DISEASE

(71 pages)

INFECTIOUS DISEASE

(8 pages)

BACTERIA & VIRUSES

(24 pages)

CONTENTS

Bacteria and Viruses as examples of pathogenic microorganisms

Bacteria

- The sigmoid growth curve of a bacterial population. The effect of temperature and nutrient availability on the growth of bacterial populations.

Viruses

- The structure of the human immunodeficiency virus (HIV) and its replication

The association of microorganisms with disease

- Diseases as a result of pathogenic organisms penetrating any of the body's interfaces with the environment
- Microorganisms causing disease by damaging the cells of the host and by producing toxins
- Illustration of these principles by reference to:

  Salmonella sp.

  Mycobacterium tuberculosis

  HIV

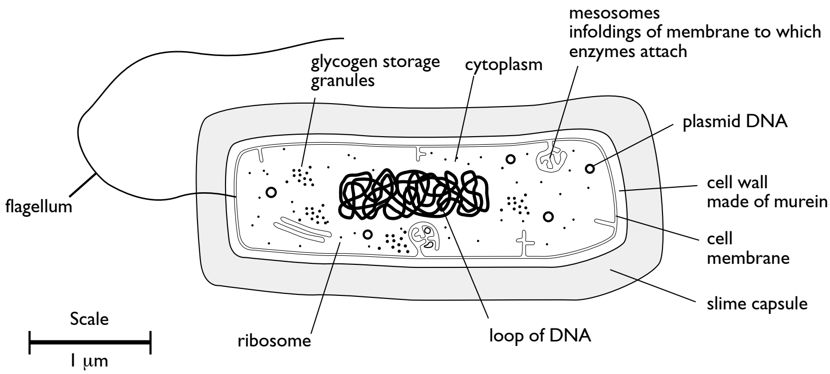
Introduction

Infectious or communicable diseases are caused by a range of organisms including viruses, bacteria, fungi, protoctists, arthropods, platyhelminthes and others which are collectively referred to as **pathogens**. The death toll from such pathogens is staggering: current estimates suggest that in 1999 diarrhoeal diseases caused by a range of bacteria killed almost 3 million people worldwide, HIV/AIDS (caused by a virus) another 2.6 million, tuberculosis (caused by a bacterium) over 1.5 million, and malaria (caused by a protoctist) a similar number. In many developing countries infectious diseases are still the most significant cause of death.

BACTERIA

Of the many thousands of species of bacteria only a relatively small proportion are human pathogens. Some common examples are *Salmonella enteriditis* a cause of food poisoning, *Mycobacterium tuberculosis*, the cause of tuberculosis (TB) and *Streptococcus sp*. a cause of throat infections. Other bacteria live freely in the soil, air or water, or mutualistically in or on animal hosts without causing them harm. Examples are forms of *Escherichia coli (E. coli)* which inhabit the large intestine of humans, and *Nitrobacter*, a soil dwelling bacterium which is involved in the nitrogen cycle.

Bacteria



Bacterial Growth

Bacteria reproduce asexually by binary fission (one cell dividing to form two identical daughter cells). The time taken for one cell to become two is highly variable, but it can be around 30 minutes. This doubling of the population every 30 minutes leads to rapid increases in numbers, and can explain why an individual may appear well one day and be severely ill or dead from a bacterial infection the next. The increase in numbers of a bacterial population is referred to as bacterial growth.

Colonies grown in a closed system, e.g. a petri dish, where there are no additions or removals of materials once growth has started, show a characteristic **sigmoid growth curve** when numbers of bacteria are plotted against time (sigmoid means curved like a capital S). Such curves can be derived from laboratory analysis of bacteria growing in a nutrient medium (a **bacterial culture**) which would require sampling the culture and counting the number of bacteria in a sample of equal size at regular time intervals. The curve has four main phases:

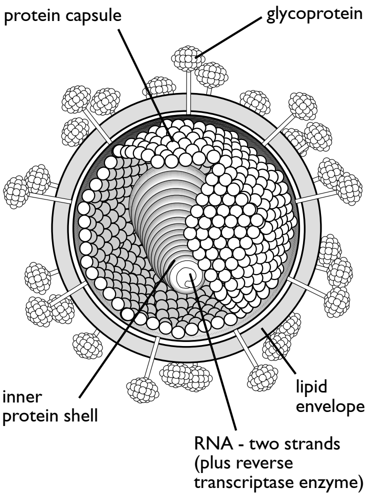
VIRUSES

Viruses are structures from 20-300 nm in size, which contain genetic material in the form of DNA **or** RNA (never both) and infect cells of other organisms (prokaryotic and eukaryotic). There is much debate as to whether they should be defined as living organisms since although they possess genetic material, they lack many of the basic features shown by all other living organisms, including the presence of a cellular structure. Viruses are incapable of reproducing themselves outside the environment of a host cell.

Whilst details vary, all viruses have similar structural features which include a central core of genetic material (DNA or RNA never both) and a capsid or protective protein coat around the core formed of units called capsomeres.

As a group, viruses cause an enormous amount of damage and death amongst organisms of all five kingdoms (bacteria, fungi, protoctista, plants and animals) yet each virus is very specific to one particular type of cell in one host species. In humans, viral diseases include chicken pox, measles, influenza, and HIV/AIDS.

Human Immunodeficiency Virus



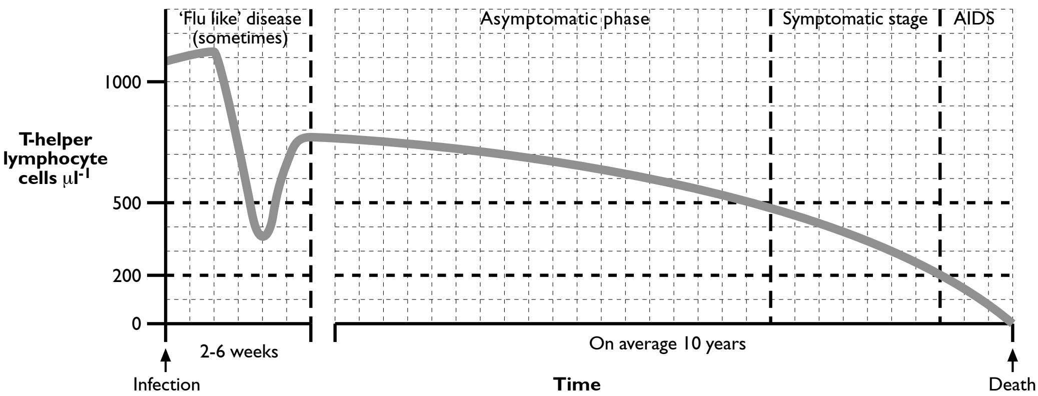
Human Immunodeficiency Virus (HIV)

HIV is a virus which causes the disease known as AIDS (Acquired Immune Deficiency Syndrome). This disease is one of the fastest growing causes of death in the world, and is currently responsible for about 3 million deaths per year. HIV infects a type of white cell known as the T-helper lymphocyte or CD4 cell. In doing so it severely damages the immune system of infected people, making them highly susceptible to infection and death from a range of infectious diseases and cancers.

Structure of HIV

HIV belongs to a group of viruses known as **retroviruses**. The main feature of such viruses is the presence of RNA rather than DNA as the genetic material in the core of the virus. The HIV virus has two identical RNA strands. Also present is the enzyme reverse transcriptase, which allows single stranded RNA to be converted to double stranded DNA. The RNA is encapsulated in layers of proteins, glycoproteins and lipids.

Decline of T-helper lymphocytes in the course of an HIV infection



Replication of HIV

Like all viruses, HIV is incapable of independent replication. It relies on inserting its genetic material into the DNA of human T-helper cells and allowing these cells to manufacture new copies of the viral RNA and proteins necessary for assembling new viruses. There are several stages in this process:

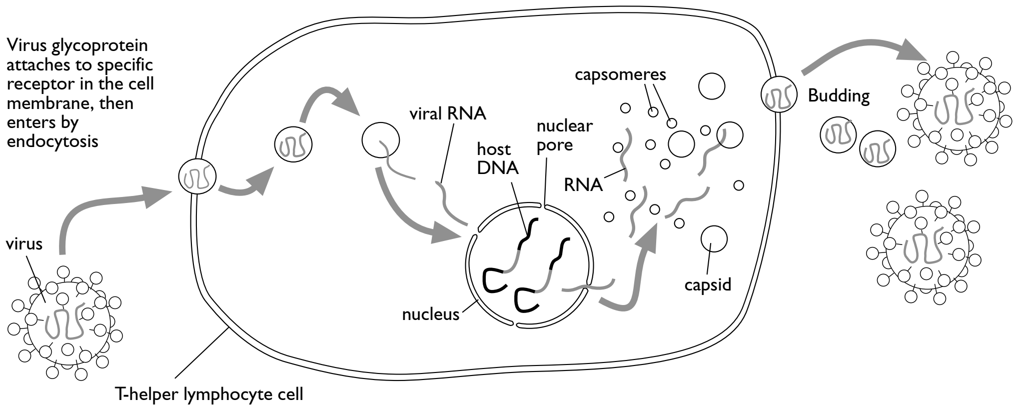
- HIV enters the body from an infected (HIV positive) person via body fluids such as blood or semen.
- It attaches to specific receptors on the cell membranes of T-helper lymphocytes.
- HIV enters the cell by endocytosis releasing its RNA and reverse transcriptase enzymes into the cytoplasm.
- The RNA strand is copied to form a double stranded DNA molecule using reverse transcriptase.
- The DNA copy inserts itself into the human DNA in the nucleus of the T-helper lymphocyte.
- After a variable period of time (latency period) the DNA is copied (transcribed) to make new viral RNA. At the same time, the viral proteins necessary for the capsid and envelope proteins are synthesised by the cell.
- New viruses are assembled from the RNA and proteins and leave the cell by exocytosis. During this process the viral envelope is constructed from the cell membrane of the host cell.

As with any virus, large numbers of new HIV viruses are made by a single cell, all of which may, in turn, infect new cells. Since HIV eventually kills the T-helper lymphocytes it has infected, one of the signs that an HIV infection has become active is a rapid decrease in the numbers of these cells. T-helper lymphocyte counts are used in the monitoring of HIV infection. Once the levels drop below 200 cells per µl of blood AIDS is diagnosed.

◆ CHECKPOINT SUMMARY

- Viruses are structures from 20-300nm in size, which contain genetic material in the form of DNA or RNA (never both) and infect cells of other organisms (prokaryotic and eukaryotic).
- Viruses are incapable of reproducing themselves outside the environment of a host cell.
- All viruses have similar structural features which include a central core of genetic material (DNA or RNA) and a capsid or protective protein coat around the core formed of units called capsomeres.
- HIV is a virus which causes the disease known as AIDS (Acquired Immune Deficiency Syndrome).
- HIV infects a type of white blood cell known as the T-helper lymphocyte or CD4 cell. In doing so it severely damages the immune system of infected people, making them highly susceptible to infection and death from a range of infectious diseases and cancers.
- HIV belongs to a group of viruses known as retroviruses. The main feature of such viruses is the presence of RNA rather than DNA as the genetic material in the core of the virus. The RNA is encapsulated in layers of proteins, glycoproteins and lipids.
- Like all viruses, HIV is incapable of independent replication. It relies on inserting its genetic material into the DNA of human T-helper cells and allowing these cells to manufacture new copies of the viral RNA and proteins necessary for assembling new viruses.

Infection of a T-helper lymphocyte with HIV



CAUSES and MEANS OF TRANSMISSION of INFECTIOUS DISEASES their WORLDWIDE IMPORTANCE PANDEMICS and the ROLES of SOCIAL, ECONOMIC and BIOLOGICAL FACTORS in the PREVENTION and CONTROL of these DISEASES

Introduction

Infectious diseases are diseases caused by pathogens (mainly bacteria, viruses, fungi and protoctists) which can be transmitted from one person to another in a variety of ways. The four diseases mentioned above, cholera, malaria, tuberculosis and HIV/AIDS, have all proved very difficult to prevent and control and there is very little chance of any of them being eradicated in the foreseeable future. There are many reasons for this, which include biological features of the pathogens themselves, as well as social and economic conditions of the human populations who suffer from them.

Reducing the number of deaths from each of these diseases involves a range of strategies which include modern medical treatments as well as simple improvements in living conditions, sanitation and education. In all cases there are two primary aims which are often closely linked. Firstly it is important to prevent people from becoming infected in the beginning (**disease prevention**). Secondly those who do catch the diseases must be managed and treated to ensure that the diseases do not spread through the population and cause epidemics. This is known as **disease control**.

PATTERNS of DISEASE DISTRIBUTION

The types of disease found in different countries are highly variable. Some diseases are always present and cause illness or death of large numbers of people every year. Others are always rare, and still others fluctuate wildly over time, killing many people one year and few in other years. In rare cases diseases can affect millions of people all over the world at the same time. Three broad terms are used to describe these patterns: **endemic**, **epidemic** and **pandemic**. It should be noted that the same diseases may be epidemic, endemic and pandemic at different times and in different regions, and that in epidemiology the use of these terms is usually restricted to infectious diseases.

Endemic

This is a term used to describe diseases which are common in populations all the time. An example is malaria in East Africa which kills thousands of children every year and shows relatively little variation in numbers of cases from one year to another.

Epidemics

These are defined as a short-term increase in the national incidence of a disease which is normally absent or occurs at a low level in that population. Regular influenza epidemics, such as the one in the winter of 1999, hit Britain. Cholera epidemics frequently occur during war or famine situations.

> ◆ CHECKPOINT SUMMARY
>
> - An endemic disease is one which is always present in a region and causes a similar number of illnesses and deaths every year.
> - Epidemics are defined as short term increases in the national incidence of a disease which normally occurs at much lower levels.
> - Pandemics are epidemics which affect most or all of the world at the same time.
> - The same diseases may be endemic, epidemic or pandemic depending on circumstances.

PANDEMICS

These are epidemics which affect most or all of the world at the same time

Plague

'The Plague' persists throughout the world, but in the 14th century it killed up to one third of the inhabitants of Europe.

Influenza

'The Flu' still persists and remains a threat throughout the world. but in 1918 it killed several million people worldwide, possibly more than the total killed in the 1914-18 WW1.

Covid 19

Covid 19 is an RNA corona virus. Coronaviruses are a large family of viruses that usually cause mild to moderate upper-respiratory tract illnesses, like the common cold common cold (which is also caused by other viruses, predominantly rhinoviruses). However, three new coronaviruses have emerged from animal reservoirs over the past two decades to cause serious and widespread illness and death.

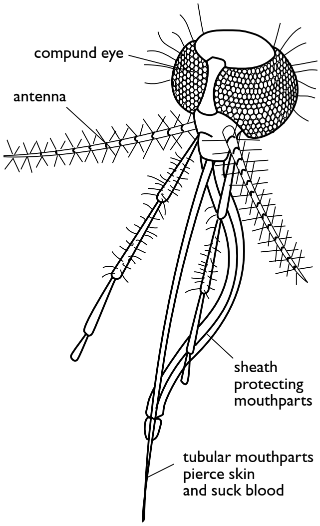
Malaria (Protozoan)

Cause - Malaria is caused by a single celled parasite, *Plasmodium*, which invades the liver cells and red blood cells of humans. There are four species which affect humans, but the most common are *Plasmodium vivax* which usually causes a relatively mild infection, and the virulent *Plasmodium falciparum* which is responsible for most malaria deaths. Although some areas which previously experienced malaria are now free of the disease (such as the United States and parts of Europe) one third of the world's population still lives in malarious regions. The disease is particularly severe in sub-Saharan Africa, where in parts, up to a quarter of children die of the disease, and almost everyone becomes infected several times during their lives. Over 1 million people died of the disease worldwide in 1999.

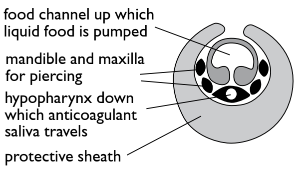
Transmission from one person to another is by the bite of an infected female *Anopheles* mosquito (the vector). As shown in the diagram below, the mosquito is not simply a passive carrier of the disease: the malarial parasite must complete part of its life cycle in humans and part inside the female mosquito.

A malaria infection of a human starts when a female mosquito injects malaria parasites known as **sporozoites** in its anti-coagulant saliva into a human on which it is feeding. These parasites migrate to the liver cells where they reproduce **asexually**, and develop into merozoites which then infect red blood cells. Here they also reproduce asexually, producing huge numbers of additional merozoites which burst out of the red blood cells and cause the characteristic fever and other symptoms of the disease. Some merozoites develop into gametocytes which can be taken up when another female mosquito feeds on the infected person's blood. Once inside the body of the mosquito these gametocytes fuse, the resulting zygotes develop into sporozoites and move into the salivary glands of the female mosquito where they can be injected into another person. The cycle thus begins again.

Diagram to show mosquito mouthparts



Section through mouthparts



Worldwide distribution of malaria

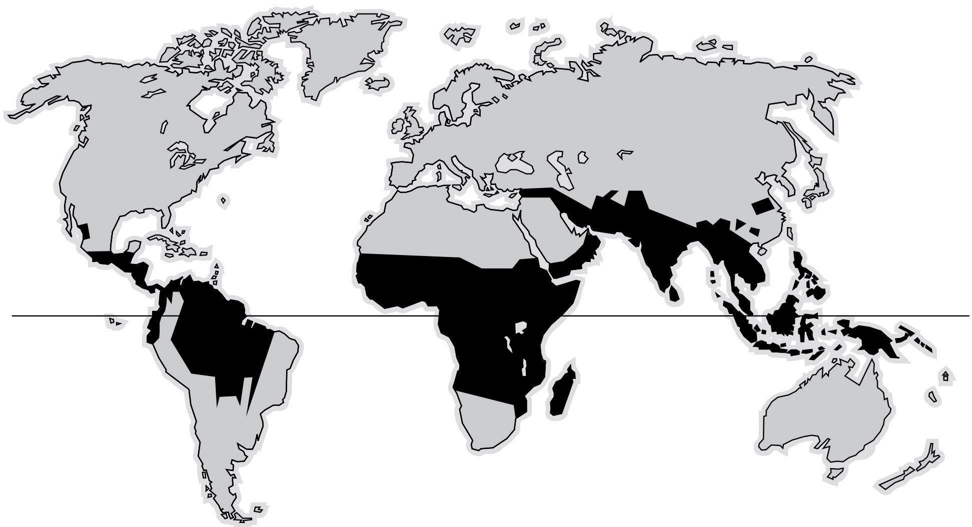
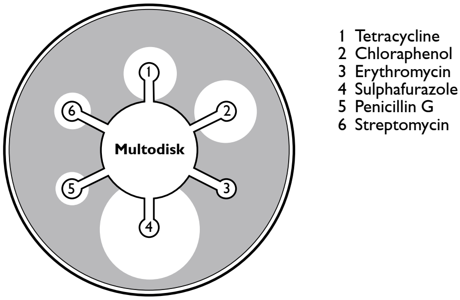


Diagram to show action of specific antibiotics on a bacterial culture



sites normally targeted by antibiotics altered so that the antibiotic cannot interfere with cellular activities. All the antibiotics are therefore less effective, and some completely ineffective at killing the bacteria. Resistance may come in two main ways: through genetic mutations in bacterial DNA, or through introduction of resistance genes via other bacteria or viruses. The very short generation time and massive (asexual) reproductive potential of bacteria allows any beneficial mutations to be passed on very rapidly. (Some bacteria can divide to produce two new bacteria about once every 30 minutes, so that a single bacterium could theoretically result in a population of 2^{47} by the end of a 24 hour period.)

Two important examples of resistant bacteria (sometimes referred to as 'superbugs') are Multiple Resistant *Staphylococcus aureus* (MRSA) which is a common cause of infection in hospitals, and some strains of *Mycobacterium tuberculosis* which causes TB. Whilst random mutations of bacterial DNA which confer antibiotic resistance can occur at any time, the problem is made worse if courses of antibiotics are not completed or if sub-optimal doses are taken. A bacterium may, for example, require two specific mutations to make it fully resistant to an antibiotic. If one mutation offering partial resistance is acquired mid-way through a course of antibiotics the remaining days of treatment may eventually kill this bacterium even though they may do so more slowly than before. However, if the antibiotics are stopped, the bacterium with one mutation for partial resistance may acquire a second mutation. Together with the first this may offer total resistance. When 'multi-drug' treatments (many different types of antibiotic together) are used the chance of a bacterium developing resistance to all types at once is very low. But it is still possible because bacteria may pass genetic material from one to another. This is again more significant if courses are not completed and mixed populations of partially resistant bacteria occur together in a patient.

Antibiotic resistance is already responsible for increasing rates of illness and death from *Staphylococcus aureus*, and T.B. Health professionals are worried that the problem will increase if more bacteria become resistant to antibiotics, allowing common infections to once again become major causes of death across the world. They are calling for a reduction in the unnecessary use of antibiotics. This could include a reduction in the number of prescriptions of the drugs for minor infections in humans, and a reduction in the use of anitibiotics in farming (60% of total antibiotic use) where they are added to feeds as growth promoters and to prevent disease.

◆ CHECKPOINT SUMMARY

- ◆ Antibiotics are substances produced by microorganisms which can kill or inhibit the growth of other organisms (usually bacteria).
- ◆ Bactericidal antibiotics kill other bacteria: bacteriostatic antibiotics inhibit the growth of other bacteria.
- ◆ Antibiotics are produced on a large scale using fermenters. Microorganisms producing them may be genetically engineered.
- ◆ Antibiotics were discovered in 1928 and have been in use since 1940s. Their use has caused an enormous reduction in severe illness and death from bacterial infections.
- ◆ Antibiotics interfere with essential functions of bacterial cells. They may upset synthesis of the bacterial cell wall, or prevent the production of proteins (enzymes) and nucleic acids.
- ◆ Antibiotics may be broad spectrum, killing most types of bacteria or specific to one particular species.
- ◆ Overuse of antibiotics in medicine and in farming industry has led to the emergence of some resistant strains of bacteria.
- ◆ Resistant strains of bacteria are not affected by antibiotics and hence can be very dangerous to humans as the infections they cause are untreatable and spread rapidly.
- ◆ Resistance often arises through random genetic mutations in bacterial DNA.
- ◆ Some strains of TB and Staphlococcus aureus are now resistant to all types of antibiotics. They are said to be 'multi-drug resistant'.

IMMUNOLOGY

(15 pages)

Content

- The immune system
- The role of vaccination in controlling disease

a)	describe the origin, maturation and mode of action of phagocytes and lymphocytes.
b)	explain the meaning of the term immune response.
c)	distinguish between the actions of B lymphocytes and T-lymphocytes in fighting infection.
d)	appreciate the role of memory cells in long term immunity.
e)	relate the molecular structure of antibodies to their functions.
f)	distinguish between active and passive, natural and artificial immunity and explain how vaccination can control disease.
g)	discuss the reasons why vaccination has eradicated smallpox but not measles, TB, malaria or cholera.
h)	outline the role of the immune system in allergies, with reference to asthma and hay fever.

Introduction

Immunology is the name given to the study of the ways in which the immune system allows the body to protect itself from disease-causing organisms (**pathogens**) which have entered the body.

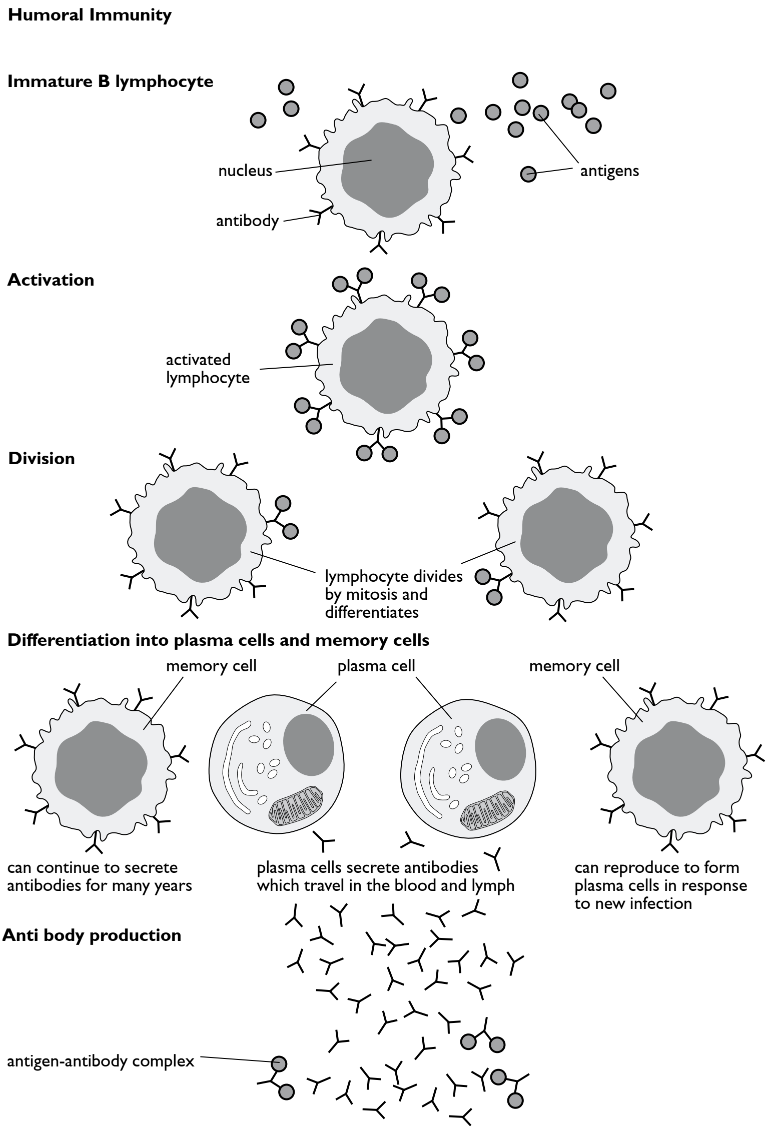
The human body is well adapted to prevent pathogens (mainly bacteria, fungi and viruses) from entering in the first place. There are several ways in which this is achieved:

- The skin forms a protective barrier against most pathogens. If it is cut, blood clotting helps to seal the wound and prevent pathogen entry.
- The mucus membranes of nose and respiratory tract filter the air using small hairs called cilia and trap pathogens in the sticky mucus for destruction by phagocytes.
- Anti-bacterial enzymes in saliva, sweat and tears help to destroy pathogens
- The stomach acid (pH 2) kills most pathogens which may enter via food or water

If however, these mechanisms fail and pathogens do enter the body tissues or blood, an **immune system** is necessary to attack and destroy these pathogens and so prevent serious disease or death. The immune system uses several specialised types of white blood cells, the most important being the phagocytes and the lymphocytes.

- Once the pathogens have been destroyed, the plasma cells eventually die and secretion of antibodies stops. But the memory cells remain in the lymph nodes and the circulation in case of a further infection with the same pathogen.

N.B. The above gives the sequence of events in response to a pathogen. It would be similar for any other foreign cell or foreign antigen.



NON-INFECTIOUS DISEASE

(28pages)

CONTENTS

MALNUTRITION

Strictly speaking malnutrition means 'poor nutrition'. It may include diets where nutrients are deficient (under nutrition) as well as those where nutrients are taken in excess (over nutrition). Both macro and micronutrients can be deficient or present in excess in a diet, and in all cases specific types of malnutrition are characterised by specific symptoms.

Protein energy malnutrition (PEM)

PEM is a term used to describe cases where the diet is severely deficient in both energy sources (fats and carbohydrates) and proteins, leading to specific deficiency symptoms. It is a common disease in many developing countries, particularly those where famines or civil wars have disrupted food production and distribution. PEM is much more common amongst children than adults, since children have smaller reserves in terms of fat stores, as well as higher energy and protein

The BIOLOGICAL BASIS of CANCER

Introduction

In 1999 7.3 million people worldwide died from cancers, of whom 1 million were in high income European countries. In such countries cancers now rank as the second most important cause of death (behind cardiovascular disease), with by far the most common being lung cancer. Other cancers which cause large numbers of deaths are prostate cancer in men, breast cancer in women and cancer of the colon in both sexes. Cancer is often classified as a degenerative disease, so it is not surprising that the vast majority of these deaths occur in older adults. It should be noted that cancer is not a single disease but rather a complex group of several hundred different diseases which share common characteristics. Chief amongst these is the presence of unregulated cell growth leading to the development of tumours.

The main characteristics of tumours and tumour cells.

A tumour is an abnormal mass of tissue, the growth of which is uncoordinated and exceeds that of normal tissue. Tumours are divided into **benign** and **malignant**. The principal difference is that malignant tumours invade their surrounding tissues and spread to distant sites via the blood stream to form secondary tumours, known as **metastases**; while benign tumours usually grow at a slower rate, they never invade organs or blood vessels/lymphatics nor do they metastasize. Such tumours are more easily removed during surgery than malignant ones.

Tumour cells, whether benign or malignant, differ from normal cells both in behaviour and appearance.