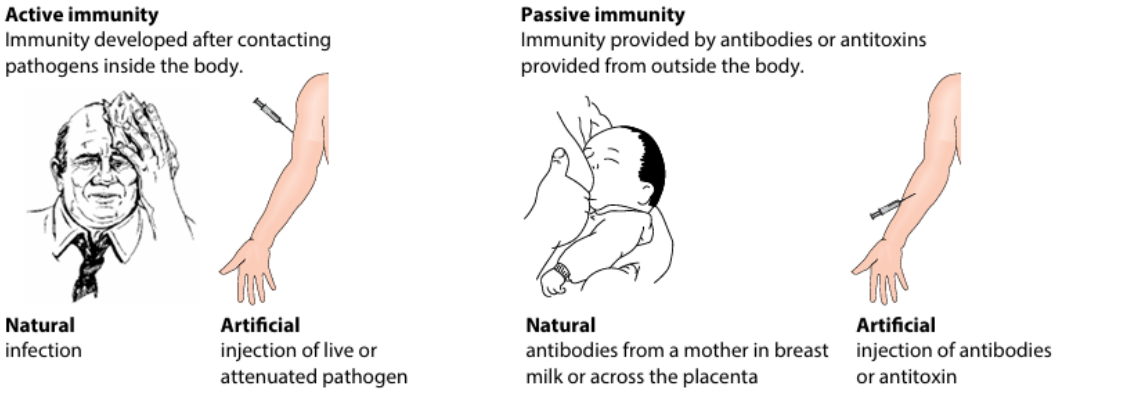


Figure 11.15 Active and passive immunity.

Problems with vaccines

Poor response

Some people do not respond at all, or not very well, to vaccinations. This may be because they have a defective immune system and as a result do not develop the necessary B and T cell clones. It may also be because they suffer from malnutrition, particularly protein-energy malnutrition (an inadequate intake of protein), and do not have enough protein to make antibodies or clones of lymphocytes.

Live virus and herd immunity

People vaccinated with a live virus may pass it out in their faeces during the primary response and may infect others. This is why it is better to vaccinate a large number of people at the same time to give **herd immunity**, or to ensure that all children are vaccinated within a few months of birth.

Antigenic variation

In spite of years of research, there are no vaccines for the common cold. When there are only minor changes in the viral antigen, memory cells will still recognise them and start a secondary response. These minor changes are called **antigenic drift.**

More serious are major changes in antigen structure – known as **antigenic shift** – when influenza viruses change their antigens considerably and the protective immunity given by vaccination against a previous strain is ineffective against the new one

Antigenic concealment

Some pathogens evade attack by the immune system by living inside cells. When Plasmodium enters liver cells or red blood cells, it is protected against antibodies in the plasma. Some parasitic worms conceal themselves by covering their bodies in host proteins, so they remain invisible to the immune system.

The eradication of smallpox

Smallpox was an acute, highly infectious disease caused by the variola virus and transmitted by direct contact. It was a terrible disease. Red spots containing a transparent f luid would appear all over the body (Figure 11.16). These then filled with thick pus.

This ring vaccination protected everyone who could possibly have come into contact with a person with the disease, reduced the chances of transmission and contained the disease.

How the eradication programme succeeded

The eradication programme was successful for a number of reasons.

■ ■ The variola virus was stable; it did not mutate and change its surface antigens. This meant that the same vaccine could be used everywhere in the world throughout the campaign. It was therefore cheap to produce.

■ ■ The vaccine was made from a harmless strain of a similar virus (vaccinia) and was effective because it was a 'live' vaccine.

■ ■ The vaccine was freeze-dried and could be kept at high temperatures for as long as six months. This made it suitable for use in the tropics.

■ ■ Infected people were easy to identify.

■ ■ The vaccine was easy to administer and was even more effective after the development of a stainless steel, re usable needle for its delivery. This 'bifurcated needle' had two prongs, which were used to push the vaccine into the skin.

■ ■ The smallpox virus did not linger in the body after an infection to become active later and form a reservoir of infection.

■ ■ The virus did not infect animals, which made it easier to break the transmission cycle.

■ ■ Many 16- to 17-year-olds became enthusiastic vaccinators and suppliers of information about cases; this was especially valuable in remote areas

Preventing measles

Measles is a preventable disease and one that could be eradicated by a worldwide surveillance and vaccination programme. However, a programme of one-dose vaccination has not eliminated the disease in any country, despite high coverage of the population.

Figure 11.16 Among the last cases of smallpox, this parent and child of the Kampa people of the Amazon region, South America, show the characteristic pustules of smallpox.

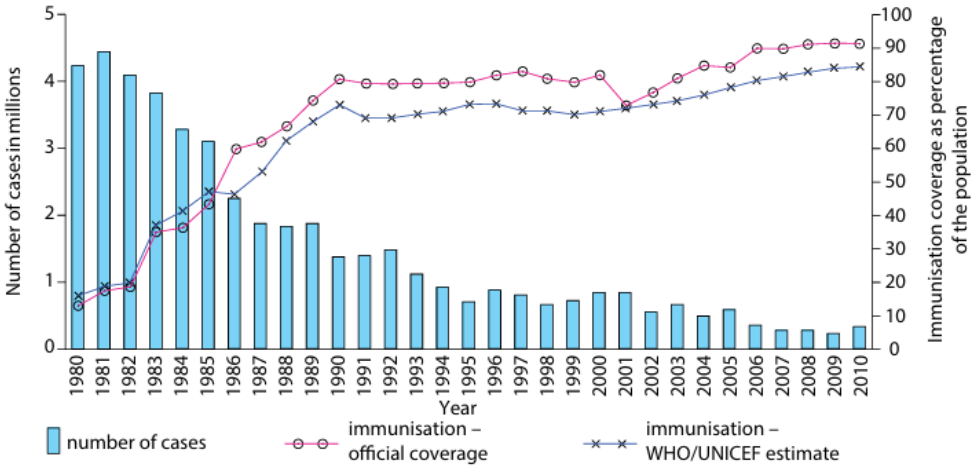


Figure 11.18 The global measles immunisation programme coordinated by the WHO, which has caused the number of cases reported each year to decrease significantly.

Autoimmune diseases – a case of mistaken identity

Not only does the body mount immune responses against pathogens and harmful substances from outside the body, but it can also attack itself leading, in some cases, to severe symptoms. Diseases of this type are autoimmune diseases.

Myasthenia gravis (MG), which means grave (serious) muscle weakness, is an autoimmune disease that targets the neuromuscular junctions between motor neurones (nerve cells) and skeletal muscle cells.

Autoimmune disease	Area of body affected	Main effects of the disease
myasthenia gravis	neuromuscular junctions	progressive muscle weakness
multiple sclerosis	central nervous system	progressive paralysis
rheumatoid arthritis	joints	progressive destruction of the joints
type 1 diabetes	islets of Langerhans – endocrine tissue in the pancreas	destruction of cells that secrete insulin
systemic lupus erythromatosus	skin, kidneys and joints	progressive deformity

Table 11.3 Five autoimmune diseases.

MG can be treated with a drug that increases acetylcholine concentration in synapses, preventing muscle fiber contraction. Surgical removal of the thymus gland is also effective. Other autoimmune diseases include multiple sclerosis, rheumatoid arthritis, and diabetes. Multiple

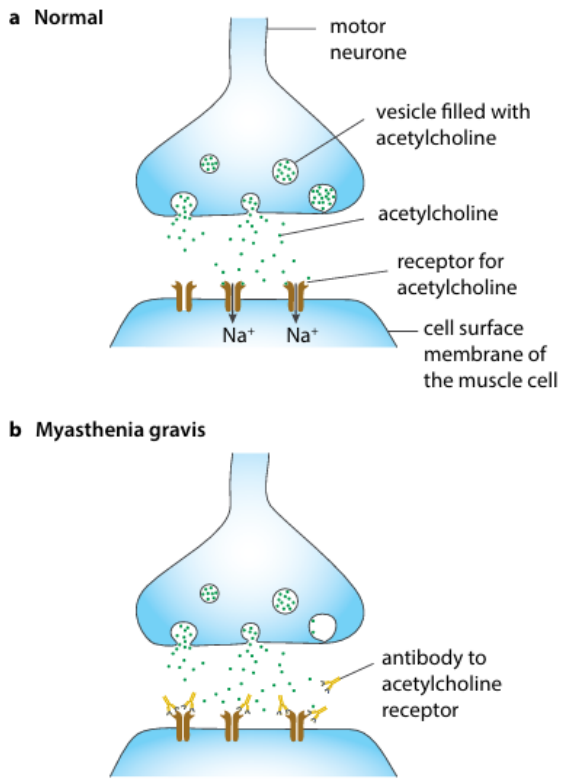


Figure 11.19 **a** Acetylcholine is released by motor neurones. It stimulates muscle cells to contract by combining with receptor proteins, which allow sodium ions into the muscle cell. **b** In myasthenia gravis, antibodies are secreted that block the receptor proteins and then cause their destruction so they do not allow the movement of sodium ions.

sclerosis develops when nerve cells lose insulating myelin sheaths, leading to muscle weakness, sensory loss, poor vision, and mental problems.

Monoclonal antibodies

Figure 11.6 (page 227) shows that, during an immune response, B cells become plasma cells that secrete antibodies in response to the presence of a non-self antigen.

For some time, though, no-one could see how to manufacture antibodies on a large scale. This requires a very large number of cells of a particular B cell clone, all secreting identical or monoclonal antibodies (Mabs). T here is a major problem in achieving this. B cells that divide by mitosis do not produce antibodies, and plasma cells that secrete antibodies do not divide.

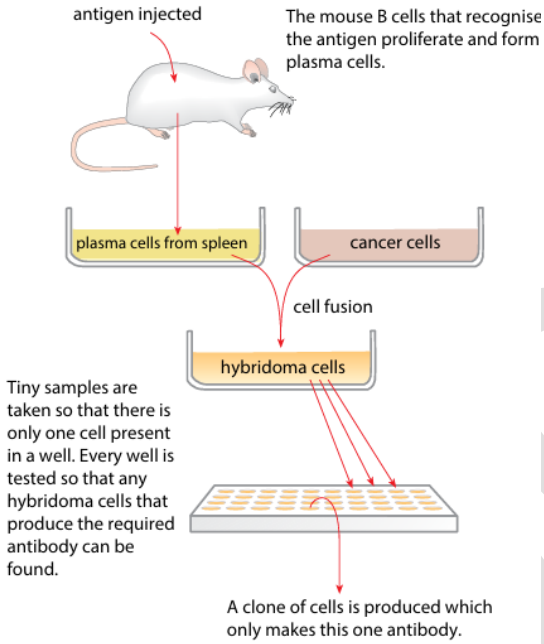


Figure 11.21 How monoclonal antibodies are produced. Monoclonal antibodies have many different uses in research and in medicine, both in diagnosis and in treatment.

Figure 11.20 Drooping eyelids are a common early symptom of myasthenia gravis. These muscles are in constant use and tire quickly. If after two years, this is the only symptom, then MG is not likely to progress to other muscles.

Using monoclonal antibodies in diagnosis

Mabs have many different uses in medicine and new applications for them are the subject of research. They are used both for diagnosis and treatment.

T here are now many Mabs available to diagnose hundreds of different medical conditions. For example, they can be used to locate cancer cells, which have proteins in their cell surface membranes that differ from the protiens on normal body cells and can therefore be detected by antibodies (Figure 11.22).

Using monoclonal antibodies in treatment

When monoclonal antibodies are used in diagnosis, they are normally administered on just one occasion. Monoclonal antibodies used as a treatment need to be administered more than once, and that presents problems.

Figure 11.22 These scientists are checking tissue samples to see whether the cells are cancerous. They do this with monoclonal antibodies specific to cancer cells.

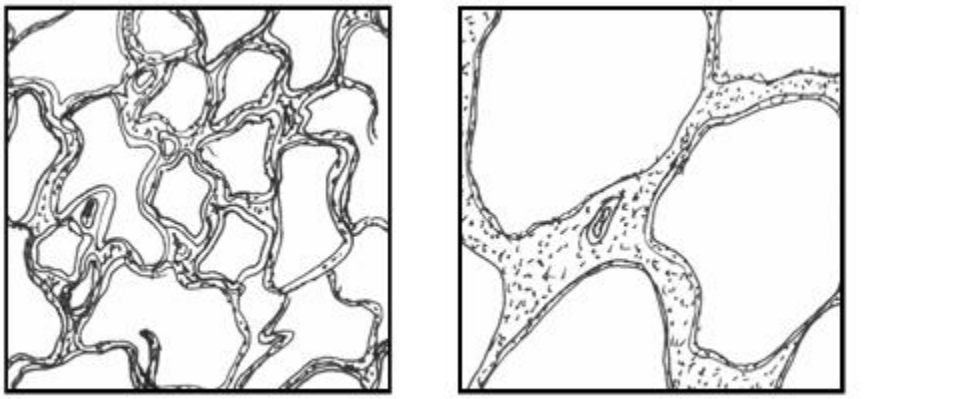
T he antibodies are produced by mice, rabbits or other laboratory animals. When introduced into humans, they trigger an immune response because they are foreign (non-self) and act as antigens. This problem has now been largely overcome by humanising Mabs in two ways:

■ ■ altering the genes that code for the heavy and light polypeptide chains of the antibodies so that they code for human sequences of amino acids, rather than mouse or rabbit sequences (Figure 11.10, page 229)

■ ■ changing the type and position of the sugar groups that are attached to the heavy chains to the arrangement found in human antibodies

Revision questions

1. The diagrams show lung tissue from a healthy person and lung tissue from a person suffering from emphysema



healthy lung tissue lung tissue from a person with emphysema

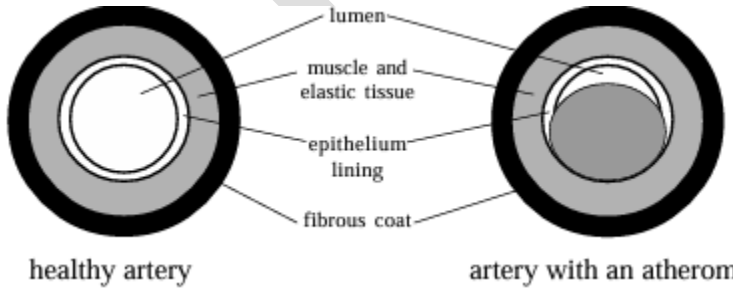
(a)(i) Describe two changes that can be seen between the lung tissue of a healthy person and the lung tissue of a person suffering from emphysema.

(ii) Explain how changes in the lung tissue might affect breathing and gas exchange

(b)Explain why a person suffering from emphysema may find it difficult to walk quickly

(c)Give two ways in which the risk of developing emphysema may be increased

2. The diagram shows a healthy artery and an artery from a person suffering from atheroma (arteriosclerosis)



healthy artery artery with an atheroma

(a)(i) Describe how atheroma has affected the structure of the artery wall

(ii) Describe and explain the effect of atheroma on blood pressure

(b)Suggest how smoking may increase the risk of atheroma

(c)Explain why changing from eating animal fats to eating plant fats may decrease the risk of developing atheroma.

(d)The coronary artery supplies blood to the tissues of the heart. Explain why the formation of an atheroma in the coronary artery may lead to heart failure.

(e)Some people may be given a heart transplant to replace a damaged heart. Explain why a transplanted heart may be rejected

3. (a)Tuberculosis is caused by a bacterium which lives in the lungs and causes destruction of tissue. Tuberculosis bacteria exposed to the air can form resistant spores. Overcrowded living conditions encourage the spread of tuberculosis.

(i) Describe how tuberculosis may spread from person to person.

(ii) Explain why tuberculosis spreads more easily in overcrowded living conditions.

(iii) During the 1950s and 60s when tuberculosis was very common in the United Kingdom, buses and railway carriages often had a notice saying “no spitting”. Explain why.

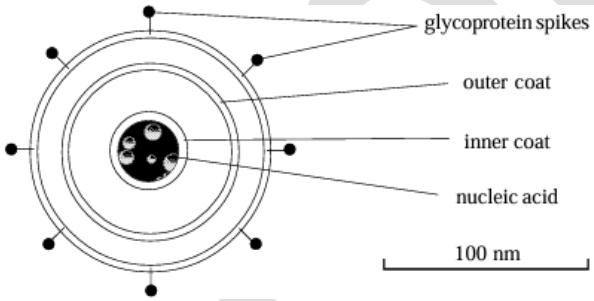
(b) The destruction of lung tissue by tuberculosis often leaves scars. Suggest why:

(i) X-rays are often used to detect tuberculosis.

(ii) mass screening by x-rays was successful in reducing the incidence of tuberculosis during the 1950s in the UnitedKingdom.

(c)Vaccination is used to control the spread of tuberculosis. Give two reasons why children should be vaccinated, even though tuberculosis is now quite rare in the United Kingdom.

4. The diagram shows the structure of HIV magnified 10,000 times



(a)Calculate the diameter of HIV in nanometers. Include the glycoprotein spikes in your measurement. Show your working

(b)HIV is a retrovirus.

(i) Name the nucleic acid present in HIV

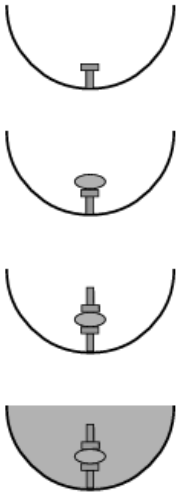
(ii) One of the genes of HIV codes for the production of reverse transcriptase. What is the role of reverse transcriptase?

(c)(i) Name the cells which are infected by HIV

(ii) Describe how HIV replicates in these cells

(d)Explain why an HIV infected person may not show any effects for several years

5. The diagram shows a system for detecting the presence of a disease organism in the blood of an infected person.



Stage 1	Antibody specific to the disease organism is bound to the surface of the well.
Stage 2	Blood of the infected person added to well. Disease organism binds to specific antibody.
Stage 3	Enzyme combined with antibody specific to disease organism added to the well. Antibody binds to disease organism.
Stage 4	Enzyme substrate added to well. Colour change occurs as a result of the reaction.

(a)Describe one method by which antibodies specific to a disease might have been produced.

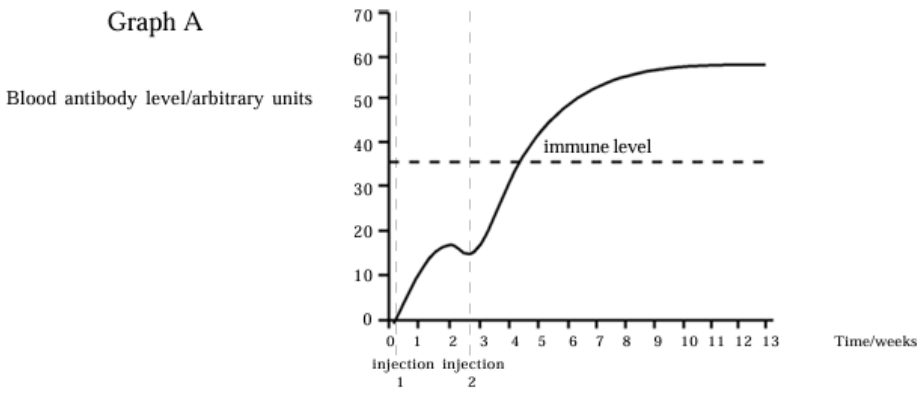
(b)(i) Explain why the disease organism binds to the specific antibody in Stage 2.

(ii) Explain the role of the enzyme combined with antibody added in stage 3 of this test system.

(c)A modification of this system can be used to detect the presence of antibodies in the blood of a person infected with syphylis. Suggest how this system could be modified to detect the presence of antibodies.

6. Graph A shows the response of person to immunisation using a vaccine containing killed pathogens.

Graph A



(a)(i) Explain the response to the first injection.

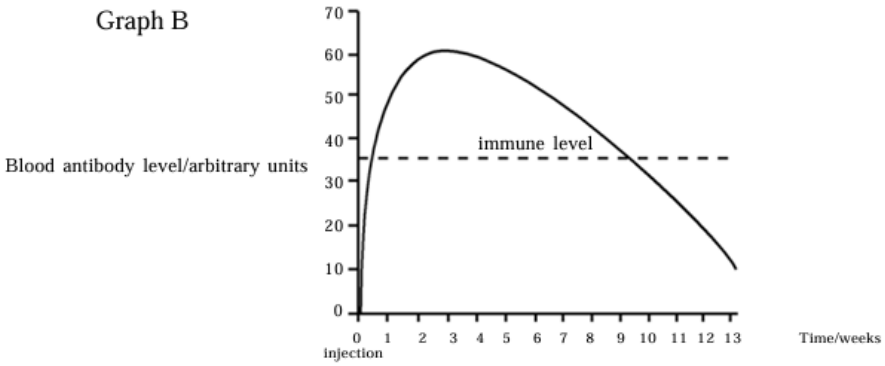
(ii) Explain why the response to the second injection was greater than the response to the second injection.

(b)Vaccination against diseases such as polio and tetanus lasts for several years. Vaccination against influenza has to be given every year. Explain why.

7.

People who have not been vaccinated against tetanus may be exposed to the bacteria causing tetanus if they cut their skin on barbed wire. Graph B shows the response of unvaccinated person to immunization against tetanus following such a cut.

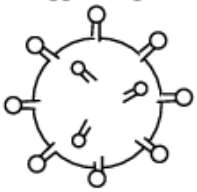
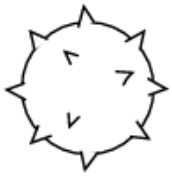
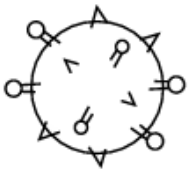
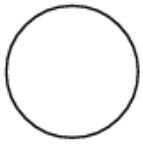
Graph B



(c) (i) What is present in the injection given to an unvaccinated person after they have been exposed to the bacteria causing tetanus?

(ii) Explain why the curve shown in graph B differs from that shown in graph A

8. The diagram below illustrates the ABO blood group system of agglutinogens on the red cells and agglutinins

Group A	Group B	Group AB	Group O
Agglutinogen A 	Agglutinogen B 	Agglutinogen A + B 	Neither agglutinogen 
Agglutinin b 	Agglutinin a 	Neither agglutinin	Agglutinins a + b 

(a)(i) In the ABO blood group system, what is an agglutinogen?

(ii) In the ABO blood group system, what is an agglutinin?

(iii) When could agglutination occur and what are its effects?

b)(i) List the blood transfusions which would be incompatible.

(ii) Group O blood contains agglutinins a and b but it is permissible to transfuse it into group A, B or AB. Explain why is this is possible