10 Infectious disease

The infectious diseases studied in this topic are caused by pathogens that are transmitted from one human host to another. Some, like *Plasmodium* that causes malaria, are transmitted by vectors; others are transmitted through water and food or during sexual activity. An understanding of the biology of the pathogen and its mode of transmission is essential if the disease is to be controlled and ultimately prevented.

10.1 Infectious diseases

While many infectious diseases have been successfully controlled in some parts of the world, many people worldwide are still at risk of these diseases.

By the end of this section you should be able to:

a) define the term disease and explain the difference between an infectious disease and a non-infectious disease (sickle cell anaemia and lung cancer)
b) state the name and type of causative organism (pathogen) of each of the following diseases: cholera, malaria, tuberculosis (TB), HIV/AIDS, smallpox and measles
c) explain how cholera, measles, malaria, TB and HIV/AIDS are transmitted
d) discuss the biological, social and economic factors that need to be considered in the prevention and control of cholera, measles, malaria, TB and HIV/AIDS
e) discuss the factors that influence the global patterns of distribution of malaria, TB and HIV/AIDS and assess the importance of these diseases worldwide

Disease: an abnormal condition affecting an organism, which reduces the effectiveness of the functions of the organism.

Non-infectious disease: a disease with a cause other than a pathogen, including genetic disorders (such as sickle cell anaemia) and lung cancer (linked to smoking and other environmental factors).

What are 'health' and 'disease'?

By disease we mean 'an unhealthy condition of the body'. There are many different diseases but good health is more than the absence of the harmful effects of disease-causing organisms. We have already seen that illness may be caused by poor lifestyle choices or unfavourable environmental conditions, such as lung cancer due to the smoking of cigarettes (page 184). Diseases of this type are called non-communicable or **non-infectious diseases**. They include conditions such as chronic obstructive pulmonary diseases (COPD) and cardiovascular disease (CVD), discussed in Topic 9. Non-infectious disease may also be caused by malnutrition. Inherited or genetic disorders such as sickle cell anaemia are included here, too.

Infectious disease

In this topic the focus is on diseases that can be 'caught' – sometimes described as contagious or communicable. These are **infectious diseases**. They are caused by invading organisms living

parasitically on or in the body. These disease-causing organisms are known as **pathogens**. Pathogens may be viruses, some types of bacteria or certain other organisms that are passed from one organism to another. The range of pathogens is introduced in Figure 10.1.

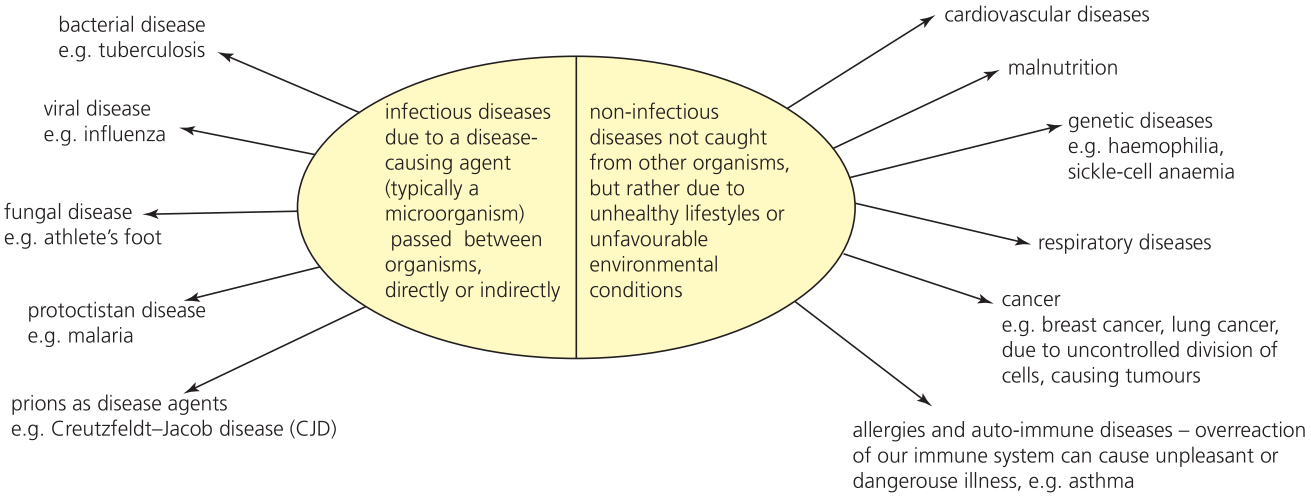


Figure 10.1 Types of human disease

Infectious disease: a disease caused by a pathogen that can be transmitted from one host organism to another.

Pathogen: a biological agent (such as a virus, bacterium, fungus or protoctist) that causes disease. A pathogen causing human diseases will have, as part of its structure, proteins that are different from those of the human host and are therefore antigens.

The pathogens that cause some infectious diseases exist permanently in a particular region or population. Such a disease is said to be **endemic** for it has a constant presence. **Malaria** is an example – a serious threat to humans living in parts of Africa and other tropical and sub-tropical regions in the world.

On the other hand, **epidemics** are diseases that appear suddenly and then spread rapidly in a specific area or within a particular population group for a time. Cases of food poisoning are examples.

A **pandemic disease** is an epidemic that spreads far more widely – typically throughout a whole country, a whole continent or throughout the whole world. It affects a huge number of people. In the twentieth century several pandemics of influenza ('flu) occurred. For example, the 'flu pandemic that occurred in 1918 was responsible for 10 million deaths worldwide.

In the **prevention of infectious disease**, knowledge of the biology of the pathogen is essential. So the fight against disease involves the work of microbiologists as well as the vigilance of the health professionals. In this topic, six specific infectious diseases of humans are examined, most of which continue to present major threats to life. There are reasons why this is so in the case of particular diseases but four general points are significant.

- We live in a 'global village' world with speedy, worldwide travel facilities available to some. A person, infected on one continent, may travel to another within hours – before any symptoms have appeared.
- The human population is in a phase in which it is increasing more and more rapidly (Figure 10.2). In ever-increasing numbers, people congregate together – many in mega-cities. Pathogens do not have far to travel!
- The work of health professionals is most effective where there is social stability, the absence of war and an equitable division of wealth. Unfortunately, these conditions are absent from many human societies.
- As natural resistance to pathogens develops and drugs to overcome them are found, so pathogens themselves evolve greater infectivity – there is a continuing 'arms race' between pathogens and **hosts**.

Extension

Accidents

Not included in any of the types of ill-health listed in Figure 10.1 is damage due to accidents, such as broken bones. A bone fracture is not a disease but it is certainly an unhealthy condition of the body which takes time to repair. Clearly, there is a borderline between health and disease that is not easy to define.

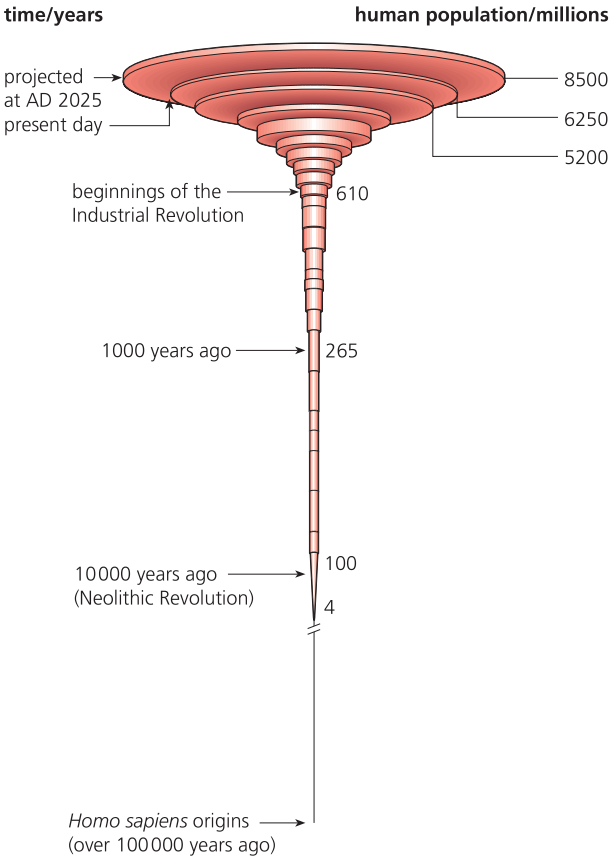


Figure 10.2 The changing pattern of the estimated world human population

Case studies in infectious disease

Cholera

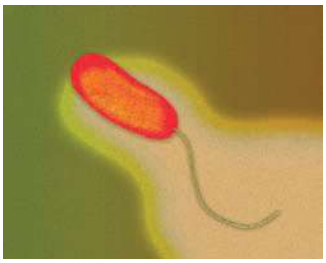


Figure 10.3 Scanning electron micrograph of *Vibrio cholerae* (×60 000)

Cholera is a dangerous disease, caused by the curved rod-shaped bacterium, *Vibrio cholerae* (Figure 10.3). This pathogen is typically acquired from drinking water that has become heavily contaminated by the faeces of patients (or from human 'carriers' of the pathogen). Alternatively, it may be picked up from food contaminated by flies that previously fed on human faeces. The consumption of raw shellfish taken from waters polluted with untreated sewage is another common source.

Cholera is endemic in many parts of Africa, India, Pakistan, Bangladesh, and Central and South America. A large number of the cholera bacteria must normally be ingested for the disease to develop; fewer than 10^8–10^9 organisms is ineffective (unless anti-indigestion tablets that neutralise stomach acid were taken beforehand). Once the bacteria has survived the stomach acid and reached the intestine, the incubation period is from 2 hours to 5 days. However, 75 per cent of those infected develop no symptoms at all – the bacteria merely remaining in their faeces for up to 2 weeks – whilst others are made very ill. This difference may arise because there are different strains of the pathogen, some mild, others virulent in their impact on the patient.

In the intestine, the pathogen increases in numbers and attaches itself to the epithelium membrane. The release of a toxin follows. This generates symptoms in susceptible patients that are mild to moderate in many people but extremely severe in about 20 per cent of people who become infected.

The effect of this toxin is to trigger a loss of ions from the cells of the epithelium. Outflow of water follows and this is constantly replaced from tissue fluid. The patient rapidly loses a massive amount of body fluid. Typically 15–20 litres may drain from the body as watery diarrhoea containing mucus and epithelium cells ('rice-water stool'), as well as vast numbers of the bacterium. At the same time, the patient has severe abdominal muscle cramp, vomiting and fever. Death may easily result from this dehydration because the severely reduced level of body fluids causes the blood circulation to collapse.

Question

1 Digestion of the proteins in the gut begins in the stomach. What is the source and role of the 'strong acid' present in the stomach when food is ingested?

How the cholera toxin works

The cholera toxin consists of a two-protein complex composed of one 'A' subunit and five 'B' subunits. The B part is the binding protein which attaches the toxin complex to a particular site, a glycolipid, on the cell surface membranes of intestine epithelium cells. The A part is an enzyme that activates other enzymes of the cell surface membrane of the epithelium cell to which it is attached. These cause the secretion of chloride ions into the gut lumen and inhibit any uptake of sodium ions. Hypersecretion of chloride ions results and is followed by water loss (Figure 10.4).

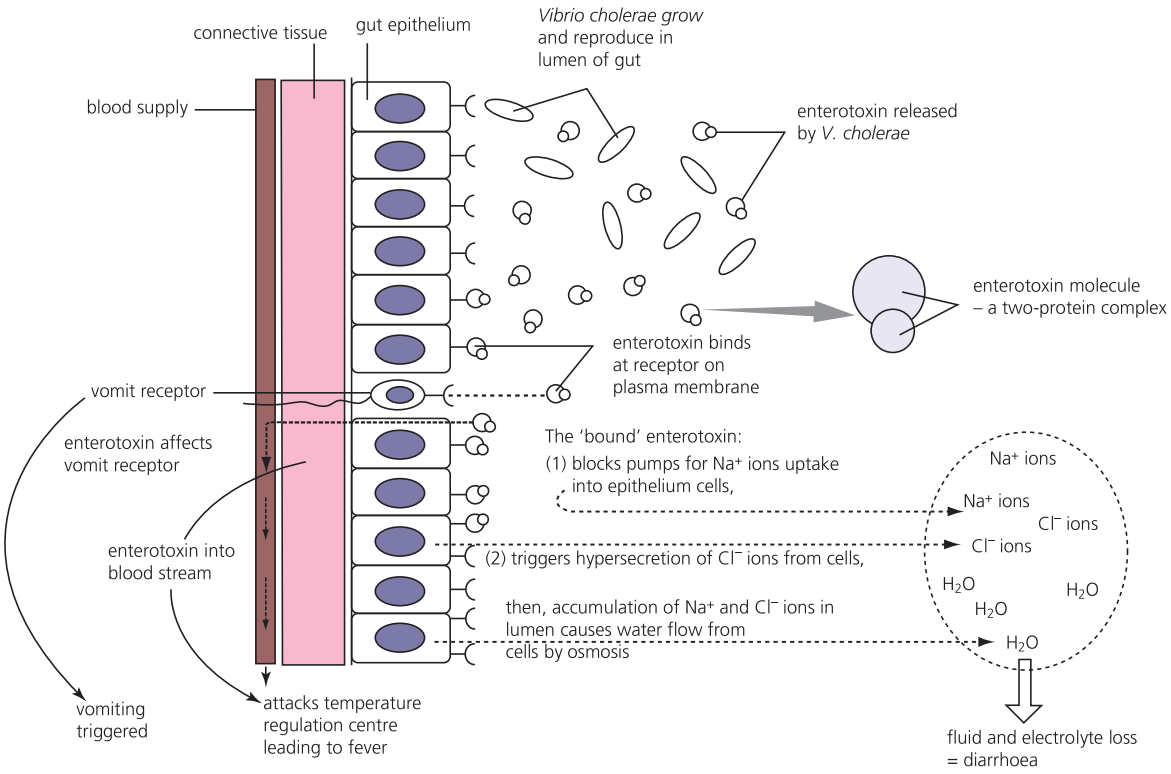


Figure 10.4 The action of the cholera toxin

Question

2 In cholera, toxic protein triggers the exit of chloride ions from the epithelium cells into the lumen of the gut. How does this movement of ions differ from the movement of water that follows ion transport?

Treatment of cholera

About 50 per cent of untreated cases of cholera are fatal but, when properly treated, generally less than 1 per cent of people are likely to die from this very unpleasant disease. A cholera patient requires immediate oral (by mouth) administration of a dilute solution of ions and glucose, present in a rehydration pack (Figure 10.5), in order to replace the fluids and ions lost from the body. The presence of glucose aids uptake of ions and compensates for energy loss. This solution prevents dehydration and restores the osmotic balance of the blood and tissue fluid. This might seem a simple process to people in the developed world but, in those places where cholera is endemic, conditions may be very different. Many who contract the disease are weakened by shortage of food. Their drinking water may be of dubious purity and have to be carried some distance. The boiling of water makes it safe to use in the rehydration fluid but this requires fuel that may be scarce.

Very severely dehydrated patients require the administration of intravenous fluids. An additional treatment, the taking of the antibiotics streptomycin or tetracycline, will assist in ridding the gut of the cholera cells. However, these drugs are of little use unless fluid, ions and glucose replacement has succeeded in restoring normal body fluid composition. An oral vaccine against cholera now exists but it is not effective against all strains.

Prevention of cholera

Figure 10.5 An oral rehydration pack for the treatment of cholera

Cholera has been eradicated where there is effective sanitation. In the longer term, the disease can be virtually eliminated by satisfactory processing of sewage and the purification of drinking water, including a chlorination phase. In endemic areas, the spreading of infection between households may be prevented by the boiling of drinking water. The faecal contamination of foods by flies must also be prevented.

However, where populations have been displaced into inadequate overcrowded refugee camps or have migrated to crowded urban slums where clean water and sanitation are not available, cholera remains a threat to life (Figure 10.6). Malnourished children and those living with HIV are at greatest risk.

Figure 10.6 A refugee camp – ideal conditions for cholera

Table 10.1 Cholera – the profile

Pathogen	**Pathogen taxonomy**	A rod-shaped bacterium, *Vibrio cholerae*
	Transmission	Via polluted water and contaminated foods
Disease parameters	**Incubation and venue**	Once in contact with the wall of the small intestine, a short incubation period of between 2 hours and 5 days
	Signs, symptoms and diagnosis	Diarrhoea, vomiting, abdominal muscle cramp, fever Confirmation by microscopic examination of faeces
	Treatment	Replacement of lost water and ions by oral rehydration with dilute solution of salts and glucose
	Prognosis	Typically 50% of untreated cases are fatal but with prompt correct treatment almost all patients recover
	Prevention and control	Boiling of drinking water, correct treatment of sewage and the prevention of food contamination by flies

Malaria

Malaria is the most important of all insect-borne diseases, posing a threat to 2400 million humans in 90 countries – 40 per cent of the world's population, in fact (Figure 10.7). About 80 per cent of the world's malaria cases are found in Africa south of the Sahara. Here, some 90 per cent of the fatalities due to the disease occur. It is estimated that around 400 million people are infected, of which 1.5 million (mostly children under 5 years) die each year. Malaria kills more people than any other communicable disease, with the exception of tuberculosis.

Malaria is caused by ***Plasmodium***, a protoctist, which is transmitted from an infected person to another by blood-sucking mosquitoes of the genus ***Anopheles***. The mosquito is described as the **vector** – an organism that transfers a disease or parasite from one host organism to another. Of the four species of *Plasmodium* that cause malaria in humans, only one (*P. falciparum*) causes severe illness. The others species trigger milder infections that are rarely fatal. Insecticides, particularly **DDT**, had been effective against mosquitoes in the past but there has been a resurgence of malaria since the 1970s.

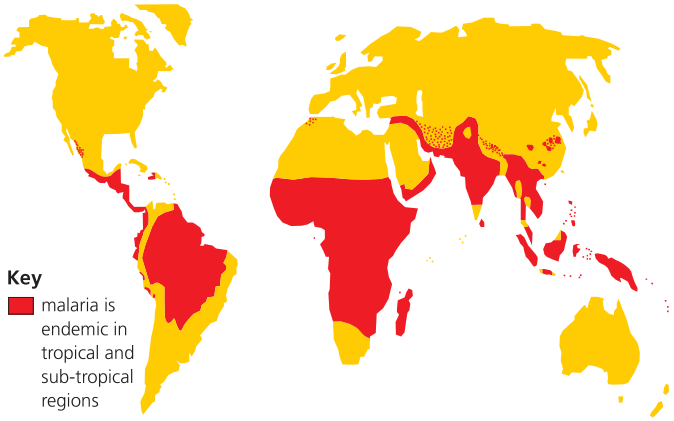


Figure 10.7 World distribution of malaria

Until 100 years ago, malaria was endemic in Europe and the USA, too. In Britain it was called 'fen ague' because it was common in communities living near marshes and because of the periodic shivering fits patients experienced. Marsh and fen drainage for agriculture changed the environment so that it was no longer favourable to mosquitoes and their transmission of the parasite. This is one reason for its disappearance in some areas.

Transmission of *Plasmodium* by the mosquito

Some pathogens need a vector to reach a new host. Stages in the life cycle of the pathogen may occur in the vector as well as the host. The female mosquito is the vector for malaria. (The male mosquito feeds on plant juices.) The mosquito is a fluid-feeding heterotroph, not a parasite, as sometimes stated. The female detects its human host, lands and inserts a long thin tube (called a proboscis) into a blood vessel below the skin surface. A 'meal' of blood is taken quickly; there is a danger that an active, alert human will 'swat' the intruder. For a blood-sucking insect, the mammalian's blood-clotting mechanism presents a problem that has to be overcome. This occurs when the mosquito's proboscis penetrates the vein and a secretion from its salivary glands passes into the victim's blood, inhibiting it from clotting. At this point *Plasmodium* may enter its human host (if the mosquito carries an infective stage). Meanwhile, the mosquito loads up with a blood meal (Figure 10.8).

Mosquitoes tend to feed at night, on sleeping victims. Those that alight on patients already ill with malaria are likely to be able to feed unhindered. The life cycle of the malarial parasite is complex. It consists of a sexual stage beginning in the human host (the primary host) and completed in the mosquito (the secondary host or vector). There is an asexual multiplication phase in the mosquito, too, and a phase of growth and multiplication in the liver cells and red blood cells of the human host. Details of this life cycle are not required here.

Question

3 The insecticide DDT is harmless to humans at concentrations that are toxic to mosquitoes. This insecticide is a stable molecule that remains active long after it has been applied and it is stored in the body rather than being excreted. Nevertheless, the use of this compound has been discontinued. Suggest why this is so?

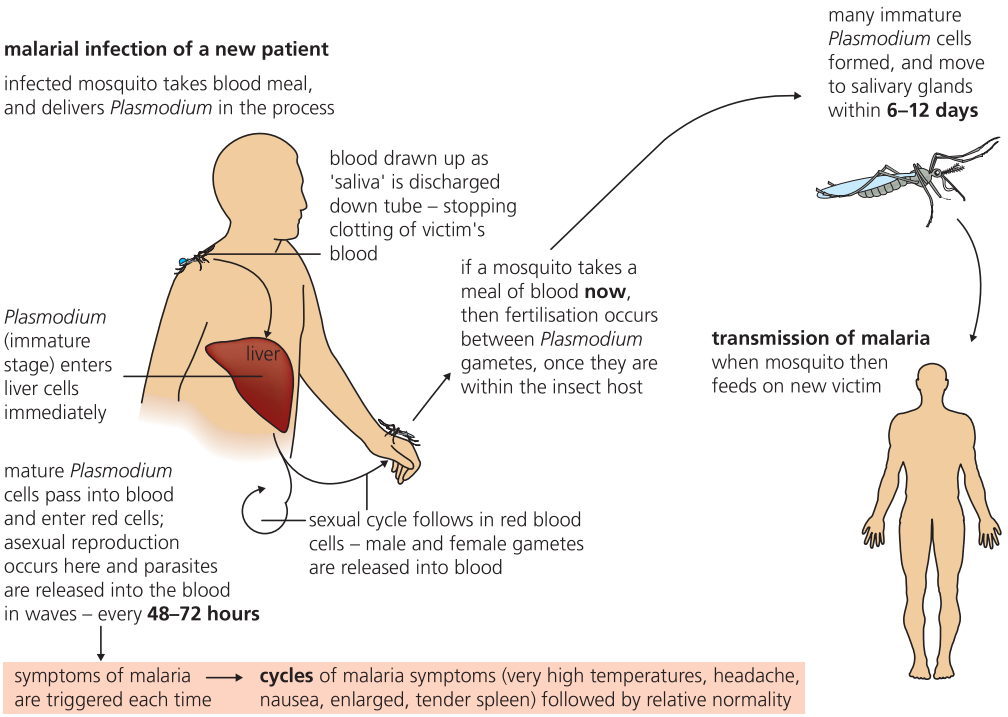


Figure 10.8 Mosquito feeding and the transmission of malaria

Control measures

Control measures currently applied include the following.

- Interruption of the mosquito life cycle by attacking the larval stage which is an air-breathing aquatic animal. Swamps are drained and open water sprayed with oil (which forms a surface film, blocking the larva's air tube), and with insecticide.
- Use of insecticides to kill adult mosquitoes on and around the buildings that humans occupy.
- Protection from mosquito bites by sleeping under insecticide-treated mosquito nets and by the burning of mosquito coils.
- Use of drugs to kill the stages of *Plasmodium* found in the blood and liver of infected people.
- Use of drugs to kill *Plasmodium* as soon as it is introduced into a healthy person's blood by an infected female mosquito whilst feeding.

The effect of the sickle cell trait on death from malaria

The malarial parasite *Plasmodium* completes its life cycle in red blood cells but it cannot do so in red blood cells containing haemoglobin-S ($\mathbf{Hb^S}$) (Figure 6.17, page 125). People with **sickle cell trait** are heterozygous for the sickle cell allele (Hb^A Hb^S). Their red blood cells contain some sickle haemoglobin so they are protected to a significant extent from malaria – they are much less likely to die from the disease. Where malaria is endemic in Africa, possession of one mutant allele is advantageous. Consequently, people with sickle cell trait are more likely to survive to pass on this allele to the next generation (Figure 10.9).

How will malaria be eradiated?

After many soldiers in the wars of the first half of the twentieth century became casualties of malaria, money was found for research into its control. Powerful insecticides (first DDT, then gamma BHC and dieldrin) became available. By the 1960s mosquito-eradication programmes had been successful in many countries. However, by the 1970s, resistant strains of mosquito had appeared (and *Plasmodium* resistant to anti-malaria drugs, too).

distribution of haemoglobin-S is virtually the same as that of malaria

distribution of malaria caused by *Plasmodium falciparum* or *P. vivax* (the forms of malaria that are most frequently fatal, especially in childhood)

distribution of sickle cell gene in the population

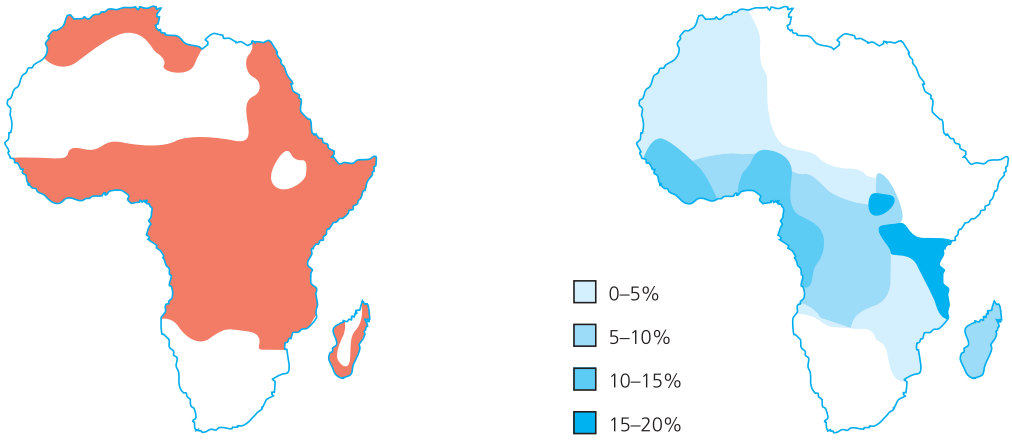


Figure 10.9 The distribution of sickle cell trait in Africa confers an advantage

A determined search for a vaccine, begun in the 1980s, led to unsuccessful trials. Now the situation is more hopeful. A huge injection of funds from the Gates Foundation into this project occurred in 1994 and recently more has been pledged. The subsequent, energetically pursued search for a vaccine that will confer lifetime active immunity for treated humans has yielded several promising 'candidates'. One is undergoing advanced trials. The malaria research community remains cautious; the complex parasitic lifestyle of *Plasmodium* makes it a difficult to eradicate and there have been many earlier set-backs. In the longer term, control of mosquitoes by the careful use of selective insecticides will be necessary, as well as the development of powerful vaccines, before this very well-adapted malarial parasite is overcome.

Active immunity: immunity resulting from exposure to an antigen. During the subsequent immune response, antibodies are produced by plasma cells and the body makes memory cells that provide ongoing long-term immunity. There is a delay before the immune response is complete, so immunity takes some days to build up.

Table 10.2 Malaria – the profile

Pathogen	**Pathogen taxonomy**	*Plasmodium*, a protoctist, with four species, of which *P. falciparum* is the most dangerous
	Transmission	Via the blood meals of the female *Anopheles* mosquito
Disease parameters	**Incubation and venue**	*Plasmodium* enters liver cells, reproduces asexually, then parasites are released into the patient's blood stream and enter red blood cells immediately. A cycle of red blood cell invasion, reproduction and release (with toxins) is then repeated.
	Signs, symptoms and diagnosis	A cycle of very high temperatures, headache, nausea and enlarged tender spleen every 48–72 hours, followed by normality
	Treatment	A combination of anti-malarial drugs
	Prognosis	Most patients improve within 48 hours after initiation of treatment and become fever-free after 96 hours. Infection by *P falciparum* causes a form of malaria with a high mortality rate if untreated.
	Prevention and control	Use of insecticides around human habitations Protection from insect bites, particularly by sleeping under insecticide-treated mosquito netting Destruction of the mosquito larva's habitat by draining swamps and spraying open water with oil to prevent larva's access to oxygen via surface air tube
WHO status	**Distribution**	Endemic in tropical and sub-tropical regions
	Global incidence and mortality	About 247 million cases per year with about 90% of the cases occurring in sub-Saharan Africa About 800 000 deaths per year with the majority being young children in remote, rural areas of Africa

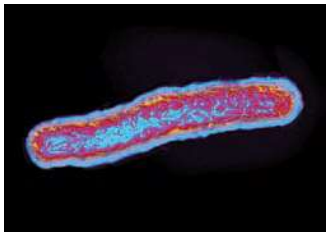


Figure 10.10 Electron micrograph of a colony of *Mycobacterium tuberculosis* (×25 000)

Tuberculosis (TB)

Tuberculosis (TB), a major, worldwide public health problem of long standing, is caused by a **bacillus** (rod-shaped bacterium) called *Mycobacterium tuberculosis* (Figure 10.10). Viewed under the microscope after staining by the Ziehl–Nielsen technique, these cells appear bright red. This red colouration is unique to bacteria of the genus *Mycobacterium* and is due to wax and other lipids in their walls. This is how the pathogen is identified in infected patients.

How tuberculosis spreads

People with pulmonary TB have a persistent cough. The droplets they inevitably spread in the air are infected with live *Mycobacterium* (Figure 10.11). Tuberculosis is chiefly spread by droplet infection in this way. Because of their lipid-rich cell walls, the bacilli are protected from drying out so the pathogen may survive for many months in the air and the dust of homes. This is another source of infection. Overcrowded and ill-ventilated living conditions are especially favourable for the transmission of the infection. However, it still requires quite prolonged contact with a viable source before people will succumb, because the bacterium is not strongly infectious.

A bovine form of TB occurs in cattle and the bacillus can enter the milk. Unpasteurised milk from infected cows is another potential source of infection. In some rural communities especially, this type of milk may be consumed by both adults and children. Today, in some countries, milk is supplied from 'tuberculin-tested' cows that are certified free of *Mycobacterium*. However, TB may still be found in dairy herds. This is because of a 'reservoir' of the bacterium that exists in wild animals that have chance contacts with the herds. Treatment of milk by pasteurisation is a major control mechanism as this heat treatment kills the bacteria without affecting the quality of the milk.

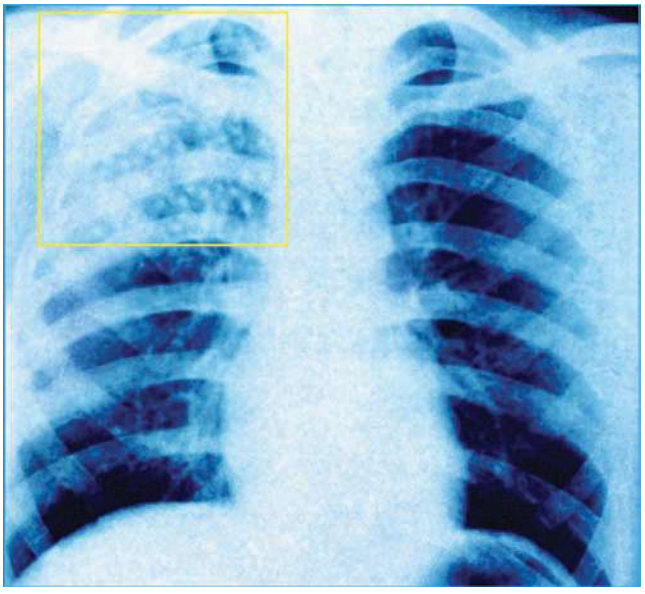
Figure 10.11 Droplet infection

How TB develops

Once inside the lungs, the bacteria are engulfed by macrophages in the alveoli and bronchioles. If the person is in good health these white blood cells (with the help of the T-lymphocytes which migrate in from lymph nodes – page 159) kill the pathogen. Alternatively, and particularly with strains of *Mycobacterium* that are more infectious, the pathogens may remain alive within the macrophage, although localised and effectively controlled by the immune system. This explains why it is that not all infections with *M. tuberculosis* result in TB – many people show no symptoms. In fact, about one-third of the world's population is infected with *M. tuberculosis*, but only 5–10 per cent becomes sick or infectious at some stage during their life.

However, if the patient is malnourished or is in inferior health with a weakened immune system, a chronic infection may develop, typically within the lungs. Cavities appear as bacteria destroy the lung tissues. Blood vessels are broken down and fluid collects. The structural damage to the lungs can be seen X-ray examination (Figure 10.12).

If the condition is not treated promptly, the pathogen may be carried in the bloodstream and lead to TB in almost any part of the body. For example, the meninges of the brain, bone tissue, the lymph glands, the liver, the central nervous system, the kidneys or the genital organs can all be attacked. Generally, patients show loss of appetite, loss of weight, excessive sweating and a decline in physical activity.



the heart is visible as a white bulge, with lung tissue on each side, enclosed in the rib cage
the white patches contain live *Mycobacterium tuberculosis* where lung structure and function are permanently destroyed

Figure 10.12 Chest X-ray showing TB in the lungs

Treatment of TB

Today, TB is treatable but it is still a 'killer' disease if not diagnosed early on in the infection. Amongst those with the disease of HIV/AIDS, TB is the leading cause of death.

Since TB is infectious, on confirmation of the diagnosis of a case of active tuberculosis, all contacts of the patient need to be traced and screened by a community public health team. Infectious patients require isolation and treatment with specific antibiotics until they cease to cough up viable bacilli. Then, antibiotics continue to be administered to the patient, now back in the community, until there is evidence the infection has been eradicated from the body.

Unfortunately, microorganisms develop resistance to antibiotics and other drugs used against them, with time. In the case of TB, this has already happened. Patients are now treated with several antibiotics simultaneously because of the emergence of multidrug-resistant TB (MDR-TB). This is particularly in the case of AIDs patients. MDR-TB is especially common in the USA and South-East Asia (see Table 10.3).

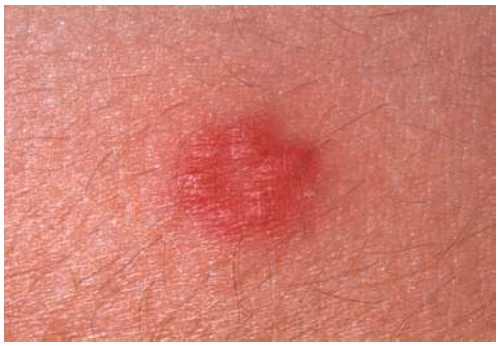
Prevention of TB

A vaccine against tuberculosis, the Bacillus Calmette–Guérin (**BCG**) vaccine, is prepared from a strain of attenuated (weakened) live bovine tuberculosis bacillus, *Mycobacterium bovis*. It is most often used to prevent the spread of TB among children.

A tiny quantity of inoculum is injected under the skin of the upper arm. Before vaccination takes place, people are tested for existing immunity, since these people will react unfavourably to the vaccine (the Haef test, Figure 10.13). Only those with no reaction may receive the vaccine. Immunity typically lasts for at least 15 years – longer if the individual is re-exposed to TB bacilli, for example, by accidental encounter with it. At best, the BCG vaccine is effective in preventing tuberculosis in a majority of people for a period of 15 years. However, immunity wanes with time and disappears entirely from the elderly.

1 instrument with six needles by which the skin is punctured and a small amount of protein, extracted from TB bacilli, is introduced below the skin (haef test)

2 after 2 or 3 days, if this test has proved positive, i.e. the patient has TB or has already acquired immunity



3 in a TB vaccination, the needle introduces the BCG vaccine just below the skin – a blister forrms and eventually subsides, leaving the patient protected against TB

Figure 10.13 Haef test and a TB vaccination

How effective the vaccine is varies according to geography. Trials of BCG in two States in the USA were only 14 per cent effective. Another trial showed no protective effect. In the UK the vaccine is 80 per cent effective. How BCG vaccination is applied in different countries is reviewed in Table 10.3.

Table 10.3 BCG vaccination policy recommended in various countries

Country	Vaccination policy/recommended for
United Kingdom	Babies and children under 16 years with parents or grandparents born in counties with high rates of TB, or where born in one themselves Those who have been in close contact with a TB patient Those under the age of 35 whose occupation puts them at risk of exposure to TB
USA	Not used
India and Pakistan	Introduced in 1948 – the first countries outside Europe to do so
Brazil	Introduced in 1967
Malaysia	Given once only, at birth, from 2001
Singapore	Given once only, at birth, from 2001
Taiwan	Given at birth and repeated at the age of 12
South Korea	Recently discontinued altogether
USSR	In the former USSR (including Russia) it was given regularly, throughout life

Deaths from TB in England and Wales, 1900–2000

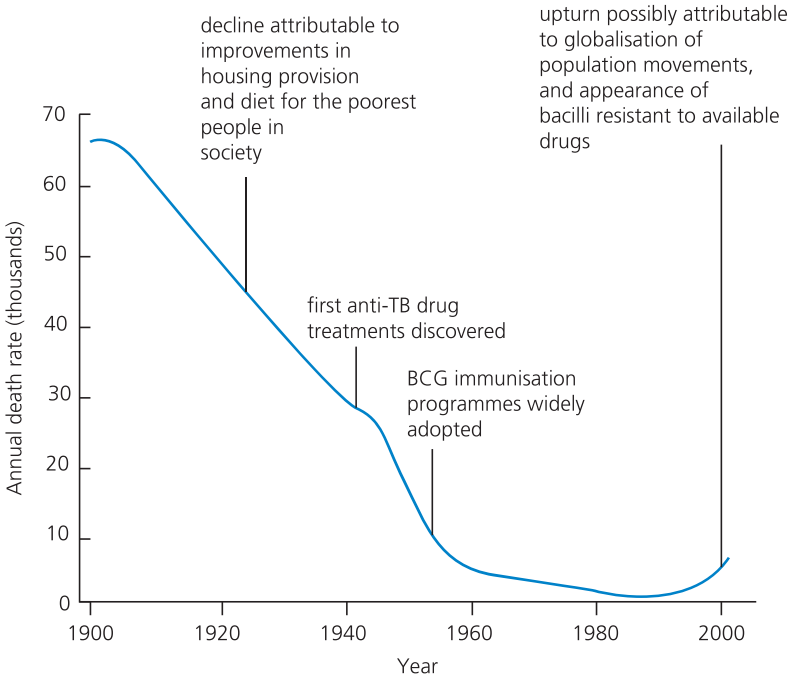


Figure 10.14 How social, economic and medical factors have influenced the occurrence of TB in developed countries

The changing pattern of the disease

There is evidence that TB was present in some of the earliest human communities and it has persisted as a major threat to health where vulnerable people lived in crowded conditions. In the nineteenth century, when the TB bacillus was first identified, one in seven of all deaths among Europeans was due to TB.

Today, in most developed countries this disease is relatively rare – in the UK for example, in 2007 the national average was about 15 cases per 100 000 of the population. In these countries, the reduction in TB throughout most of the past century has been due to steadily improving living conditions, particularly in housing and diet (Figure 10.14). However, today there is evidence of a resurgence of the disease due to inward migration of new citizens, to the globalisation of travel and to the emergence of multidrug-resistant TB (MDR-TB).

Globally, almost 14 million people have active TB, with approaching 2 million deaths due to the bacillus annually. In developing countries with a high incidence of this disease it primarily affects young adults. In developed countries where TB had ceased to be a major health threat, the rising incidence of the disease is largely among those described as immunocompromised (page 205), particularly those with HIV/AIDS, and among new migrants from developing countries – specially where they are now living in poorer housing in large cities, such as New York and London.

The World Health Organisation's Stop TB strategy – DOTS

In their vision for a TB-free world, the World Health Organisation (WHO) goal is to dramatically reduce the global burden of TB by 2015 by:

- achieving universal access to high-quality care for all people with TB, so reducing the human suffering and socioeconomic burden associated with TB
- protecting vulnerable populations from TB, co-infection with TB and HIV, and multidrug-resistant TB by supporting the development of new tools and enabling their timely and effective use
- protecting and promoting human rights in TB prevention care and control.

Direct Observation, Treatment, Short course (**DOTS**) is an approach aimed at health workers and family members who are responsible for patients taking prescribed medicines, to see that they do so regularly. The drugs now used (isoniazid and rifampicin, typically with a combination of others) cure the majority of patients with multidrug-resistant strains of TB, provided they are taken for 6–8 months.

Question

4 Examine the data in Table 10.4 concerning the disease TB in selected WHO Regions. Then suggest what factors are mostly likely to account for these contrasting figures.

Table 10.4 Estimated prevalence and mortality from TB in 2009

Selected WHO region	Prevalence/rate per 100 000 of the population	Mortality/rate per 100 000 of the population
Africa	450	50
South-East Asia	280	27
Europe	63	7

Table 10.5 Tuberculosis – the profile

Pathogen	**Pathogen taxonomy**	A rod-shaped bacterium, *Mycobacterium tuberculosis*
	Transmission	Droplet transmission from lung-infected patients and from contaminated dust of homes Prolonged contact is required – the bacterium is not strongly infectious (Also *M. bovis* from infected cows via unpasteurised milk)
Disease parameters	**Incubation and venue**	Within weeks or months, typically in the lungs of patients already vulnerable due to malnutrition or inferior health
	Signs, symptoms and diagnosis	A persistent cough, producing sputum (phlegm), with fatigue, loss of appetite, weight loss and fever Confirmation by a skin test, a chest X-ray and bacteriological test of sputum
	Treatment	A combination of antibiotics, particularly isoniazid and rifampicin, for at least 6 months
	Prognosis	Improvement within 2–3 weeks of early diagnosis and treatment, full recovery in 6–12 months An ignored infection that spreads to other organs is likely to be fatal For patients with HIV/AIDS, TB is likely to be the cause of death
	Prevention and control	BCG vaccination often protects younger people and is typically given to children and young adults at risk
WHO status	**Distribution**	Worldwide; strains resistant to anti-TB drugs have emerged in all countries
	Global incidence and mortality	About 8.8 million, for 1.4 million per year of whom the condition proves fatal Within the UK there are over 8000 cases per year, most non-UK born, from Sub-Saharan Africa (37%) and South Asia (47%)

HIV/AIDS

Auto-immune deficiency syndrome (AIDS) is a disease caused by the human immunodeficiency virus (**HIV**, Figure 10.15). **Viruses** are disease-causing agents, rather than 'organisms'.

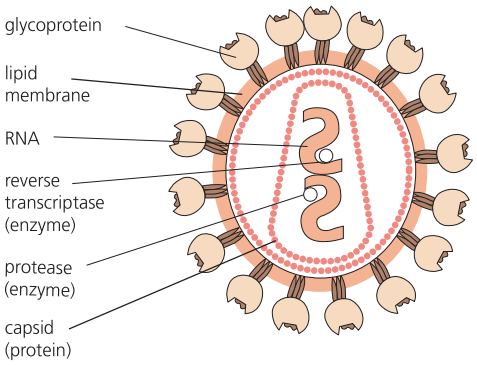


Figure 10.15 The structure of the human immunodeficiency virus (HIV)

Infection with HIV is only possible through contact with blood or body fluids of infected people, such as may occur during sexual intercourse, sharing of hypodermic needles by intravenous drug users, and during pregnancy, labour, delivery and breast feeding of a newborn baby. Also, blood transfusions and organ transplants will transmit HIV but donors are now screened for HIV infection in most countries. HIV is *not* transferred by contact with saliva on a drinking glass, nor by sharing a towel, for example. Nor does the female mosquito transmit HIV when feeding on human blood.

The spread of HIV and the eventual onset of AIDS in patients are outpacing the current efforts of scientists and doctors to prevent them. The World Health Organisation WHO records the current state of this pandemic (Figure 10.16).

Antibiotics are not effective against viruses. What antibiotics are and why this is so is explained on pages 210–16.

Antigen: a protein (normally – some carbohydrates and other macromolecules can act as antigens) that is recognised by the body as foreign (non-self) and that stimulates an immune response. The specificity of antigens (which is a result of the variety of amino acid sequences that are possible) allows for responses that are customised to specific pathogens.

T-lymphocytes (CD4 helper cells) and the development of AIDS

T-lymphocytes are a particular type of white blood cell (page 153). An **antigen** is, normally, a protein that is recognised by the body as foreign (**non-self**, see page 221) and that stimulates an immune response (page 231). HIV attacks T-lymphocytes.

HIV is one of a minority of viruses that has an additional external envelope – a membrane of lipids and proteins. (This membrane is actually 'borrowed' from the last cell that it infected.) Once in the bloodstream, specific proteins on the outer membrane of the virus are antigens. These proteins attach the virus to protein receptors of the surface of T-lymphocytes (CD4 helper cells of the immune system, page 221) and the core of the virus penetrates to the cytoplasm (Figure 10.17).

Estimated number of adults and children newly infected with HIV during 1998 – Total: 2.7 million

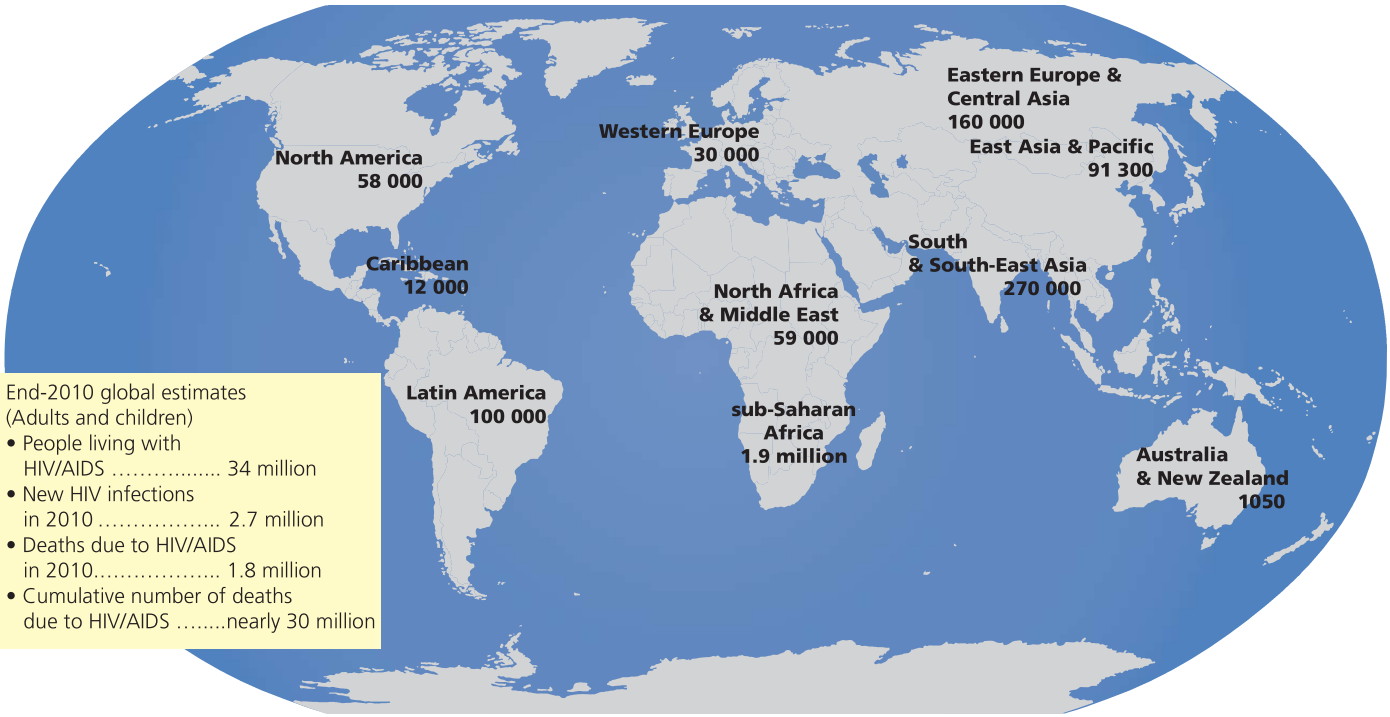


Figure 10.16 HIV/AIDs – global estimates (WHO data)

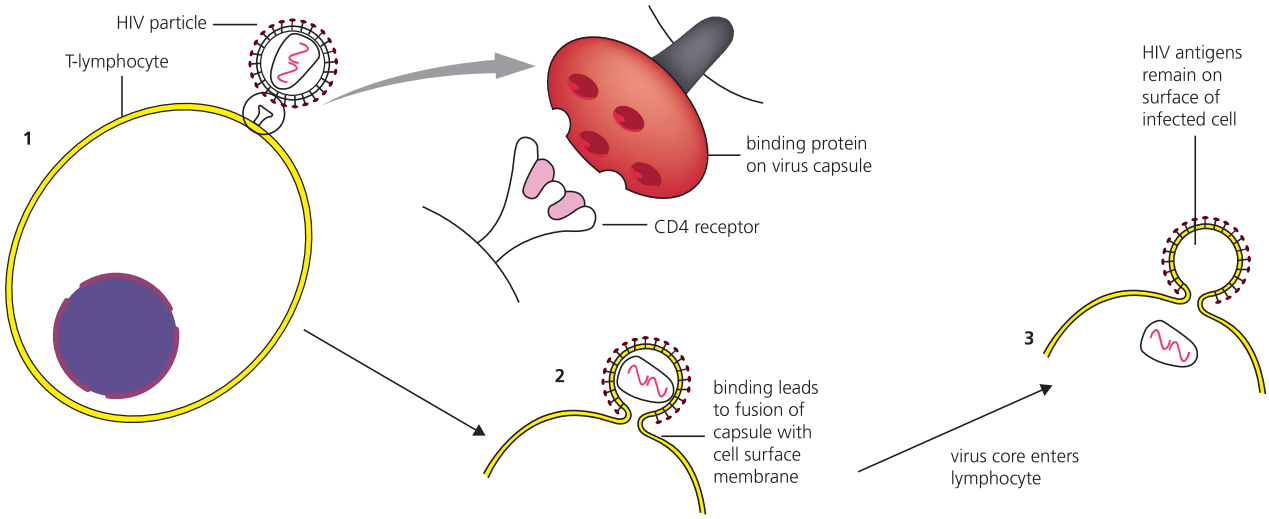


Figure 10.17 HIV infection of a white blood cell

HIV is a virus belonging to a group known as retroviruses. **Retroviruses** are RNA viruses with a unique 'infection process'. On entering the cytoplasm of a host cell the virus RNA is translated into DNA which then attaches to that of a chromosome in the host's nucleus (Figure 10.18). The steps to this are as follows.

Inside the lymphocyte, the RNA strands and an enzyme called reverse transcriptase are released from the core of the virus. Then, using the viral RNA as the template, a DNA copy is formed by the action of the reverse transcriptase. (Remember, RNA is single stranded but DNA is a double-stranded molecule, page 112).

This DNA enters the nucleus of the lymphocyte and attaches itself to a chromosome. It becomes a permanent part of the host cell's genome. It is known as a provirus. After an initial, mild form of AIDS (a brief 'flu-like illness within a few weeks, or possibly the development of a rash or swollen glands) the provirus remains dormant (called the latency period).

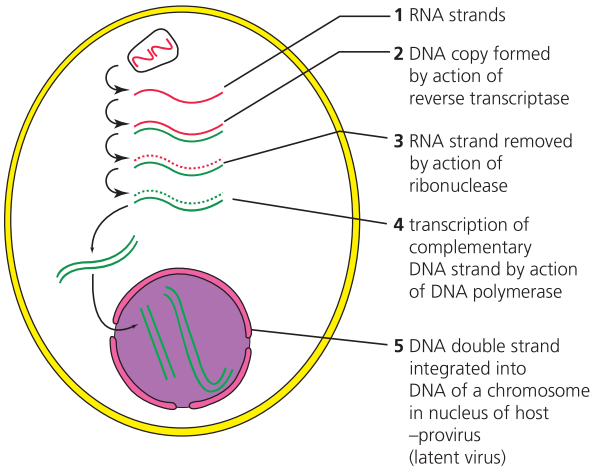
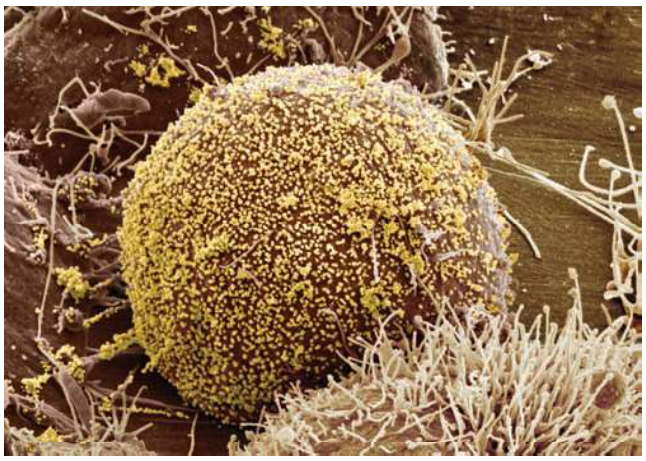


Figure 10.18 How HIV becomes part of the white blood cell's genome

However, at some later time the viral DNA replicates, leading to the production of new viruses which then invade and kill other lymphocytes (Figure 10.19). It is not clear whether infected T-lymphocytes are killed by the virus they harbour or by the actions of the patient's immune system against these infected cells. However, AIDS-related symptoms follow, caused by pathogens that are around us all the time. These are normally resisted by a healthy immune system but, without it, the body cannot effectively resist (Figure 10.20). We say the patient has now become **immunocompromised**.

SEM of a white cell from which HIV are budding off



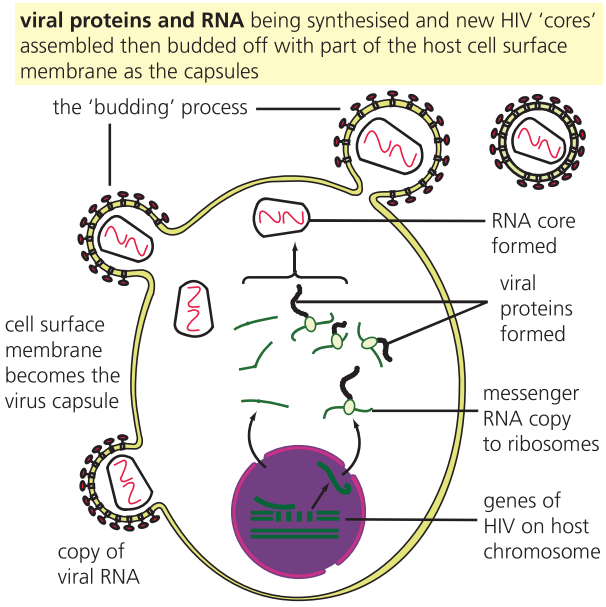


Figure 10.19 Activation of the HIV genome and the production of new HIV

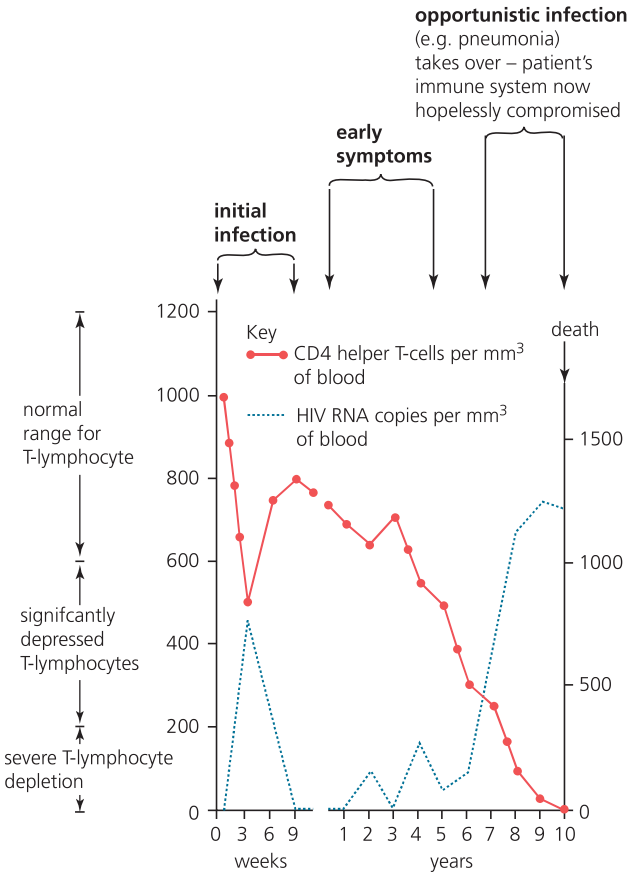


Figure 10.20 The profile of an AIDS infection

Social, economic and biological factors in the prevention and control of HIV/AIDS

AIDS is difficult to treat because viruses are not controlled by antibiotics. AIDS patients are offered **drugs** that slow down the progress of the infection. The three most popular drugs (AZT and two protease inhibitors) interrupt the reverse transcription of nucleic acid. A combination of drugs is used to prevent HIV from rapidly developing resistance to any one drug. This also helps to avoid dangerous or unpleasant side effects that some patients experience.

However, there is no cure for HIV/AIDS. Ideally, a **vaccine** against HIV would be the best solution – one designed to wipe out infected T-lymphocytes and free virus particles in the patient's bloodstream. The work of several laboratories is dedicated to this solution. The problem is that infected T4 cells in the latent state frequently change the membrane marker proteins they carry due to the HIV genome within. Effectively, HIV can hide from the body's immune response by frequently changing its identity.

Current effective measures to prevent the spread of HIV include **male circumcision**. Recent studies have shown that the incidence of AIDS is significantly higher in uncircumcised males. Circumcised males were seven times less likely to transmit to or receive HIV from their partner. The reason for this is that the mucous membrane of the inner surface of the foreskin has cells with receptors that HIV can exploit. Consequently, it is possible that infection of future generations with HIV might be reduced if male circumcision was practised more widely. However, if this were to encourage males to participate in unsafe sex with numerous partners, it would defeat the object.

Table 10.6 The prevention and control of HIV/AIDS

Factors	Prevention	Control
Social	Effective education programmes so that the vulnerable understand the cause and effects of HIV infection, and the best steps to remain healthy, whether or not they are literate Encouraging faithfulness to one partner	Contact tracing, where a person diagnosed as HIV-positive is willing and able to identify those who have been put at risk by contact
Economic	Condoms being made freely available to the sexually active population Sterile needles being made freely available to intravenous drug users	Funding of testing of the sexually-active population to identify HIV-positive people (if people will accept this invasion of their privacy) Funding and supply of the drugs that prevent the replication of the virus inside host cells
Biological	The practice of 'safe sex' by the use of condoms to prevent the transmission through infected blood or semen Screening of blood donors for HIV, so that infected blood is not taken and used	Drug therapy Research on the development of a vaccine Replacement of breast feeding by bottle feeding of infants of HIV-positive mothers, and other WHO strategies for helping HIV-infected mothers

Question

5 Suggest what features of the HIV virus and the disease it causes create particular problems for the people and the economies of less-developed countries such as Zimbabwe or Zambia?

Table 10.7 HIV/AIDS – the profile

Pathogen	**Pathogen taxonomy**	A single-stranded RNA retrovirus, human immunodeficiency virus (HIV)
	Transmission	Contact with blood or body fluids of infected people, via sexual intercourse, the sharing of hypodermic needles by intravenous drug users or during breast feeding of infants
Disease parameters	**Incubation and venue**	Once in the blood, the virus immediately enters T-lymphocytes (CD4 cells) – components of the immune system
	Signs, symptoms and diagnosis	Early symptoms typical of mild 'flu occur in a few weeks Presence of HIV can only be confirmed by HIV blood test The patient's terminal vulnerability to any opportunistic infections typically delayed months or years
	Treatment	A combination of drugs that interrupt reverse transcription of nucleic acid (AZT and two protease inhibitors)
	Prognosis	There is no cure for HIV/AIDS but an effective vaccine is sought Patients ultimately succumb to other infection, e.g. TB or measles
	Prevention and control	Safe sex using condoms Needle exchange schemes for intravenous drug users Male circumcision
WHO status	**Distribution**	Worldwide, after the first cases of the disease came to light in the 1980s in the USA
	Global incidence and mortality	Estimated annual total of newly-infected individuals of the order of 6 million, two-thirds are in sub-Saharan Africa Estimated annual death rate approaching 3 million

Measles

Measles is a highly infectious disease that people of any age can get. It is most commonly contracted by children aged between one and four years. Unlike other childhood diseases, such as mumps and rubella, it can generate severe complications. Measles is a virus disease entirely specific to humans and with a long history. For example, there is a tenth-century record of it being '*more dreaded than smallpox*'. In fact, in the past most people contracted measles. The incidence of this infection and the dangers it posed were abruptly diminished only as recently as the 1960s. A cheap and reliable vaccine became available then but it was effective only when taken up by 95 per cent of the population. This is often the case in the developed world (but not always – see below). Today, over 95 per cent of fatalities due to measles occur in less-developed countries where health infrastructures are poor. Measles is also a major killer of those in an advanced stage of HIV/AIDS.

The disease and its transmission

Measles is caused by an RNA virus belonging to the *Morbilivirus* genus. It is closely related to the canine distemper virus but both viruses are host-specific. The disease is spread by droplet transmission when infected individuals cough or sneeze. It infects the upper respiratory tract or conjunctiva of the eyes. There is an incubation period of 10–14 days before the symptoms appear. Initially these are a cold-like condition, red eyes that are sensitive to light, fever, and grey or white spots appearing in the throat and mouth. Subsequently, a red-coloured rash spreads from the head to the rest of the body, starting behind the ears. The patient is most infectious for about four days before the appearance of the rash and then remains mildly infectious for a further four days after its appearance. The result is that measles is often spread before the condition is recognised or confirmed.

In susceptible patients the complications that arise include pneumonia, hepatitis, and encephalitis (inflammation of the brain). The latter occurs in only 1 in 5000 cases but it can be fatal.

Question

6 What is meant by a disease-causing agent being 'host-specific'?

Prevention and control of measles

The first measles vaccines became available in 1963 and were then replaced by a superior version in 1968. The effect of the widespread use of these vaccines was dramatic, including in the USA (Figure 10.21).

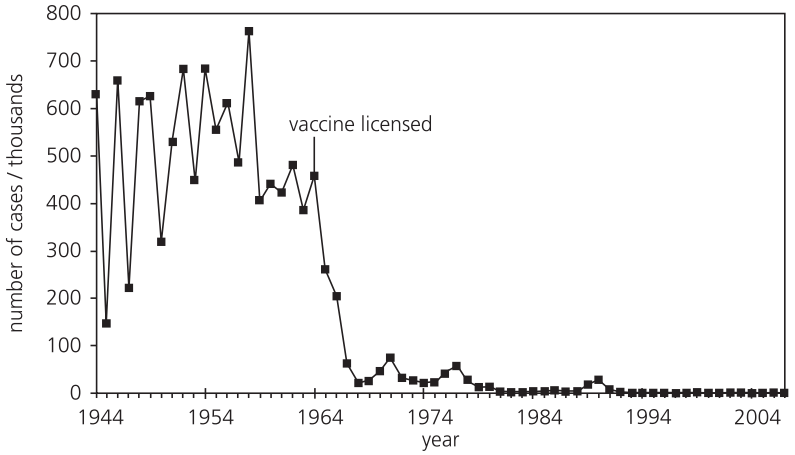


Figure 10.21 Number of measles cases in the USA, 1944–2007

A combined vaccine against three common childhood illness, referred to as the **MMR vaccine**, became available in 1971. The MMR vaccine is made by using live, attenuated (weakened) strains of the measles, mumps and rubella viruses. Infants in the UK, for example, are now offered a first MMR injection aged 15–24 months and then receive a booster injection between 3 and 5 years' of age. (A baby under 6 months is protected by antibodies received from the mother, via the placenta, whilst *in utero*; conferring what is known as '**passive immunity**'.) The success of vaccines has made measles a rare disease, at least where the vaccination regime has been adhered to.

Passive immunity: immunity involving the transfer of antibodies (already made in the body of another organism or *in vitro*) into the body where they will bind to their specific antigen if it is present. This gives instant immunity but does not lead to the development of memory cells, so the immunity only lasts for a few weeks.

Table 10.8 Measles – the profile

Pathogen	**Pathogen taxonomy**	A single-stranded RNA virus of the *Morbilivirus* genus
	Transmission	Droplet transmission when an infected person coughs or sneezes The virus has a short survival time outside its host
Disease parameters	**Incubation and venue**	10–14 days Respiratory mucous membranes, lymph glands and other body tissues
	Signs, symptoms and diagnosis	Cold-like symptoms, red eyes that are sensitive to light, fever, grey or white spots in the mouth and throat, followed by red skin rash
	Treatment	Pain and fever-reducing medications, e.g. paracetamol Anti-viral drugs in the (rare) case of complications
	Prognosis	In the absence of complications, recovery occurs within 7 days of the appearance of the rash
	Prevention and control	Measles can kill or leave severe complications Avoided by prior vaccination The MMR vaccine has made measles rare in developed countries
WHO status	**Distribution**	Worldwide
	Global incidence and mortality	Estimated 900 000 deaths from measles (2008), in countries with low incomes and limited health infrastructures

Extension

The MMR–Autism controversy

Recently, a controversy over the MMR vaccine has influenced some parents' choices.

Dr Andrew Wakefield, a gastroenterologist employed at the Royal Free Hospital in London, studied 12 children who had all apparently developed autism within 14 days of being given MMR. He published his opinion (in the medical journal *The Lancet* in 1998) that for some children, inoculation with the MMR vaccine triggered an inflammatory bowel condition. In this state the gut might become leaky, allowing 'rogue peptides' into the blood circulation, quickly leading to brain damage – in particular, to **autism**. (Autism is a life-long disorder in which children withdraw into themselves, reject human contact and often become difficult to handle. To the families in which it occurs, autism is most distressing. The film '*Rain Man*', in which Dustin Hoffman starred, helped raise the profile of this disease so it is more widely recognised now.)

Dr Wakefield noted '*We did not prove an association*', meaning this was a suggestion that needed following up (and it was). However, his ideas immediately received widespread publicity and created public anxiety sufficient to cause a marked fall in the take-up of MMR vaccine.

Why did some parents confidently blame MMR for their child's condition?

Autism, when it arises, does so at about 18 months. When this occurs soon after the MMR inoculation, it is inevitable that there may *appear* to be a connection. In fact, no study has produced evidence that MMR causes autism. Major investigations and follow-up studies have been undertaken with large samples of children in Australia, in Finland, and in Japan. In communities where autism appears to be on the increase, the increase began before MMR was introduced, and the incidence of autism continued to rise even when the numbers of children receiving MMR reached a plateau. There is no doubt in the minds of health authorities that vaccination is the safest option for children and their parents.

The measles vaccine is not universally available; there are several less developed countries where many people are not vaccinated. This is despite the fact the disease is targeted by the WHO in an expanded programme of immunisation. It is estimated there may be up to 900 000 measles-related deaths annually – many HIV/AIDs-related. Unfortunately, some children who recover are left with serious, permanent complications.

Question

7 The coincidence of autism onset and MMR administration may be described as circumstantial evidence. What part, if any, can it play in scientific discovery?

Those patients that survived smallpox were typically disfigured by scabs. These resulted from red spots that had formed on their skin and became filled with thick pus before drying out. Eyelids often swelled up and became glued together, leaving many patients blind.

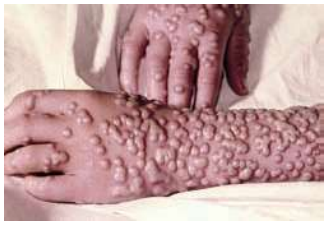


Figure 10.22 Skin vesicles on a smallpox patient

Question

8 Outline how it has been possible to eradicate smallpox but not other infectious diseases like malaria.

Smallpox

Smallpox, a highly contagious disease, was once endemic throughout the world. It killed or disfigured all those who contracted it (Figure 10.22). Smallpox was caused by a DNA *Variola* virus. The virus was stable, meaning it did not mutate or change its surface antigens.

Eventually, a suitable vaccine was identified – made from a harmless but related virus – *Vaccinia*. This was used in a 'live' state and could be freeze dried for transport and storage. Consequently, the virus vaccine was relatively easy to handle and stable for long periods in tropical climates.

How eradication came about

This disease has been eradicated (the last case of smallpox occurred in Somalia in 1977). The development of a vaccine played an important part in this achievement, which was the outcome of a determined World Health Organisation programme, begun in 1956. This involved careful surveillance of cases in isolated communities and within countries sometimes scarred by wars – altogether a most remarkable achievement. How was smallpox eradicated when so many other diseases continue? The reasons include:

- patients with the disease were easily identified as they had obvious clinical features
- transmission was by direct contact only
- on diagnosis, patients were isolated, all their contacts traced and all were vaccinated
- it had a short period of infectivity, about 3–4 weeks
- patients who recovered did not retain any virus in the body ('carriers' did not exist)
- there were no animals that acted as a vectors or 'reservoirs' of the infection (and so be able to pass on the virus to humans).

Other reasons, relating to the virus, its antigens and the vaccine that was used in the eradication campaign are identified on page 231.

10.2 Antibiotics

The 'age of antibiotics' began in the 1940s with the availability of penicillin. With an increase in antibiotic resistance is this age about to come to an end?

By the end of this section you should be able to:

a) outline how penicillin acts on bacteria and why antibiotics do not affect viruses
b) explain in outline how bacteria become resistant to antibiotics with reference to mutation and selection
c) discuss the consequences of antibiotic resistance and the steps that can be taken to reduce its impact

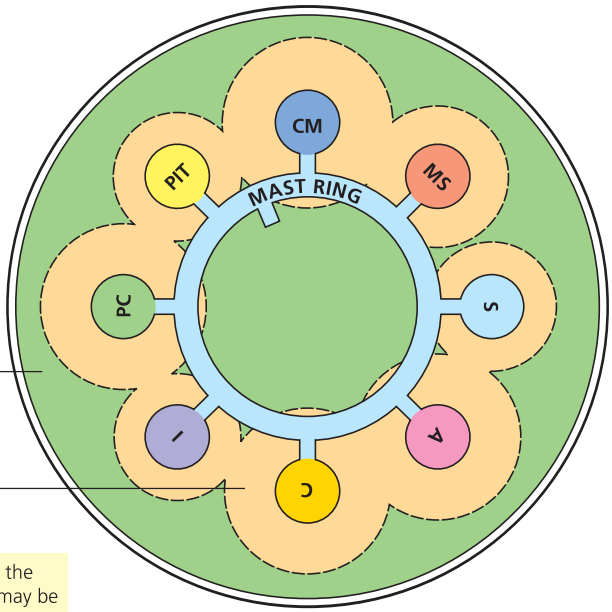
Introducing antibiotics

Antibiotics were discovered relatively recently – with a chance observation in 1928. By the 1950s, it became possible to treat patients with courses of antibiotics that cured many bacterial infections. More recently, the excessive use of antibiotics has generated problems, as we shall see later.

Antibiotics are naturally occurring chemical substances obtained mainly from certain fungi and bacteria commonly found in the soil. When antibiotics are present in low concentrations they inhibit the growth of other microorganisms or cause their outright death, as demonstrated in Figure 10.23.

The discovery, isolation and development of the first antibiotic, penicillin, was not an easy task. (It took from 1929 until 1944.) Since then, over four hundred different antibiotics have been isolated and tested. Of these, only about 50 have proved to be non-toxic to patients. These antibiotics have achieved wide usage. Those effective against a wide range of pathogenic bacteria are called **broad-spectrum antibiotics**. These include chloramphenicol. Others, including streptomycin, are effective against a limited range of bacteria.

To a known species of bacteria growing on nutrient agar was added a mast ring with each 'arm' impregnated with a different antibiotic (colour coded). Then the plate was closed and incubated. From the result (opposite) there is evidence that growth of this bacterium is more sensitive to certain antibiotics (e.g. CM, A) than to others (e.g. S, I).



Different antibiotics are contained in the arms of the mast ring, so that sensitivity to many antibiotics may be tested simultaneously.

Figure 10.23 Investigating sensitivity to antibiotics

How antibiotics work

Antibiotics work by disrupting the metabolism of prokaryotic cells. It is in these division and growth phases that bacteria are vulnerable to antibiotic action – an effective antibiotic specifically disrupts one of three major aspects of the growth or metabolism of bacteria. Since the particular components, metabolites or enzymes concerned are not found in eukaryotic cells in the same form, the antibiotic is not toxic to the mammalian host tissues.

1 Cell wall synthesis inhibition

The most effective antibiotics work by interfering with the synthesis of bacteria's cell walls. Once the cell wall is destroyed, the delicate plasma membrane of the bacterium is exposed to the destructive force generated by excess uptake of water by osmosis, and possibly, as well, to attack by antibodies and phagocytic macrophages.

Several antibiotics, including **penicillin**, ampicillin, and bacitracin, bind to and inactivate specific wall-building enzymes. These are the enzymes required to make essential cross-links between the linear polymers of the walls in particular species. In the presence of the antibiotic, wall polymers continue to be synthesised by the pathogens, but the individual strands are not linked and bound together. The walls fall apart.

2 Protein synthesis inhibition

Other antibiotics inhibit protein synthesis by binding with ribosomal RNA. The ribosomes of prokaryotes (known as 70S) are made of particular RNA sub-units, together with many polypeptides (which mainly function as enzymes). The ribosomes of eukaryotic cells are larger (80S), and are built with different RNA molecules and polypeptides. Antibiotics like streptomycin, chloramphenicol, tetracyclines and erythromycin all bind to prokaryotic ribosomal RNA subunits unique to bacteria. Here their presence causes protein synthesis to be terminated.

3 Nucleic acid synthesis

A few antibiotics interfere with DNA replication or transcription, or they block mRNA synthesis. These antibiotics, for example the quinolones, are not as selectively toxic as other antibiotics. This is because the processes of replication and transcription do not differ so greatly between prokaryotes and eukaryotes as wall synthesis and protein synthesis do.

Why antibiotics do not affect viruses

We have seen that viruses are non-living particles (page 26). A virus lacks cell structure and has no metabolism of its own to be interfered with or disrupted. Instead, viruses reproduce using metabolic pathways in their host cell that are not affected by antibiotics. Antibiotics cannot be used to prevent viral diseases.

How bacteria become resistant to antibiotics

Before antibiotics became available to treat bacterial infections the typical hospital ward was filled with patients with pneumonia, typhoid fever, tuberculosis, meningitis, syphilis and rheumatic fever, for example. These diseases, all caused by bacteria, claimed many lives, sometimes very quickly. The discovery of antibiotics brought a significant change. Patients with bacterial infections were treated with an antibiotic, and quickly overcame their infection. In fact, antibiotics have been very widely used – to great success.

However, in any large population of a species of pathogenic bacteria, some of the bacteria may acquire or carry a gene for resistance to the antibiotic in question. Sometimes this gene has arisen by a spontaneous mutation. Sometimes the gene has been acquired in a form of sexual reproduction between bacteria of different populations, or when the bacterium itself has been parasitised by a virus that brought the resistance gene within its nucleic acid (Figure 10.24).

When an individual bacterium has acquired resistance it confers no selective advantage at all *in the absence of the antibiotic*. The resistant bacterium must compete for resources with non-resistant bacteria. However, when an antibiotic is administered, most bacteria of the population are killed off. Only at this stage will the bacteria with resistance to the antibiotic flourish, and then come to create the future population, all of which now carry the gene for resistance to the antibiotic. At this point, the genome has been changed abruptly, and the future effectiveness of that antibiotic is compromised.

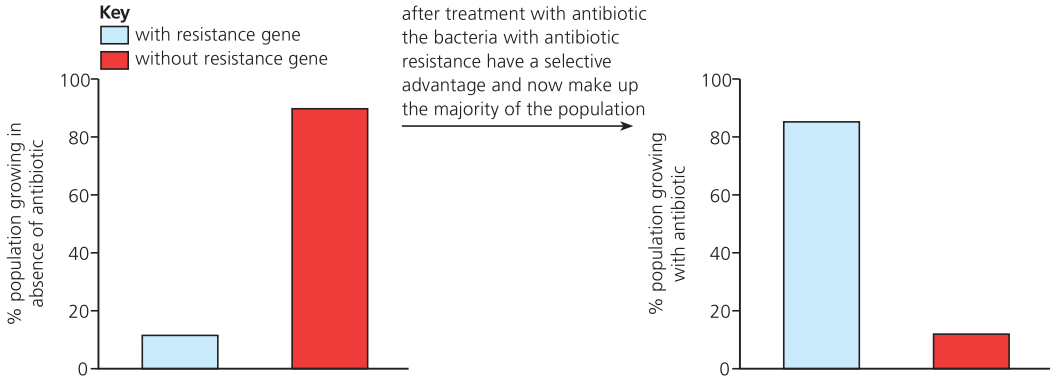


Figure 10.24 Development of antibiotic resistance in bacteria

Today, the issue of bacterial resistance to antibiotics in healthcare has become a major problem. As pathogenic bacteria developed genes for resistance to antibiotic actions, different antibiotics were used in response. The inevitable outcome of this is that pathogenic bacteria slowly acquire **multiple resistance** (Figure 10.25). For example, a strain of *Staphylococcus aureus* has acquired resistance to a range of antibiotics including methicillin. Now, so-called methicillin-resistant *Staphylococcus aureus* (MRSA) is referred to as a 'hospital superbug' because of the harm its presence has inflicted in these places. (Actually, 'superbugs' are found everywhere in the community, not just in hospitals.) MRSA poses the greatest threat to patients who have undergone surgery. With cases of MRSA to treat, the intravenous antibiotic called vanomycin is prescribed, but recently there have been cases of partial resistance to this drug, too (Figure 10.26).

Similarly, a strain of the bacterium *Clostridium difficile* is now resistant to all but two antibiotics. This bacterium is a natural component of our gut 'microflora'. It is only when *C. difficile's* activities are no longer suppressed by the surrounding, huge, beneficial (i.e. 'friendly') gut flora that it may multiply to life-threatening numbers and then may trigger toxic damage to the colon.

Suppression of beneficial gut bacteria is a typical consequence of heavy doses of broad-spectrum antibiotics, administered to overcome infections by superbugs.

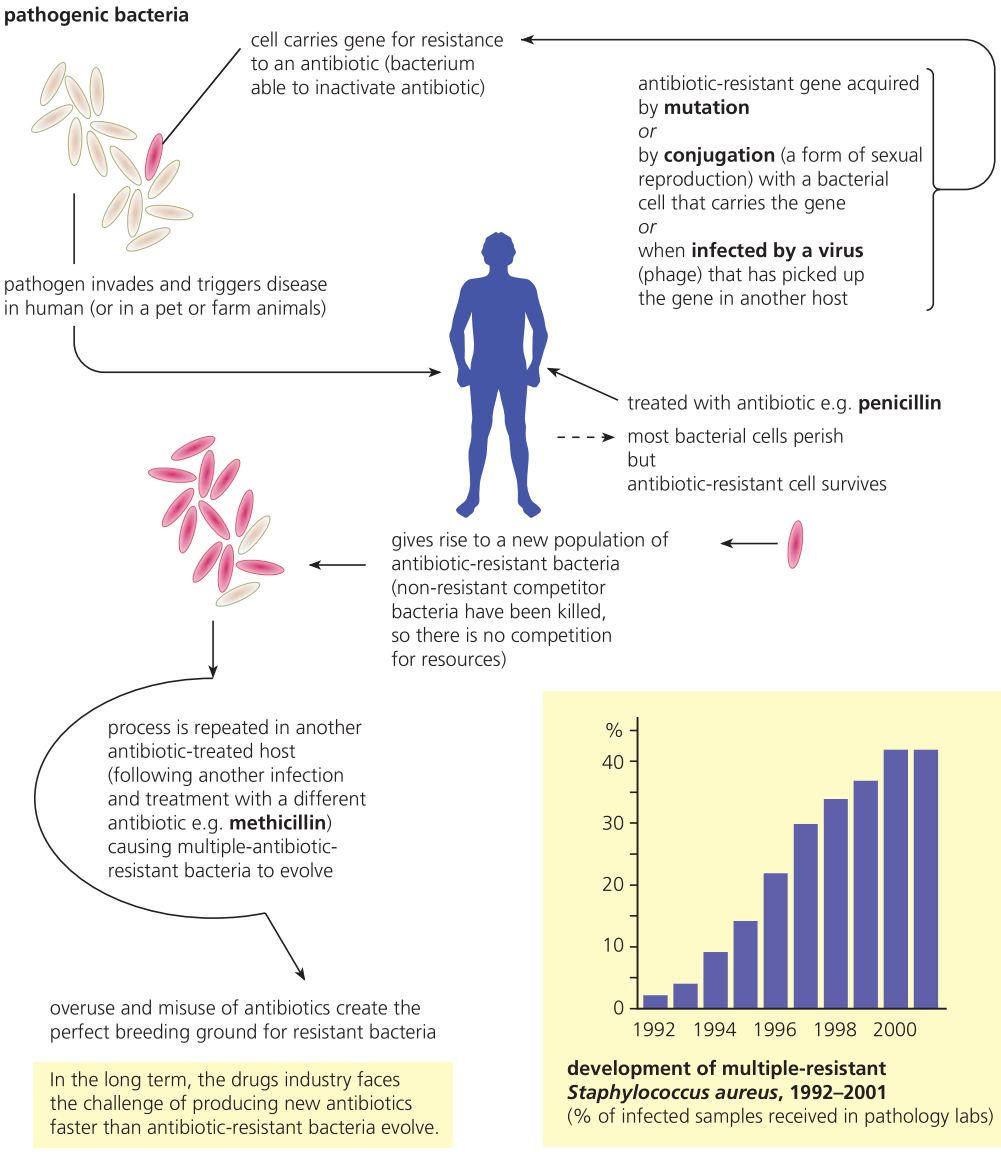


Figure 10.25 Multiple antibiotic resistance in bacteria

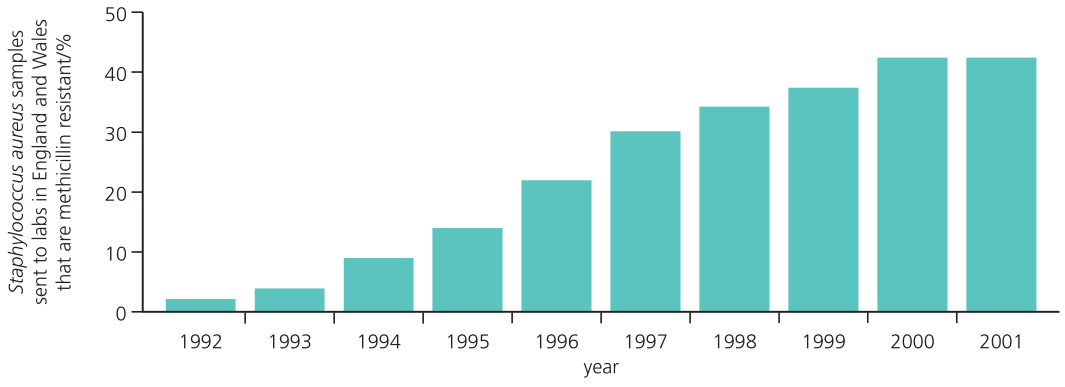


Figure 10.26 The increasing incidence of MRSA

Question

9 Explain:

a why doctors ask patients to ensure that they complete their course of antibiotics fully

b why the medical profession tries to combat resistance by regularly alternating the type of antibiotic used against an infection.

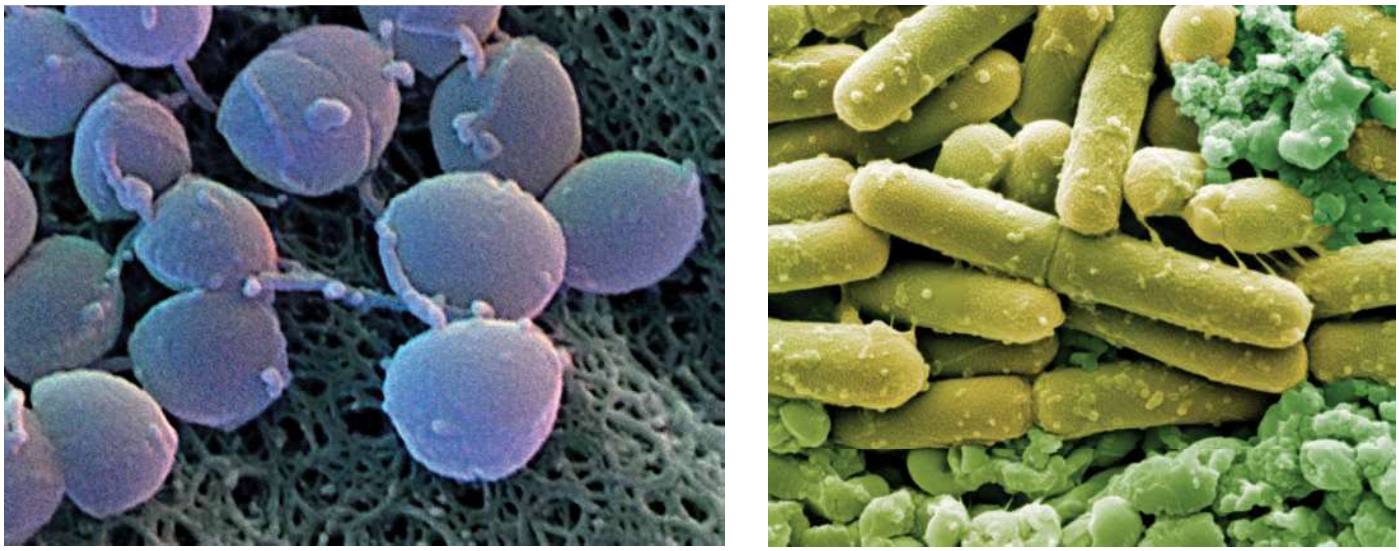


Figure 10.27 False-colour SEMs of *Staphylococcus aureus* (x000) and *Clostridium difficile* (x10 000)

THE TIMES | Thursday May 1 2014

Antibiotics crisis means scratch could kill

Common infections will once again kill as the rise of antibiotic-resistant superbugs has a "devastating" effect on modern medicine, the World Health Organisation said yesterday.

Resistance to commonly used drugs is increasing across the planet and is now a problem that could affect "anyone, of any age, in any country", the WHO said in a report tracking the rise of superbugs in 114 countries.

Patients are already suffering because those infected by superbugs are twice as likely to die as those with non-resistant infections. Routine operations, minor scratches and common infections could all become fatal, the report warns.

Doctors said the problem demanded an international effort modelled on the fight against Aids, including a clampdown on the use of antibiotics, the end of their use in agriculture and the urgent development of new drugs. Patients must only use antibiotics prescribed by a doctor and complete a full course even if they are feeling better, the WHO said.

Chris Smyth Health Correspondent

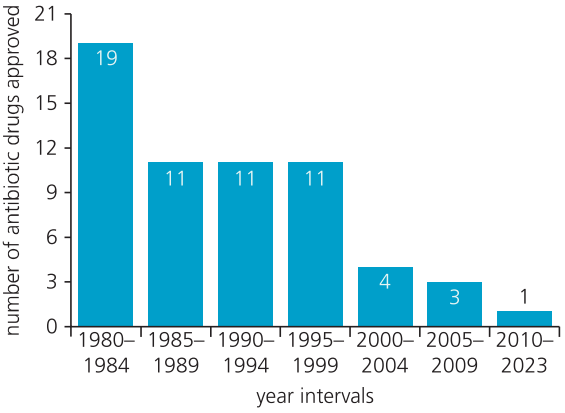


Figure 10.28 The number of new antibiotics developed and approved in the past three decades

The consequences of antibiotic resistance

A natural response to this challenging situation is to search for new and more effective antibiotics to replace those that have become ineffective. This has been the response of pharmaceutical firms – and continues to be so. However, this is proving increasingly difficult – the number of new antibiotics being developed each year has fallen dramatically (Figure 10.28). Pathogens tend to develop resistance faster than new antibiotics can be found.

In this situation the strategy to combat the problem includes:

- **Prudent antibiotic use.**
  Avoidance of the unnecessary and inappropriate exposure of microorganisms to antibiotics in medical clinics, veterinary clinics, animal husbandry and agriculture. These drugs must be used sparingly, and only in situations where there is no alternative appropriate treatment. When a course of antibiotics is prescribed, the antibiotics should be taken to completion, and not abandoned as soon as the patient feels some improvement. The widespread prophylactic use of antibiotics in animal husbandry should be minimalised and preferably discontinued. Animals reared intensively have been fed antibiotics as a component of their diet, following the discovery that they grew faster and reached marketable weights more quickly. However, antibiotic residues have accumulated in the food chain, and many more bacteria have been exposed to situations where resistance may evolve and emerge.
- **Surveillance.**
  The monitoring of the appearance of new cases of resistance to antibiotics, and prompt circulation of the data to healthcare professionals and institutions.
- **Infection control.**
  A renewed focus on the reduction in the spread of infection in general, so that the need for the use of antibiotics is reduced – on the principle that prevention is better than cure.

Question

10 Antibiotics are widely used as prophylactics in animal husbandry. What does this mean, why does this happen, and what possible dangers arise from this use of antibiotics?

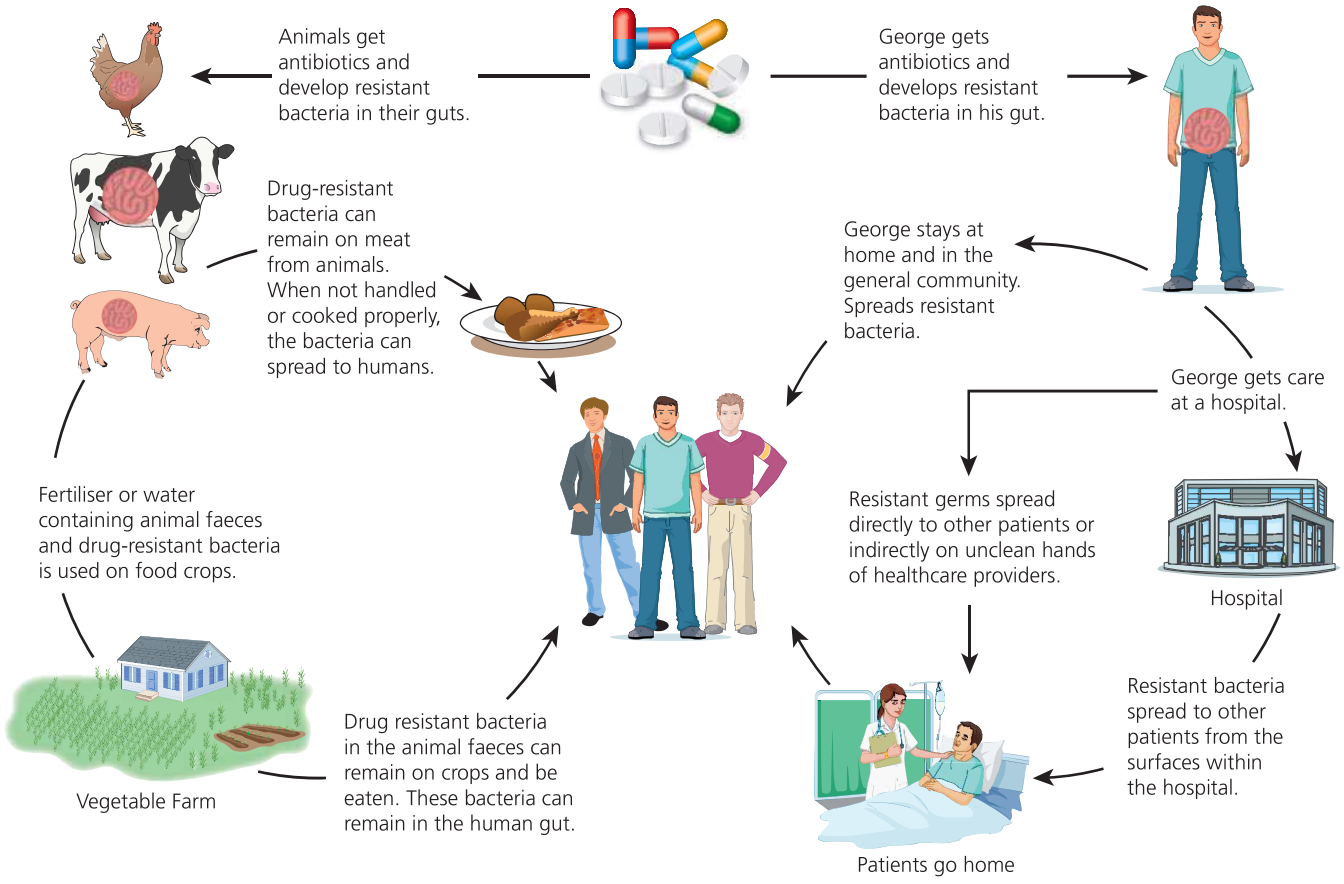


Figure 10.29 How antibiotic resistance spreads

Summary

- **Health** is a state of physical, mental and social well-being, not merely the absence of disease. Diseases caused by disease-causing agents are **infectious diseases** since they may be transferred. **Non-infectious diseases**, such as lung cancer and sickle cell anaemia, are not 'caught' from other organisms.
- **Viruses** consist of DNA or RNA, wrapped in a protein coat. Viruses take over host cells and convert the cellular machinery to produce more viruses which escape and may repeat the process. Human viral diseases include HIV/AIDS, measles and smallpox.
- **HIV** is transmitted by contact with blood or body fluids. It enters lymphocytes of the immune system and ultimately destroys them and the body's resistance to other diseases. Treatment with drugs that interfere with the replication of the virus delays the onset of AIDS but there is no vaccine as yet and therefore no cure. Transmission may be controlled by barrier methods of contraception but HIV/AIDS especially harms societies when young, economically active members and their children are infected. The distribution of the disease is global.
- The **measles** virus is transmitted by droplets discharged via coughs and sneezes, and attacks the respiratory mucous membranes and other tissues. Distinctive symptoms appear within 10 days or so, including a body rash and grey or white spots in the mouth. Contracting measles can be avoided by prior vaccination, now via the MMR vaccine, but untreated infections can kill or leave severe complications.
- **Bacterial diseases** are caused by pathogenic bacteria. They are vulnerable to antibiotics, unlike viruses. Examples of bacterial diseases include cholera and tuberculosis (TB) but most bacteria are not disease-causing at all.
- The **cholera** bacterium is principally transmitted in water or foods contaminated by human faeces. The bacterium releases a toxin that triggers the loss of water and salts from the intestines, causing diarrhoea and severe dehydration. Cholera has been eradicated where there is effective processing of sewage and the purification of drinking water. Vaccines are available but prompt treatment by rehydration with a dilute solution of glucose and salts is essential once the disease is diagnosed. About 50 per cent of untreated cases are fatal.
- The **TB** bacterium is transmitted by droplets from infected lungs during persistent coughing. In the lungs of people weakened by malnutrition or ill-health the bacterium overcomes resistance and attacks the alveoli. Prolonged treatment with a combination of antibiotics leads to recovery but, untreated, TB will attack other body systems and cause death. A vaccine is available and is given to people in some countries, particularly children, but how effective the vaccine is varies according to geography. Distribution of the disease is worldwide but it is a particular threat to HIV/AIDS patients. Strains resistant to anti-TB drugs have emerged in all countries.
- Diseases caused by eukaryotic organisms include **malaria**, due to the protoctist *Plasmodium*, transferred by the mosquito. The life cycle of *Plasmodium* is acted out in the liver and red blood cells and results in periodic release of toxins and high fever. Protection from mosquito bites is critical but a combination of anti-malarial drugs permits a patient with malaria to improve within 48 hours. Malaria is endemic in tropical and sub-tropical regions and kills thousands of children in remote areas of sub-Saharan Africa. A well-funded drive to find a vaccine continues.
- **Antibiotics** are developed from naturally-occurring chemicals obtained from certain bacteria and fungi and that inhibit the growth of other microorganisms. They work by destroying the pathogenic bacteria or by interfering in their metabolism so that the body's own defences can work effectively. Unfortunately, pathogens develop resistance so new antibiotics are constantly sought.

Examination style questions

1 a) i) Name the organism that causes tuberculosis (TB). [1]

ii) Explain how TB is transmitted from an infected person to an uninfected person. [2]

The World Health Organisation (WHO) collects data on TB from its six different regions as shown in Table 1.1.

In 2003, it used these figures to estimate

- the total number of people with the disease in each region
- the number of deaths from TB.

Many of those who died from TB were also infected with HIV.

Table 1.1

WHO region	Number of cases per 100 000 population	Number of deaths from TB (including TB deaths in people infected with HIV) per 100 000 population
Africa	345	78
The Americas	43	6
Eastern Mediterranean	122	28
Europe	50	8
South-East Asia	190	38
Western Pacific	112	19

b) Explain the advantage of expressing the number of cases and the number of deaths as 'per 100 000 population'. [2]

c) Using the information in Table 1.1, outline the reasons why TB has a greater impact on the health of people in some regions rather than others. [3]

d) The number of cases of TB decreased considerably in many countries during the 20th century. Over the past 20 years, the number of cases worldwide has increased very steeply. A vaccine against TB has existed since 1921.

Explain why TB has not been eradicated even though a vaccine has existed since 1921. [3]

[Total: 11]

(Cambridge International AS and A Level Biology 9700, Paper 02 Q5 November 2007)

2 a) Moves to prevent the spread of infectious disease within a local community have included:

A an improved supply of water, including sewage treatment

B insect control

C milk pasteurisation.

For each of these preventative measures, describe a disease they are effective against and explain why. [12]

b) What features of the lifecylce of the pathogen that causes malaria make the development of an effective vaccine especially difficult? [4]

c) Explain why malaria is endemic in tropical and sub-tropical regions but absent or rare elsewhere in the world. [2]

d) What is the significant difference between a disease outbreak which is classified as an epidemic and as a pandemic? [2]

[Total: 20]

3 a) The human immunodeficiency virus (HIV) is a retrovirus that is responsible for the disease of AIDs. Explain what 'retrovirus' means.

b) With the onset of AIDs, the immune system is said to be 'hopelessly compromised'. Explain this, and outline how HIV brings this about.

c) Ideally, a vaccine is sought against HIV. Why is the development of an effective vaccine proving difficult in this case?

4 a) Explain the mechanism by which antibiotics may be effective against pathogenic bacteria but that results in them having no effect on viruses.

b) Antibiotics have been thought of as 'wonder drugs' but today are used selectively and sometimes with restraint. What are the reasons for this change in attitudes and practice?