11 Immunity

An understanding of the immune system shows how cells and molecules function together to protect the body against infectious diseases and how the body is protected from further infection by the same pathogen. Phagocytosis is a more immediate non-specific part of the immune system, while the actions of lymphocytes provide effective defence against specific pathogens.

11.1 The immune system

The immune system has non-specific and specific responses to pathogens. Auto-immune diseases are the result of failures in the system to distinguish between self and non-self.

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

a) state that phagocytes (macrophages and neutrophils) have their origin in bone marrow and describe their mode of action
b) describe the modes of action of B-lymphocytes and T-lymphocytes
c) describe and explain the significance of the increase in white blood cell count in humans with infectious diseases and leukaemias
d) explain the meaning of the term immune response, making reference to the terms antigen, self and non-self
e) explain the role of memory cells in long-term immunity
f) explain, with reference to myasthenia gravis, that the immune system sometimes fails to distinguish between self and non-self

Responses to infection

Pathogens do not gain easy entry to the body because:

- externally, the keratinised protein of the dead cells of the epidermis are tough and impervious unless broken, cut or deeply scratched
- internal surfaces, in particular the trachea, bronchi and the bronchioles of the breathing apparatus, and the gut are all lined by moist epithelial tissue. These internal barriers are protected by mucus, by the actions of cilia removing the mucus, and some by digestive enzymes or strong acid (as in the stomach).

However, these barriers are sometimes crossed by pathogens. In response, there are internal 'lines of defence'. Firstly, the body responds to localised damage (cuts and abrasions, for example) by **inflammation**. If a blood vessel is ruptured then the blood clotting mechanism is activated. In the blood and tissue fluid, the **immune system** is triggered, which is covered in more detail shortly.

Inflammation

Inflammation is the initial, rapid, localised response the tissues make to damage, whether due to a cut, scratch, bruising, or a deep wound. We are quickly aware that the site of a cut or knock (contusion) has become swollen, warm and painful. Inflammation is triggered by the damaged cells themselves, which release 'alarm' chemicals, including **histamine** and prostaglandins.

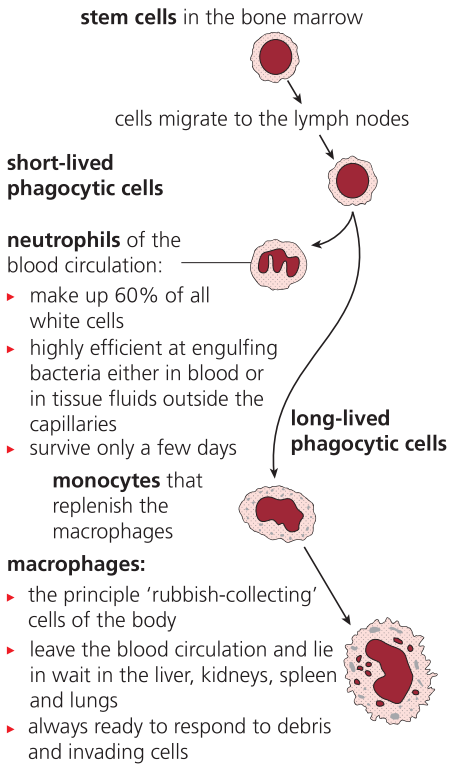


Figure 11.1 The phagocytic cells of the body's defence mechanism

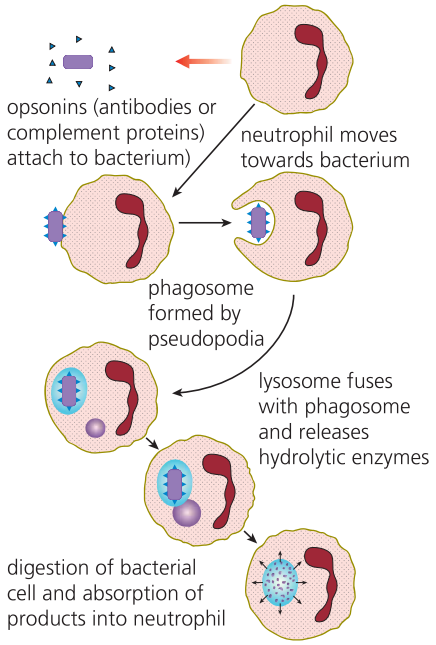


Figure 11.2 Phagocytosis by a white cell – a neutrophil

The initial outcome is that the volume of blood in the damaged area is increased, and **white blood cells** and **plasma** accumulate outside the enlarged capillaries. Ultimately, tissue repair is initiated, also.

The blood circulation plays a complex part in the resistance to infection that will result if microorganisms enter the body. The **increased blood flow removes toxic products** released by invading microorganisms and by damaged cells (Figure 11.3).

The white blood cells that accumulate at the site of tissue damage or invasion of pathogens fall into two functional groupings depending on their roles in the defence against disease.

General **phagocytic white cells** engulf 'foreign' material. These are the **neutrophils** and the **macrophages**. Neutrophils make up 60 per cent of all white blood cells in the blood, but they are short-lived. Macrophages are the principal 'rubbish-collecting cells' found throughout the body tissues (Figure 11.1). These responses to infection destroy any invading pathogen.

Other white blood cells called **lymphocytes**, produce the **antibody reaction** to infection or invasion of foreign matter. This, the immune response, is triggered by and directed towards *specific* pathogens.

You can see some phagocytic white cells and a lymphocyte in the photomicrograph of a blood smear, in Figure 8.2. You will probably have already seen them in a prepared microscope slide of mammalian blood.

All these white blood cells originate by division of stem cells in the bone marrow and in certain cases they mature in the lymph nodes. On average, they spend only about 10 per cent of their short lives in the blood, but all are concerned with the body's protection against infection.

The blood also delivers special proteins (**complement proteins**), which are activated by the presence of infection. Complement proteins enhance the work of white blood cells in overcoming infections. Some trigger the lysis of invading microorganisms, and others, the opsonins, bind to pathogenic bacteria and so increase phagocytosis.

Cells infected with viruses produce proteins called **interferons**. These bind to neighbouring, healthy cells and trigger synthesis of antiviral proteins. Viral replication is halted.

Non-specific responses to infection

The above responses to infection are referred to as **non-specific responses** because they help to destroy any invading pathogen. By contrast, the immune response we discuss next is triggered by and directed towards *specific* pathogens.

The immune response

The immune response is our main defence once invasion of the body by harmful microorganisms or 'foreign' materials has occurred. It is particular leucocytes (white blood cells) called **lymphocytes** that are responsible for the immune response. They make up 20 per cent of the leucocytes circulating in the blood plasma (or found in the tissue fluid – remember, white blood cells also move freely through the walls of blood vessels).

Lymphocytes detect any 'foreign' matter entering from outside our bodies, including macromolecules as well as microorganisms, as different from out body cells and our own proteins. Any molecule the body recognises as a foreign or **'non-self** substance is known as an **antigen**.

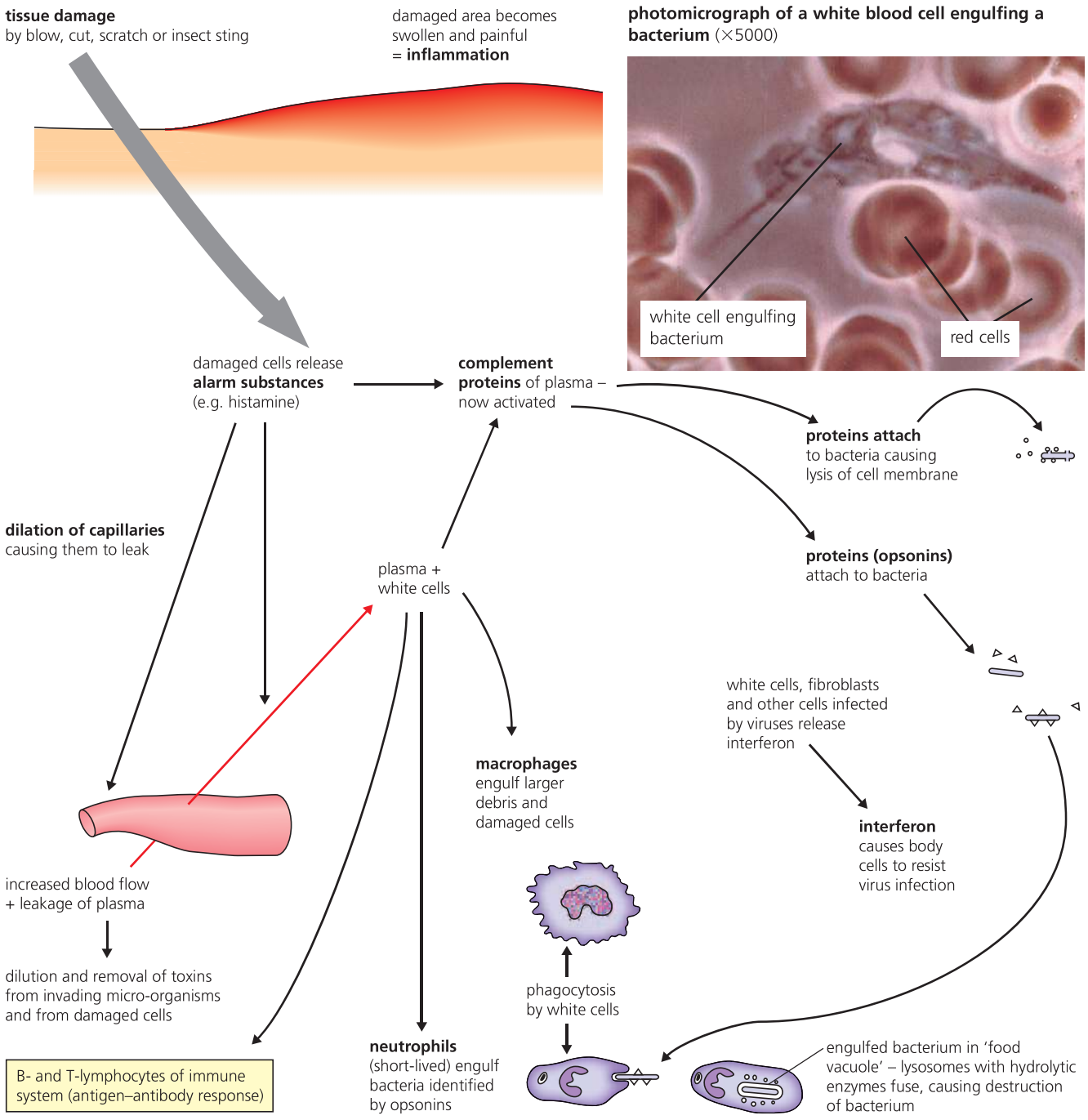


Figure 11.3 Inflammation at a damage site, the processes

What recognition of 'self' entails

All cells are identified by specific molecules – markers, if you like – that are lodged in the outermost surface of the cell. In fact, these molecules include the highly variable **glycoproteins** on the cell surface membrane. Remember, glycoproteins occur attached to proteins there. Look at Figure 4.3, page 76 and remind yourself of the 'fluid mosaic' structure of this membrane.

The glycoproteins that identify cells are also known as the **major histocompatibility complex** antigens – but we can refer to the major histocompatibility complex as **MHC** from now on. There are genes on one of our chromosomes (chromosome 6, actually) that code for MHC antigens. Each individual organism's MHC is genetically determined – it is a feature we inherit. As with all inherited characteristics that are products of sexual reproduction, variation occurs. So each of us

has distinctive MHC antigens present on the cell surface membrane of most of our body cells. Unless you have an identical twin, your MHC antigens are unique.

Lymphocytes of our immune system have **antigen receptors** that recognise our own MHC antigens and can tell them apart from any 'foreign' antigens detected in the body. After all, it is critically important that our own cells are not attacked by our immune system.

Self: the products of the body's own genotype, which contain proteins (normally – some carbohydrates and other macromolecules can act as antigens) that do not trigger an immune response in the body's own immune system. Inside the body that produced them, self proteins do not act as antigens (and so do not stimulate an immune response) but, if introduced into another body, they become non-self.

Question

1 Explain the significance of the role of the thymus gland in destroying T-lymphocytes that would otherwise react to body proteins.

Lymphocytes and the antigen–antibody reaction

We have two distinct types of lymphocytes (Figure 11.4), based on the ways they function. Both cell types originate in the bone marrow where they are formed from **stem cells**. As they mature they undergo different development processes in preparation for their distinctive roles.

- **B-lymphocytes** secrete antibodies.
- **T-lymphocytes**, some of which assist B-lymphocytes, and others which may attack infected cells.

How do these distinctive roles develop?

T-cells leave the bone marrow early during development and they undergo differentiation in the **thymus gland**. Here they mature. The thymus gland is found in the chest, just below the breast bone (sternum). It is an active and enlarged gland from birth to puberty. The gland then shrinks in size, its task completed.

It is whilst T-lymphocytes are present in the thymus gland that the body selects out all the lymphocytes that would otherwise react to the body's own cells. The surviving T-lymphocytes then circulate in the plasma and are stored in lymph nodes.

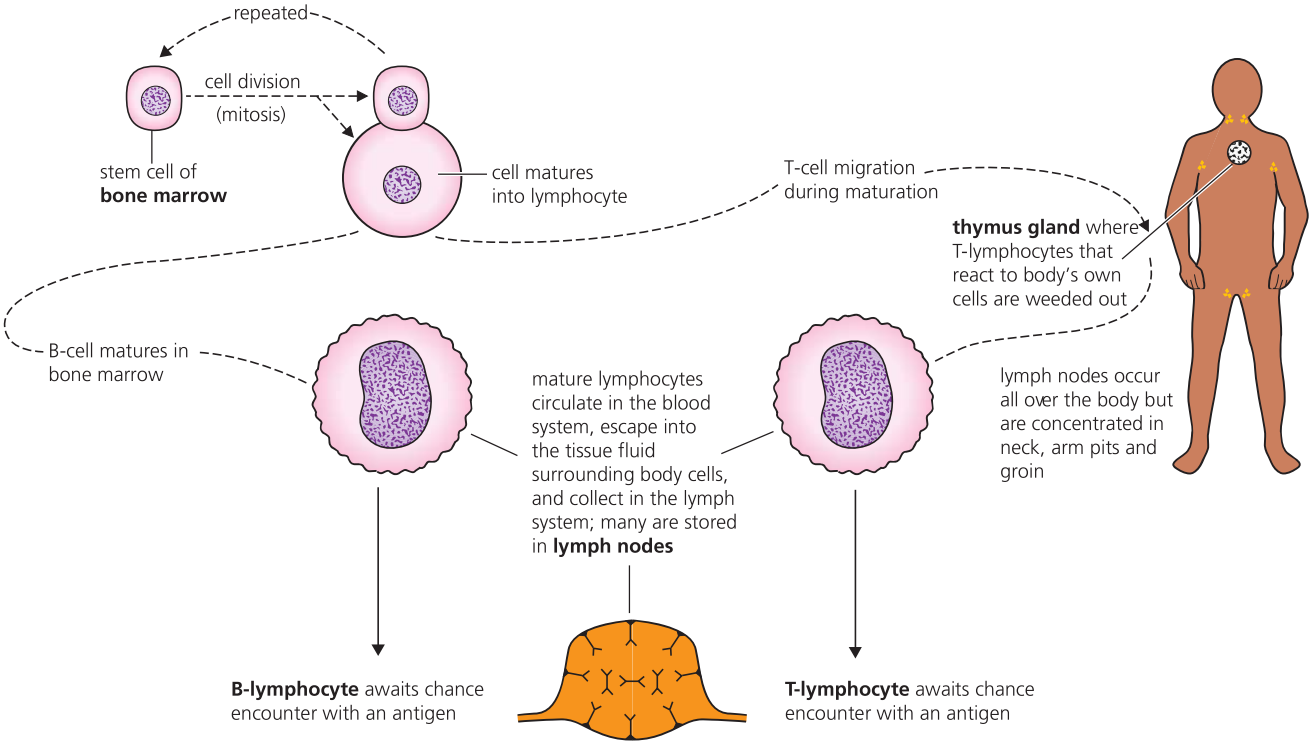


Figure 11.4 T- and B-lymphocytes

Antibody: A glycoprotein secreted by a plasma cell. An antibody binds to the specific antigen that triggered the immune response, leading to destruction of the antigen (and any pathogen or other cell to which the antigen is attached). Antibodies have regions that vary in shape (variable regions) that are complementary to the shape of the antigen. Some antibodies are called antitoxins and prevent the activity of toxins.

The T-lymphocytes do not secrete antibodies. The role of T-lymphocytes is **cell-mediated immunity** – meaning their role in the immune response does not directly involve antibodies, although some have a role in the activation of B-lymphocytes, as we shall see shortly.

B-lymphocytes complete their maturation in the bone marrow, prior to circulating in the blood and being stored in lymph nodes. The role of the majority of B-lymphocytes, after recognition and binding to a specific antigen, is to proliferate into cells (called **plasma cells**) that secrete antibodies into the blood system. This is known as **humoral immunity**.

Now whilst both T- and B-cells have molecules on the outer surface of their cell surface membrane that enable them to recognise antigens, each T- and B-lymphocyte has **only one type** of surface receptor. Consequently, **each lymphocyte can recognise only one type of antigen**.

How do B- and T-lymphocytes respond to an infection?

When an infection occurs the leucocyte population increases enormously and many collect at the site of the invasion. The complex response to infection is begun. The special roles of T- and B-lymphocytes in this response are given below.

Refer to Figure 11.6 as you follow these steps.

1 On the arrival of a specific antigen in the body, **B-lymphocytes** with surface receptors (antibodies) that recognise that particular antigen, **bind** to it.
Antibodies initially occur attached to the cell surface membrane of B-lymphocytes but later are also mass produced and secreted by cells derived from the B-lymphocyte, but only after that B-lymphocyte has undergone an **activation step** (step 4, below).

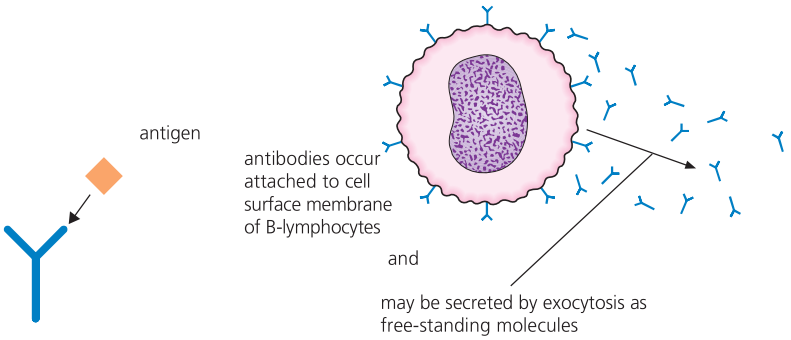


Figure 11.5 The structure of an antibody

2 On binding to the B-lymphocyte, the antigen is taken into the cytoplasm by endocytosis, before being expressed on the cell surface membrane of the B-lymphocyte.

3 Meanwhile, **T-lymphocytes** can only respond to antigens when presented on the surface of other cells. Phagocytic cells of the body, including **macrophages**, engulf antigens they encounter. This may occur in the plasma, lymph or tissue fluid. Once these antigens are taken up, the macrophage presents them externally by attaching the antigen to their surface membrane proteins, **MHC** antigens. This is called **antigen presentation** by a macrophage.

4 T-cells come in contact with these macrophages and briefly bind to them. The T-lymphocyte is immediately activated. They become **activated helper T-lymphocytes**.

5 Activated helper T-lymphocytes now bind to B-lymphocytes with the same antigen expressed on their cell surface membrane (step 2 above). The B-lymphocyte is activated by the binding of this chemical. It is now an **activated B-lymphocyte**.

6 Activated B-lymphocytes immediately divide very rapidly by mitosis forming a clone of cells called **plasma cells**. Plasma cells are packed with rough endoplasmic reticulum (RER). It is in these organelles that the antibody is mass produced. The antibody is then exported from the plasma cell by exocytosis. The antibodies are normally produced in such numbers that the antigen is overcome. The production of an activated B-lymphocyte, its rapid cell division to produce a clone of plasma cells and the resulting production of antibodies that react with the antigen is called **clonal selection**. Sometimes several different antibodies react with the one antigen – this is **polyclonal selection**.

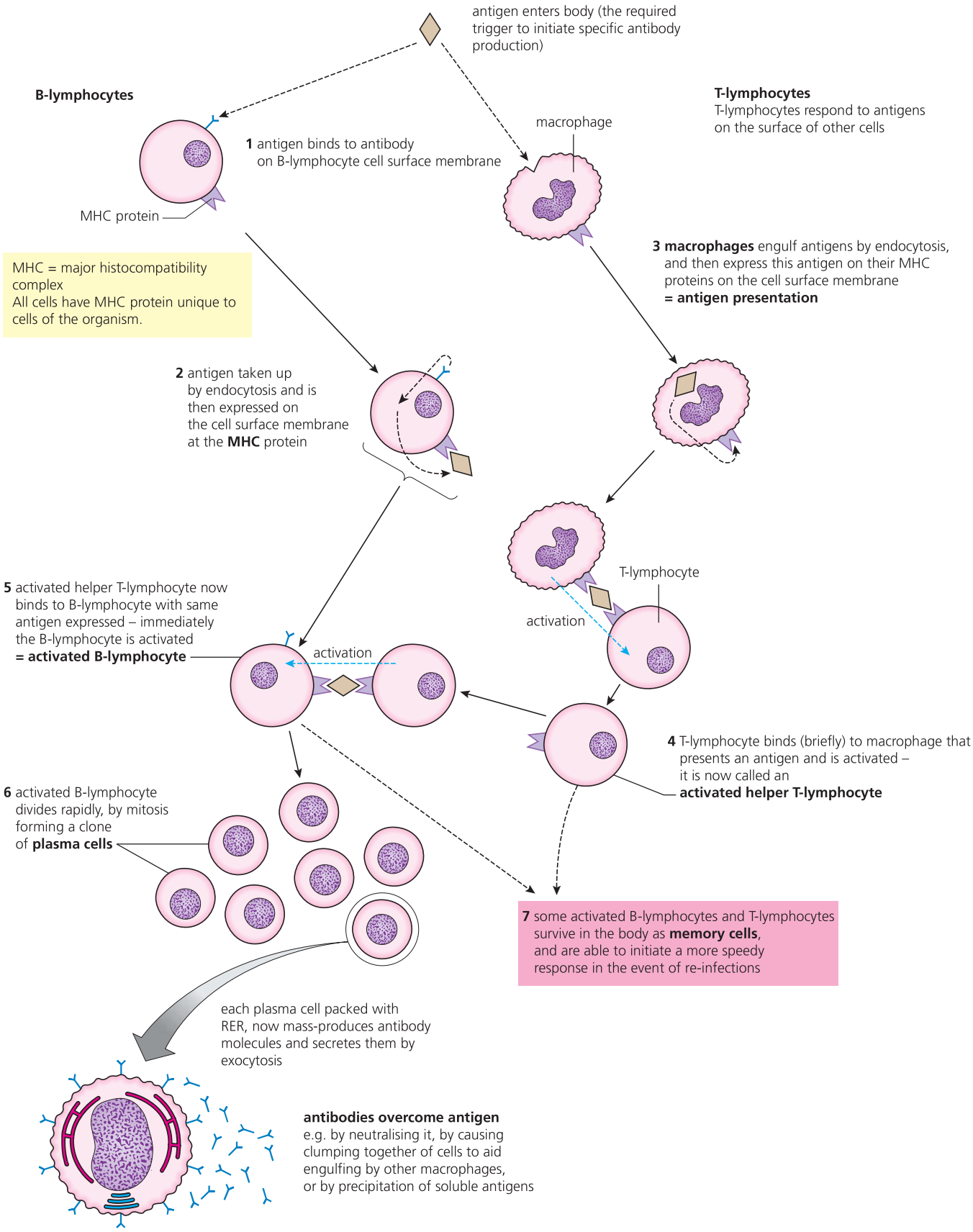


Figure 11.6 The stages in antibody production

Natural immunity: immunity that is acquired by the individual as a natural part of their life. This includes natural passive immunity following transfer of maternal antibodies into a fetus through the placenta and into a newborn infant in the first milk (colostrum). It also includes the natural active immunity that follows natural infection by a pathogen involving the production of memory cells (for example, natural infection with chicken pox, giving long-term protection against this virus).

7 After these antibodies have tackled the foreign matter and the disease threat is overcome, the antibodies disappear from the blood and tissue fluid. So too do the bulk of the specific B-lymphocytes and T-lymphocytes responsible for their formation.
However, certain of these specifically activated B- and T-lymphocytes are retained in the body as **memory cells**. These are long-lived cells, in contrast to plasma cells and activated B-lymphocytes. Memory cells make possible an early and effective response in the event of a re-infection of the body by the same antigen (Figure 11.7). This is the basis of natural immunity.

Memory cells are retained in lymph nodes. They allow a quick and specific response if the same antigen reappears.

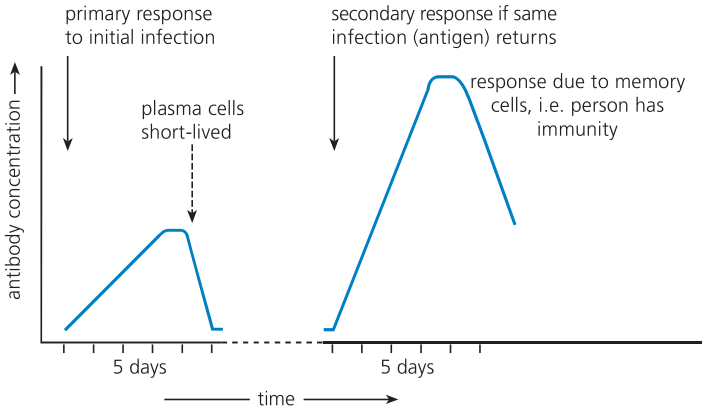


Figure 11.7 The profile of antibody production on infection and re-infection

Questions

2 Identify where antigens and antibodies may be found in the body.
3 Remind yourself of the appearance of the types of white blood cells observed in a blood smear preparation. See for example, the photomicrograph in Figure 8.2 (page 153). Compare this image with a prepared slide of a human blood smear so that you are familiar with the appearance of phagocytic white blood cells and lymphocytes. Make a fully annotated drawing of representative white blood cells that makes clear the differences between them.

It is now helpful to summarise the complex roles of B- and T-lymphocytes in the immune system (Figure 11.8).

The significance of white blood cell counts

A normal white blood cell count is between 4500 to 10000 cells per μl, but during active infections in the body the number rises and may be considerably higher. Given the roles of white blood cells when in the presence of pathogens within the body, this relationship is of no surprise. Another cause of raised white blood cell count is leukaemia – a cancer of the bone marrow cells. The stem cells from which white blood cells are normally formed proliferate but fail to differentiate. Here the numbers can be very high indeed, but with a variety of abnormal cells present.

Myasthenia gravis – a failure to distinguish 'self' from 'non-self'

Myasthenia gravis is an usual auto-immune disorder in which specific antibodies attack and destroy the acetylcholine receptors at the post-synaptic junctions, thereby inhibiting the effect of the neurotransmitter acetylcholine (page 319). This disease is one of the less common auto-immune disorders, affecting about two people in every 10000 of the population. It causes muscle weakness. The effects of the disease may be localised in the body, involving just the eye muscles for example. Alternatively, many muscle systems may be affected, leaving the sufferer susceptible to general fatigue. In the presence of this condition, muscles weaken during periods of activity but improve with resting. Some patients with myasthenia gravis are found to have a tumour of the thymus gland. These are often benign, but the gland is then removed as a precaution, and typically symptoms of myasthenia gravis improve.

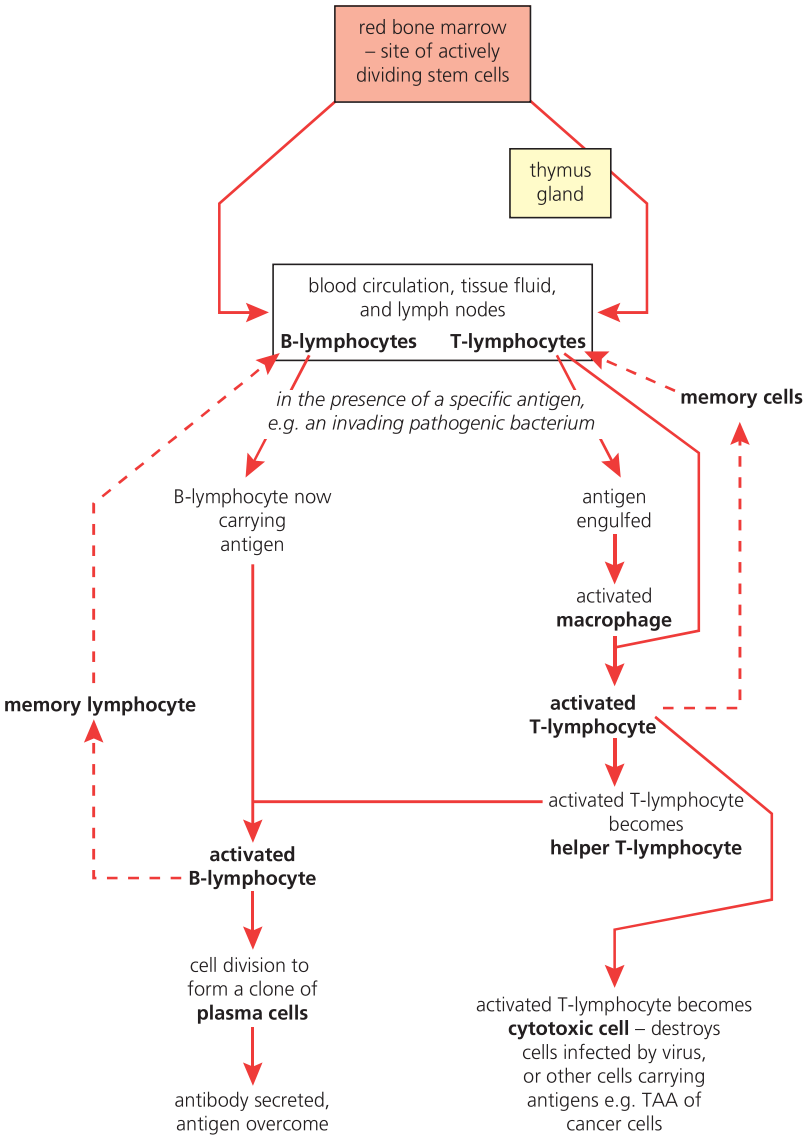


Figure 11.8 The roles of B- and T-lymphocytes in the immune system – a summary

Immune response: the complex series of reactions of the body to an antigen, such as a molecule on the outside of a bacterium, virus, parasite, allergen or tumour cell.

- The immune response begins with an innate first response, carried out by phagocytic white blood cells, which can destroy and engulf (by phagocytosis/endocytosis) many different foreign organisms.
- At the same time, the primary phase of the adaptive immune system response begins, in which specific clones of B-lymphocytes and T-lymphocytes divide and differentiate to form antibody-secreting plasma cells (from B-lymphocytes) and T helper cells and T killer cells (from T-lymphocytes) that are specific to the antigen, contributing to its destruction or preventing its activity.
- This leads into the secondary phase of the adaptive immune system response, where memory cells retain the capability to secrete antibodies or act as T helper or T killer cells as soon as the specific antigen is detected again.

11.2 Antibodies and vaccination

Active and passive immunisations are effective ways to treat and prevent infectious diseases. Smallpox has been eradicated; other diseases may soon follow, but vaccine development has proved more difficult for diseases such as malaria.

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

a) relate the molecular structure of antibodies to their functions
b) outline the hybridoma method for the production of monoclonal antibodies
c) outline the use of monoclonal antibodies in the diagnosis of disease and in the treatment of disease
d) distinguish between active and passive, natural and artificial immunity and explain how vaccination can control disease
e) discuss the reasons why vaccination programmes have eradicated smallpox, but not measles, tuberculosis (TB), malaria or cholera

The antibody molecules – structure in relation to function

Antibodies are proteins called **immunoglobulins**. Each antibody consists of four polypeptide chains held together by disulfide bridges (–S–S–), forming a molecule in the shape of a **Y**. The arrangement of amino acids in the polypeptides that form the tips of the arms of the Ys in this molecule are unique to that antibody. It is these regions that hold the highly specific **binding site** for the antigen. Antibodies initially occur attached to the cell surface membrane of B-lymphocytes, but later are also mass-produced and secreted by cells derived from the B-lymphocyte (Figure 11.9), but only after that B-lymphocyte has undergone an **activation step**.

The structure of the antibody molecule demonstrates the four levels of protein structure, discussed earlier (page 45):

The **primary structure** of a protein is the long chain of amino acids in its molecule – amino acid residues joined by peptide linkages. You can see that there are four polypeptide chains that make up each antibody, two described as 'heavy chains' and two as 'light chains'. The polypeptides differ in the variety, number and order of their constituent amino acids.

The **secondary structure** of a protein develops when parts of the polypeptide chain take up a particular shape, immediately after formation at the ribosome. Parts of the chain become folded or twisted, or both, in various ways. The most common shapes are formed either by coiling to produce an **α-helix** or folding into **β-sheets**, and both shapes are permanent, held in place by hydrogen bonds.

The **tertiary structure** of a protein is the precise, compact structure, unique to that protein that arises when the molecule is further folded and held in a particular complex shape. This shape is made permanent by four different types of bonding, established between adjacent parts of the chain (Figure 2.22, page 47).

The **quaternary structure** of a protein arises when two or more proteins are bound together, forming a complex, biologically active molecule. In an antibody, four polypeptide chains are combined, held together in a characteristic shape by sulfide bridges (Figure 11.9).

Monoclonal antibodies

We have seen that white blood cells in the blood provide our main defence against the invasion of the body by harmful microorganisms. Special cells among the white blood cells, called **lymphocytes**, are responsible for the immune response. Among these it is the **B-lymphocytes** that secrete antibodies. Antibodies are very effective in the destruction of antigens within the body (Figure 11.7). **Monoclonal antibodies** are produced by a single clone of B-lymphocytes. They are identical antibodies effective against a single, specific antigen.

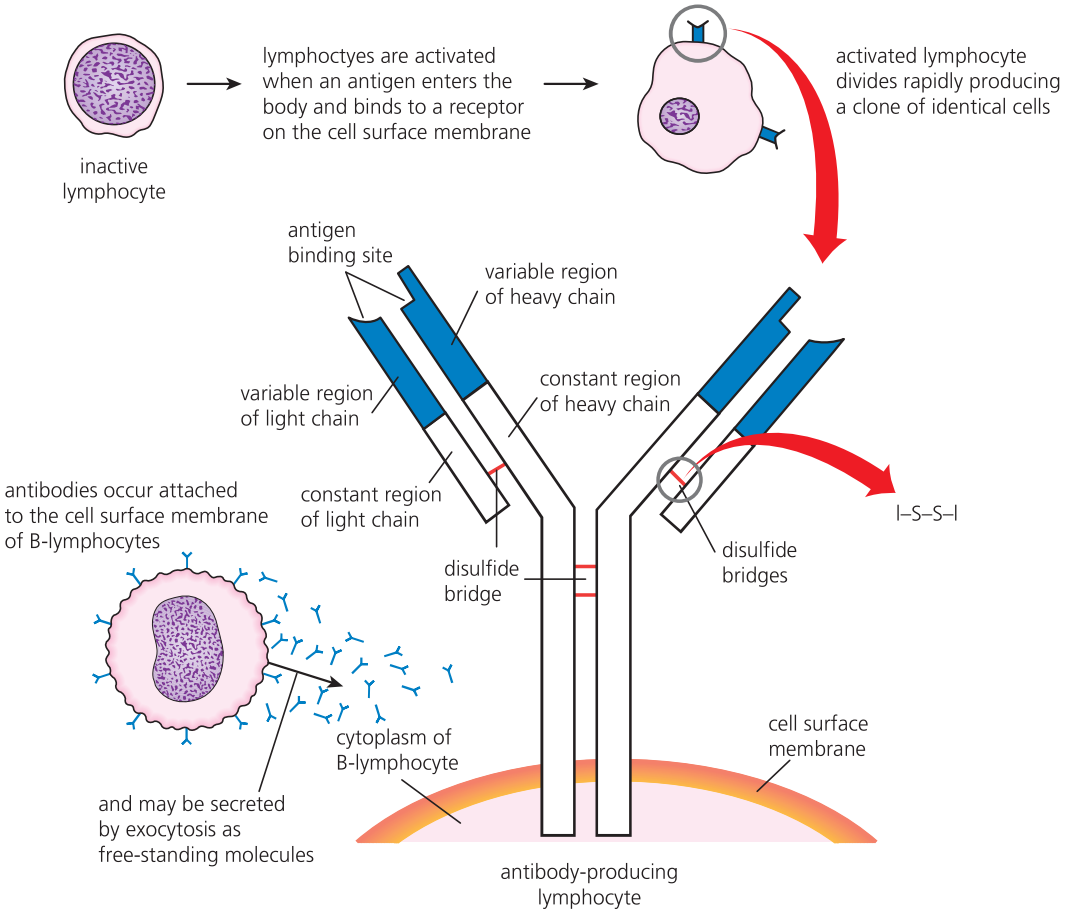


Figure 11.9 The antibody – a quaternary protein

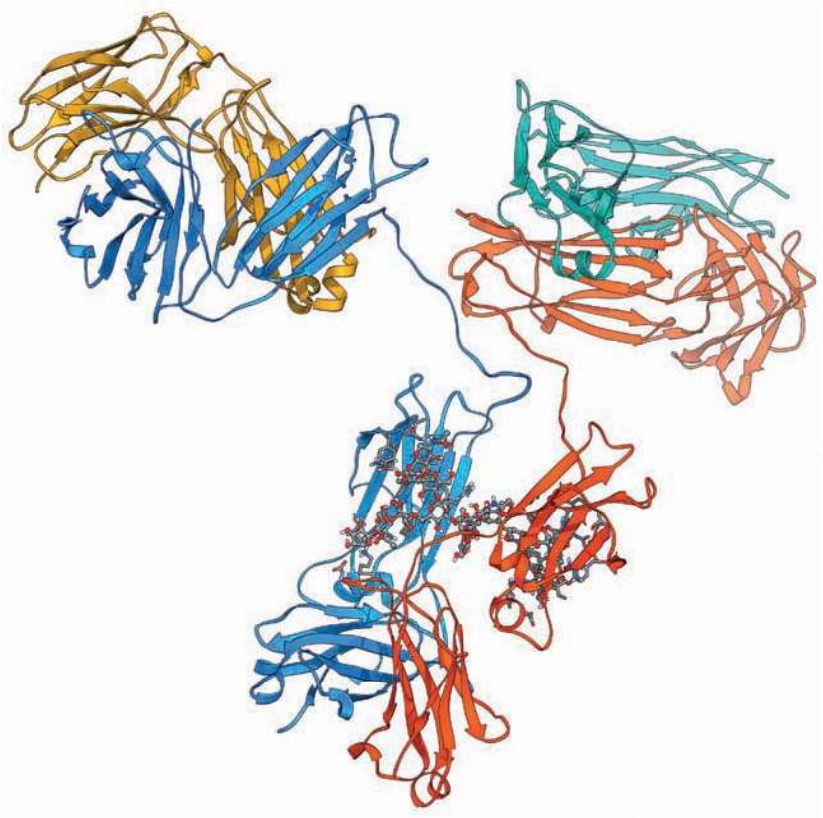


Figure 11.10 Computer-generated image of an antibody molecule

The production of monoclonal antibodies

Antibodies have great potential in modern medicine, if they can be made available. The problem has been that B-lymphocytes are short-lived. This issue of the normally brief existence of a B-lymphocyte is overcome by fusing the specific lymphocyte with a **cancer cell** (a malignant myeloma of a B-lymphocyte) which, unlike non-cancerous body cells, goes on dividing indefinitely. The fused cells, called **hybridoma** cells, are separated and each hybridoma is cultured individually. Each cell divides to form a clone of cells which persists and which conveniently goes on secreting the antibody in significant quantities. The outcome is a single antibody that is stable and that can be used over a period of time. How a specific monoclonal antibody is made is illustrated in Figure 11.11.

The use of monoclonal antibodies in medicine is already established and is under further development.

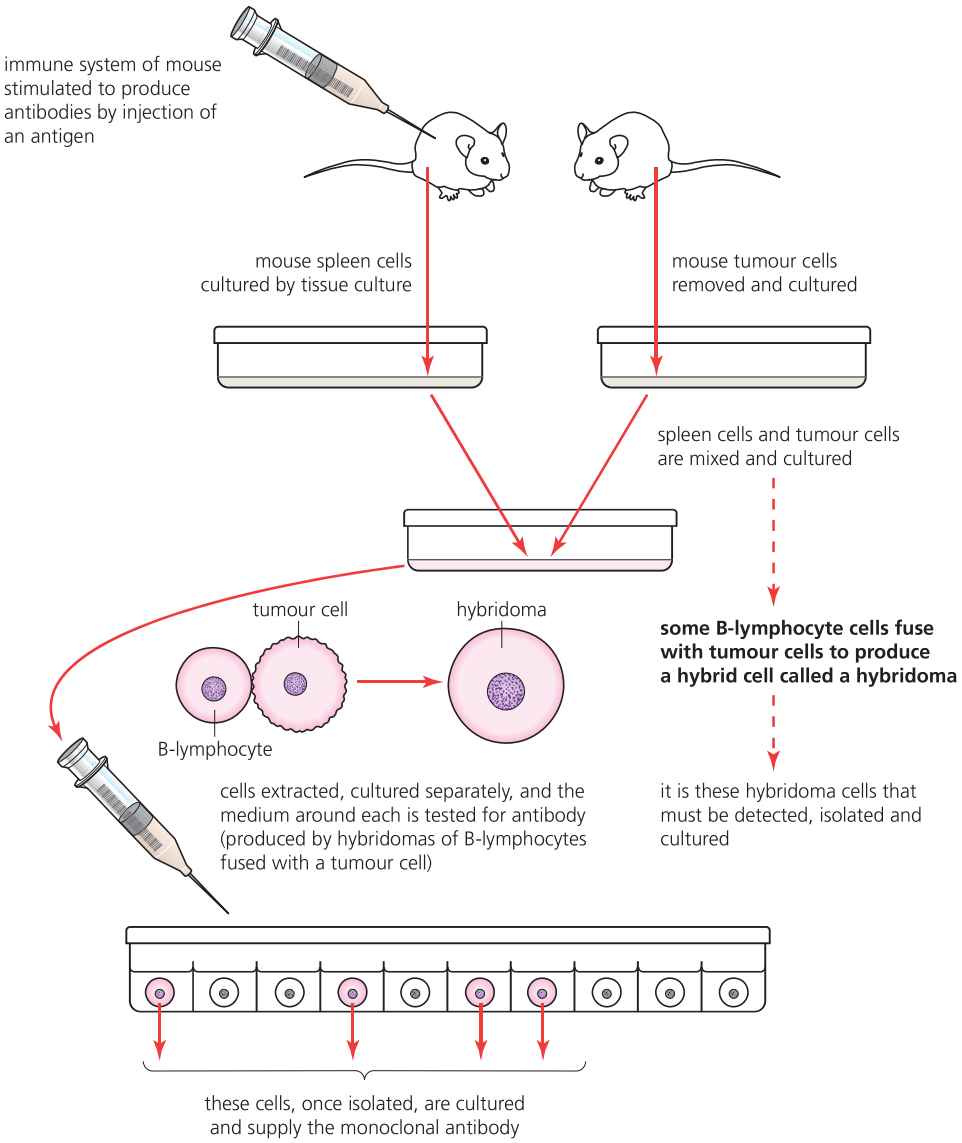


Figure 11.11 The formation of monoclonal antibodies

Question

4 Study the production of monoclonal antibodies illustrated in Figure 11.11. Make a concise list of the sequence of steps in their production.

The use of monoclonal antibodies in the treatment of disease

It is known that cancer cells carry specific **tumour-associated antigens (TAA)** on their cell surface membrane. Monoclonal antibodies to TAA have been produced. Then, drugs to kills cells or inhibitors to block key tumour proteins have been attached. The monoclonal antibodies specifically target and kill the cancer cells. The advantage is that whereas many drugs and treatments effective against cancer are also harmful to other, healthy cells, the specificity of antibodies avoids this problem. These developments are sometimes referred to as 'magic bullets'.

Monoclonal antibodies have already been developed to treat certain cancers, as described in Table 11.1. Now, monoclonal antibodies are under investigation in clinical trials for nearly every type of cancer. Perhaps this is the most important way that monoclonal antibodies are currently being used in the treatment of disease.

Table 11.1 How monoclonal antibodies are used to treat cancers

Making cancer cells 'visible' to the immune system	Cancer cells are 'self' cells – they have not invaded the body from outside. The immune system only targets non-self cells. Monoclonal antibodies that recognise and attach to cell surface membrane proteins that have resulted from the specific cancer condition present have been produced. Once introduced into the body they attach, making the cell visible to the immune system and therefore vulnerable to destruction by it.
Blocking growth signals of the cell surface membrane of cancer cells	Monoclonal antibodies have been produced that attach to and block the growth signal molecules on the cell surface membrane of cancer cells. Unblocked, these growth factors signal the cancer cell to grow. Cancer cells produce additional growth factors, enhancing their growth rate. Such 'blocking' monoclonal antibodies have been produced to treat colon cancer, for example.
Stopping the formation of new blood vessels	The growth signals manufactured by cancer cells which stimulate the growth of fresh blood vessels to supply the developing malignant tumour can be blocked by specific monoclonal antibodies. One such is in use in the treatment of breast cancer.
Delivering radiation to cancer cells	Radiation sufficient to destroy a cancer cell can be delivered specifically to the cells of a malignant tumour by combining radioactive particles with monoclonal antibodies that attach exclusively to cancer cells. These monoclonal antibodies deliver a low level of radiation over a long period of time, without damage to the surrounding cells. Such monoclonal antibodies are in use against non-Hodgkin's lymphoma.

Another application of monoclonal antibodies in the treatment of disease is as 'passive vaccines'. A monoclonal antibody specific to a particular pathogen may be produced and injected into a patient's blood circulation to good effect.

The use of monoclonal antibodies for pregnancy testing

Another application of monoclonal antibodies is in pregnancy testing. A pregnant woman has a significant concentration of **HCG hormone** in her urine whereas a non-pregnant woman has a negligible amount. Monoclonal antibodies to HCG have been engineered which also have coloured granules attached. In a simple test kit, the appearance of a coloured strip in one compartment provides immediate, visual confirmation of pregnancy. How this works is illustrated in Figure 11.12.

Because all the monoclonal antibodies produced by a clone of a B-lymphocyte are identical they can be used to identify other specific macromolecules, too.

Other examples of the use of monoclonal antibodies in diagnosis

- Since a B-lymphocyte recognises a specific antigen, monoclonal antibodies can be used to distinguish between different strains of a disease-causing microorganism
- Detection of HIV in a patient's blood sample
- Blood typing before a blood transfusion, for example to determine A, B, AB or O and Rhesus negative or Rhesus positive groupings
- Tissue typing before a transplant operation
- Identification of the particular type of leukaemia (a cancer) that a patient has contracted to determine the most appropriate treatment
- Location of tumours.

Extension

An issue to note is that, because the original monoclonal antibodies were developed from mice cells (Figure 11.11), a patient may develop an adverse reaction to an antibody. This is because the monoclonal antibody is itself a foreign protein to the patient's immune system. Genetically engineered antibodies that are compatible with the human immune system are sought to avoid the triggering of the immune response.

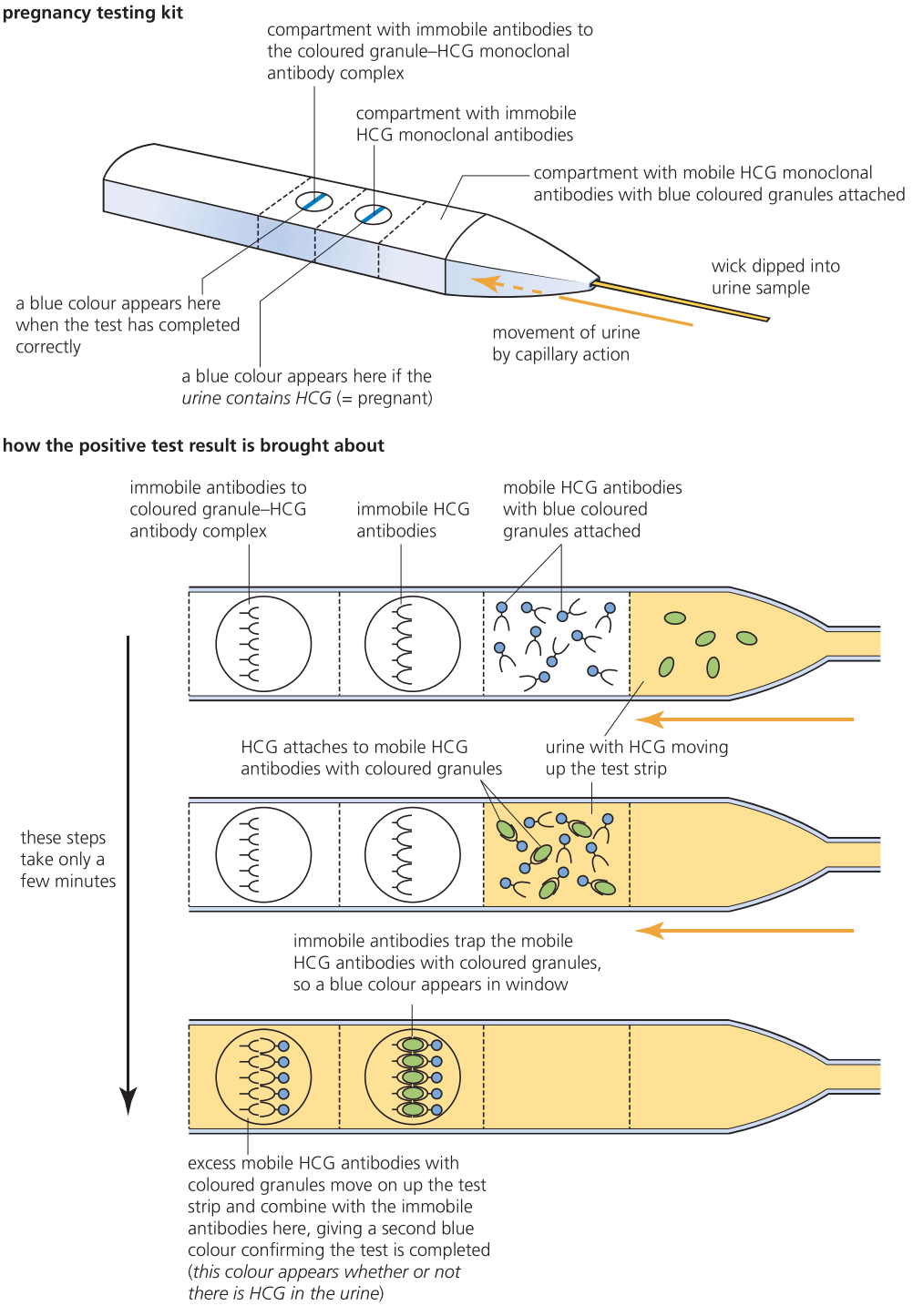


Figure 11.12 Detecting pregnancy using monoclonal antibodies

Vaccination: the medical giving of material containing antigens, but with reduced or no ability to be pathogens, in order to give long-term active immunity as a result of the production of memory cells.

Artificial immunity: immunity that is acquired by a person as a result of medical intervention. This includes artificial passive immunity following injection of antibodies (for example monoclonal antibodies, to treat acute life-threatening infections, such as tetanus or rabies). It also includes the long-term immunity that results from the injection of antigens (such as those attached to killed or weakened pathogens) where memory cells are made.

Questions

5 **a** Identify the steps to plasma cell formation that the existence of memory cells avoids in the event of re-infection.
b Why is it quicker to respond on re-infection in these cases?

6 State what we mean by immunity.

Vaccination

Vaccination is the deliberate administration of antigens that have been made harmless, after they are obtained from disease-causing organisms, in order to confer immunity in future. The practice of vaccination has made important contributions to public health (see TB, page 200; measles, page 208; smallpox, page 210).

Vaccines are administered either by injection or by mouth. They cause the body's immune system to briefly make antibodies against the disease (*without becoming infected*), and then **to retain the appropriate memory cells**. Active artificial immunity is established in this way (Table 11.2). The profile of the body's response in terms of antibody production, if later it is exposed to the antigen again, is exactly the same as if the immunity was acquired after the body overcame an earlier infection.

Vaccines are manufactured from dead or attenuated (weakened) bacteria, or from inactivated viruses, or purified polysaccharides from bacterial walls, or toxoids, or even recombinant DNA produced by genetic engineering.

In communities and countries where vaccines are widely available and have been taken up by 85–90 per cent of the relevant population, vaccination has reduced some previously common and dangerous diseases to very uncommon occurrences. As a result, in these places, the public there has sometimes become casual about the threat such diseases still represent.

A summary of the types of immunity

Our immune system may provide protection to the body from the worst effects of many of the pathogens that may invade. This immunity may be acquired **actively**, as when our body responds to invasion by a pathogen, or **passively**, as when ready-made antibodies are injected into our body. Also, immunity may be acquired **naturally**, as when our bodies respond to a natural pathogen invasion, or **artificially**, as follows vaccination.

In Table 11.2 the differences between active and passive immunity, and natural and artificial immunity are identified and illustrated.

Table 11.2 Types of immunity that humans display

Types of immunity	Natural	Artificial	*. . . and their longevity*
Active immunity • Results from exposure to an antigen. During the subsequent immune response, antibodies are produced by plasma cells. • There is a delay before the immune response is complete. (Immunity takes some days to build up.)	e.g.: Immunity that follows natural infection by a pathogen involving the production of memory cells (for example, natural infection with chicken pox, giving long-term protection from this virus).	e.g.: Immunity that results from the injection of antigens (such as those attached to killed or weakened pathogens) where memory cells are made (for example, after vaccination).	Active immunity persists for a prolonged period, and possibly throughout life, after it has been acquired because the body makes memory cells.
Passive immunity • Involves 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. • Gives instant immunity.	e.g.: Immunity following transfer of maternal antibodies into a fetus through the placenta, and into a newborn infant in the first milk (colostrum).	e.g.: Immunity following injection of antibodies (for example, monoclonal antibodies, to treat acute life-threatening infections, such as rabies).	Passive immunity fades with time because the recipient does not acquire memory cells and so is unable to make the antibodies in future.

Question

7 **a** By means of a table such as Table 11.2, show the ways that immunity may arise according to whether it is actively or passively obtained, and by natural or artificial means. Place these terms in your table:

polio vaccine

measles infection

antibodies received via the placenta

monoclonal antibodies to treat tetanus

b Underline those terms in which memory cells are *not* formed (and therefore the effects are short term).

Issues with vaccines and vaccination

The many uses that the body has for proteins that it builds from the pool of amino acids are identified in Figure 2.26 (page 51). The antibodies (immunoglobulins) secreted by B-lymphocytes are only one of these demands. So, if our diet is deficient in proteins, and especially if we are generally malnourished, our amino acid pool is diminished and the body has difficulty in meeting all of these demands. So underfed and starving people typically have a defective immune system and they are at risk of contracting infectious diseases and of passing them on to others.

Nevertheless, *one* infectious disease, once common among people throughout the world has been eradicated. This is smallpox. This is partly for reasons that relate to the virus and the vaccine produced, including:

- the virus was stable – it did not mutate or change its surface antigens. (Minor changes in antigens (**antigenic shift**) will cause memory cells to fail to recognise a pathogen.)
- transmission was by direct contact only, so the people possibly infected by an isolated outbreak were limited and were easily identified. (The vaccine could be quickly given to all contacts to achieve **herd immunity**. In this way, transmission within any community is interrupted.)
- the vaccine was freeze dried and stocks could be distributed and held at high temperatures (as in the tropics) and remain effective.
- the made-up vaccine could be administered with a reusable (stainless steel) needle.

Other reasons why smallpox has been eradicated relate to the impact of the disease on patients and their contacts and to the ways the eradication campaign was administered and delivered, for example. They are identified earlier in the topic, on page 210.

Other diseases we have discussed in this topic have not been eradicated. The reasons are due to particular features of these diseases and the pathogens or factors that cause them. These have been identified and discussed earlier in this topic. They are summarised in Table 11.3.

Table 11.3 Why vaccination has not eradicated measles, TB, malaria, sickle cell anaemia or cholera

Disease	Impact (or other otherwise) of vaccination – and why
Cholera – vaccines exist	The cholera-causing bacterium and its toxin are active in the intestine – a region of the body where the vaccine administered by injection cannot operate. The oral vaccine that has been developed offers protection from some but not all strains of the cholera bacterium. (Standard hygiene precautions – clean water and efficient sewage disposal – if they can be achieved, are the most effective protection. Cholera is endemic only in countries where these conditions cannot be maintained.)
Malaria – no vaccine exists as yet	No effective vaccine has been produced as yet. The difficulties are: • the pathogen is a protoctist, with many more genes than bacteria and viruses. The alleles of these genes result in vast numbers of antigens being present on the surface of the pathogen – including different antigens on the separate stages in the life cycle. • the pathogen spends a very short time in the blood plasma, before 'hiding' from the immune system in liver or red blood cells in the human host. This **antigenic concealment** leaves little time for an effective immune response.
Sickle cell anaemia	This is a genetic disease expressed in people who are homozygous for the sickle cell haemoglobin allele (Hb^S). Vaccines and the immune response cannot effect changes in the genetic constitution (the genome).
TB – a vaccine exists	The effectiveness of the vaccine against tuberculosis (BCG vaccine) varies according to geography – 80% in the UK, 14% in the USA and in some places it shows no protective effect. (Strains of the pathogenic bacterium resistant to anti-TB drugs have emerged in all countries.)
Measles – a vaccine exits	The disease persists because the virus is highly infectious and the vaccine is about 95% effective, so a whole infant population needs to be treated within 8 months of birth in order to prevent transmission of the virus. Some children require one or more 'booster' injections before full immunity is achieved, too. Many countries now have about 80% of the population vaccinated but in African countries it is currently less than 50% that receive the vaccine. For most communities, **herd immunity** has not been established. In less-developed countries with a high birth rate the living conditions of many people are crowded – ideal conditions for transmission of the virus. Also, many victims are malnourished and the diets of infants are low in protein (and deficient in vitamin A). Any natural resistance to infection by the measles virus is minimal.

Summary

- Defence against disease that enters when the body is wounded and then invaded by a pathogen is provided by **phagocytic white blood cells**. These are able to engulf and destroy foreign matter.
- The **immune system** is provided by **B- and T-lymphocytes** which, when sensitised by foreign material (**antigens**), respond in complex ways to overcome the invasion, including by the production of specific **antibodies** that destroy or inactivate the foreign matter. Memory cells are formed and retain the ability to respond again in the event of re-infection.
- **Vaccination** is the deliberate administration of antigens that have been rendered harmless but nevertheless are able to stimulate antibody production and the retention of appropriate memory cells.
- **Monoclonal antibodies** are a source of a single antibody made by a particular type of B-lymphocyte fused with a cancer cell to form a **hybridoma.** This divides indefinitely and so secretes the antibody in significant quantities. Monoclonal antibodies are used in the treatment of cancer by targeting specific **damaged** or **diseased cells** and killing them by the delivery of a 'magic bullet'. They are used in diagnosis to identify the presence of **specific macromolecules**, as in pregnancy testing, and in several other medical applications.

Examination style questions

1 During an immune response, plasma cells secrete antibody molecules. Fig.1.1 is a diagram of an antibody molecule. The diagram is **not** complete.

Fig. 1.1

a) On a copy of Fig. 1.1:

i) Draw a circle around a variable region. [1]

ii) Draw in and label the position of the disulfide bonds in the molecule. [1]

iii) Explain the importance of disulfide bonds in protein molecules, such as antibodies. [3]

b) Describe how antibodies provide protection against pathogens. [4]

c) Other proteins are found in cell surface membranes.

Describe three roles of the proteins in cell surface membranes. [3]

[Total: 12]

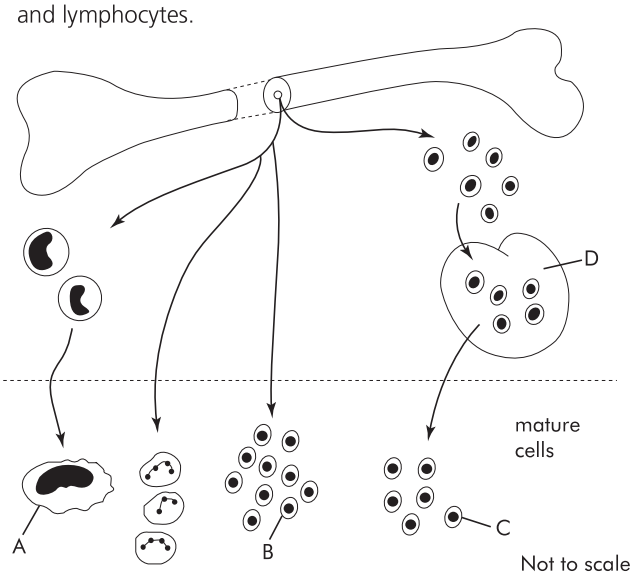
(Cambridge International AS and A Level Biology 9700, Paper 21 Q1 November 2009)

2 **a)** Plasma cells secrete specific antibodies but are short-lived in the body. Explain, with use of a diagram, how a plasma cell is made 'immortal' in the production of a monoclonal antibody. [8]

b) Detail the use of monoclonal antibodies in one application of their use in diagnosis and one application in the treatment of diseases. [8]

[Total: 16]

3 Phagocytes and lymphocytes are part of the body's cellular response to infection by pathogens.
The diagram shows the origin and maturation of phagocytes and lymphocytes.



a) Name the site of origin of phagocytes and lymphocytes. [1]

b) Name:

i) cells **A**, **B** and **C** [3]

ii) organ **D**. [1]

c) Explain the roles of the cells, **A**, **B** and **C** in an immune response.
In your answer use the terms *antigen* and *non-self*. [5]

[Total: 10]

(Cambridge International AS and A Level Biology 9700, Paper 21 Q6 November 2011)