10 DEFENCE AGAINST INFECTIOUS DISEASE

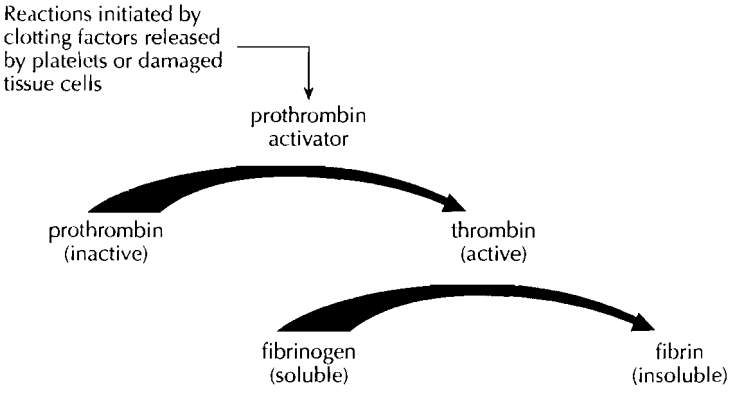
Types of defence

BLOOD CLOTTING

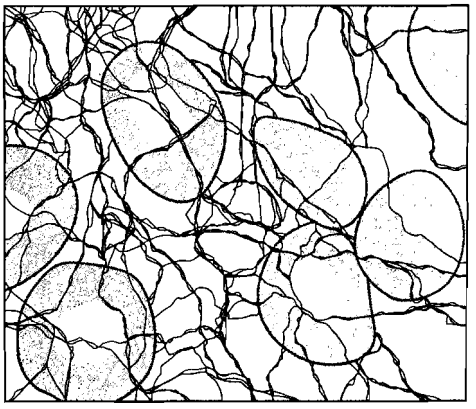
When human tissue is injured and blood escapes from blood vessels, a semi-solid is formed from liquid blood to seal up the wound and prevent entry of pathogens. The semi-solid is called a **blood clot** and the process is called **clotting**.

Platelets have an important role in clotting. Platelets are small cell fragments that circulate with erythrocytes and leukocytes in the blood plasma. The clotting process begins with the release of clotting factors either from damaged tissue cells or from platelets. These clotting factors set off a series of reactions in which the product of each reaction is the catalyst of the next reaction. This system helps to ensure that clotting only happens when it is needed and it also makes it a very rapid process. In the last reaction fibrinogen, a soluble plasma protein is altered by the removal of sections of peptide that have many negative charges. This allows the remaining polypeptide to bind to others, forming long protein fibres called fibrin. Fibrin forms a mesh of fibres across wounds. Blood cells are caught in the mesh and soon form a semi-solid clot. If exposed to air the clot dries to form a protective scab, which remains until the wound has healed.

Final reactions in blood clotting



Fibrin and blood cells in a blood clot



IMMUNITY

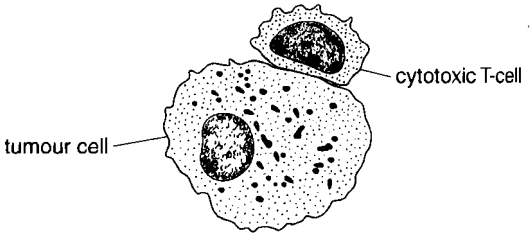
The human body is able to resist infection by many types of pathogenic organism. This resistance to infection is called **immunity**. Barriers to infection such as the skin provide immunity to a wide range of pathogens. Phagocytes are able to ingest and kill many organisms and chemicals including acids in the stomach and lysozyme in tears kill others. These defences are not adequate to resist the most potent pathogens. Specific immunity by production of antibodies is needed. Immunity to specific pathogens can be either natural or artificial and either active or passive.

Type of immunity	Definition	Examples
Natural or artificial	*Natural immunity is the result of infection with a pathogen*	The body becomes immune to the measles virus after being infected by it
	Artificial immunity is the result of inoculation with a vaccine	The body becomes immune to the measles virus after being inoculated with measles vaccine
Active or passive	*Active immunity is due to antibodies produced by the body's own immune system, following invasion of the body by pathogens*	Infection with rubella virus causes the development of immunity to rubella and re-infection is very rare
	Passive immunity is due to antibodies received from another organism, which made them as a result of active immunity	During pregnancy, antibodies are passed across the placenta from mother to the fetus and the first milk produced after birth, called colostrum, contains antibodies that can be absorbed into the newborn baby's blood through the stomach wall

THE ROLE OF CYTOTOXIC T-CELLS

Viruses multiply inside body cells, where they are out of reach of antibodies. One class of lymphocyte, called cytotoxic T-cells, can detect viral proteins in the membrane of infected body cells and then destroy these infected cells. Cytotoxic T-cells can also identify and destroy some types of cancer cell in the body.

The figure (right) shows a small cytotoxic T-cell preparing to kill a large cancer cell.



Antibody production

DEVELOPING IMMUNITY

Antibodies are made by lymphocytes called B-cells. The immune system as a whole can make 10^{15} different types of antibody. It would be impossible to make large quantities of all of these antibodies. Instead, a few B-cells that can make each type of antibody are produced and if these cells encounter an antigen to which their antibody binds, they multiply to form a clone of many cells. This is called **clonal selection**. Sometimes, several different types of antibody can bind to the same antigen, so more than one clone of cells is formed. This is called polyclonal selection.

A clone of B-cells can produce large amounts of antibody quickly and so give immunity to the disease with which the antigen is associated. Immunity to a disease is only developed if the immune system is challenged by the disease. This is called the principle of **challenge and response**.

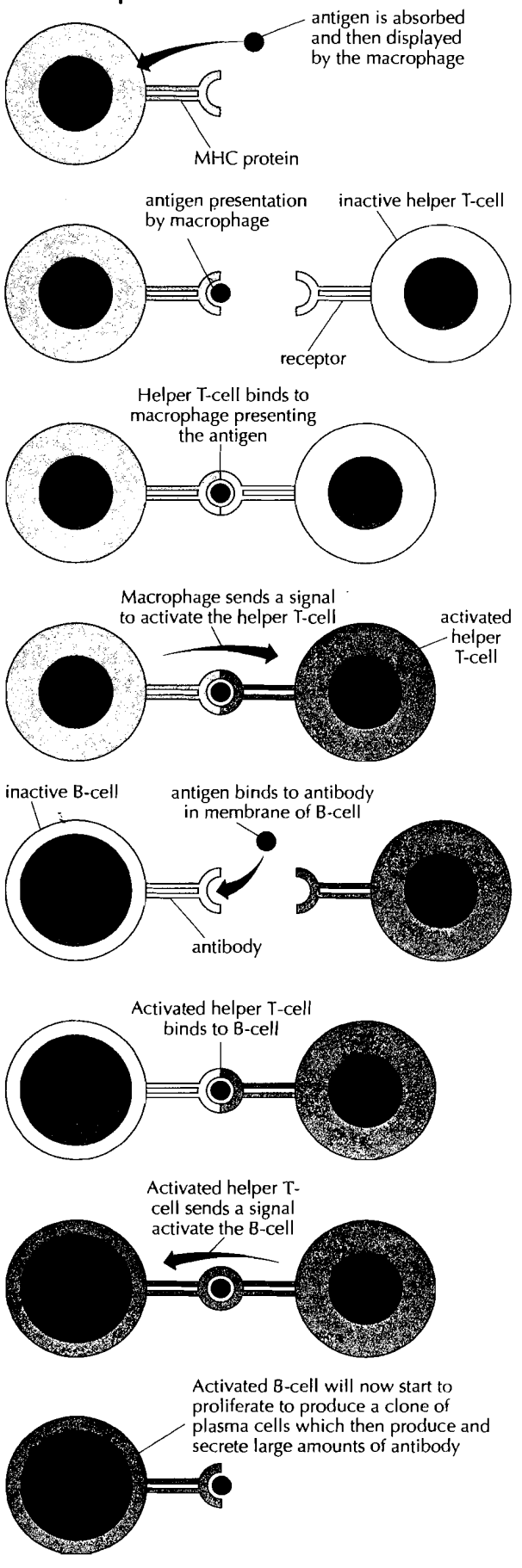
STAGES IN ANTIBODY PRODUCTION

The figure on page 50 summarizes the production of antibodies by B-cells. Antibody production by B-cells usually depends on other types of lymphocyte, including macrophages and helper T-cells.

1. Macrophages take in antigens by endocytosis, process them and then attach them to membrane proteins called MHC proteins. The MHC proteins carrying the antigens are then moved to the plasma membrane by exocytosis and the antigens are displayed on the surface of the macrophage. This is called **antigen presentation**.
2. Helper T-cells have receptors in their plasma membrane that can bind to antigens presented by macrophages. Each helper T-cell has receptors with the same antigen-binding domain as an antibody. These receptors allow a helper T-cell to recognize an antigen presented by a macrophage and bind to the macrophage. The macrophage passes a signal to the helper T-cell changing it from an inactive to an active state. This is called **activation of helper T-cells**.
3. B-cells have antibodies in their plasma membrane. These antibodies recognize an antigen and the antigen binds to the antibody. An activated helper T-cell with receptors for the same antigen binds to the B-cell. The activated helper T-cell sends a signal to the B-cell, causing it to change from an inactive to an active state. This is called **activation of B-cells**. Activated B-cells start to divide by mitosis to form a clone of plasma cells.
4. Plasma cells are active B-cells with a very extensive network of rough endoplasmic reticulum. This is used for synthesis of large amounts of antibody, which is then secreted by exocytosis.
5. Memory cells are B-cells and T-cells that are formed at the same time as activated helper T-cells and B-cells when a disease challenges the immune system. After the activated cells and the antibodies produced to fight the disease have disappeared the memory cells persist and allow a rapid response if the disease is encountered again. Memory cells give long-term immunity to a disease.

The figure (right) shows the events that lead to the production of a clone of plasma cells.

Production of plasma cells

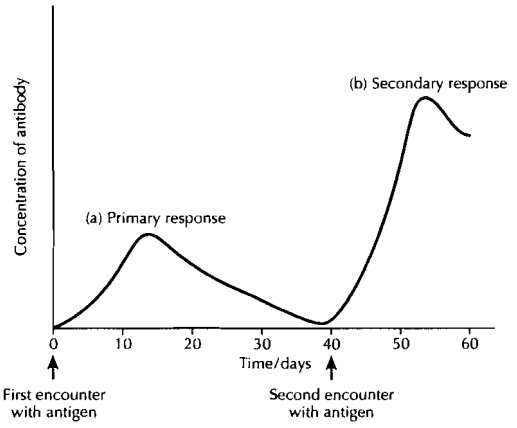


Helping to defend the body

VACCINATION

A vaccine is a modified form of a disease-causing micro-organism that stimulates the body to develop immunity to the disease, without fully developing the disease. Vaccines contain weakened forms of the micro-organisms, killed forms or chemicals produced by the micro-organism that act as antigens. The vaccine is either injected into the body or sometimes swallowed. The principle of vaccination is that antigens in the vaccine cause the production of the antibodies needed to control the disease. Sometimes two or more vaccinations are needed to stimulate the production of enough antibodies. The figure (right) shows a typical response to a first and second vaccination against a disease. The first vaccination causes a little antibody production and the production of some memory cells. The second vaccination, sometimes called a booster shot, causes a response from the memory cells and therefore faster and greater production of antibodies. Memory cells should persist to give long-term immunity.

Response to first and second vaccinations



BENEFITS AND DANGERS OF VACCINATION

Vaccination has enormous benefits but also possible dangers.

Benefits

1. Some diseases may be completely eradicated. Smallpox, for example, has already been eradicated by vaccination, reducing human suffering and future costs of treatment
2. Deaths due to disease can be prevented. For example measles is a major cause of death of small children in some parts of the world
3. Long-term disabilities due to disease can be prevented. For example, if pregnant women are infected with rubella their babies can be born with deafness, blindness and heart and brain damage. Mumps can cause infertility in men

Dangers

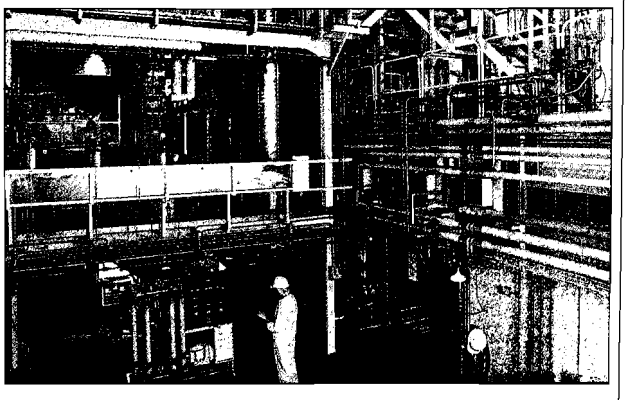
1. Excessive amounts of vaccination may reduce the ability of the immune system to respond to new diseases. It has been suggested that the soldiers who have felt ill since the Gulf war were harmed by having too many vaccinations in a short time.
2. The immunity developed after vaccination may not be as effective as immunity due to actually catching a disease. Vaccination of children might make them vulnerable to more severe infection as adults, for example with measles
3. There is a danger of side effects from some vaccines, which can cause long-term disability. Whooping cough vaccination sometimes causes brain damage and MMR vaccine (combined measles, mumps and rubella vaccine) may increase the chance of autism.
4. Pregnant women, cancer patients and other vulnerable groups can be harmed by cross-infection from people vaccinated with live virus e.g. smallpox vaccine.

PRODUCTION OF MONOCLONAL ANTIBODIES

Large quantities of a single type of antibody can be made using an ingenious technique.

- Antigens that correspond to a desired antibody are injected into an animal.
- B-cells producing the desired antibody are extracted from the animal.
- Tumour cells are obtained. These cells grow and divide endlessly.
- The B-cells are fused with the tumour cells, producing hybridoma cells that divide endlessly and produce the desired antibody.
- The hybridoma cells are cultured and the antibodies that they produce are extracted and purified.

The figure (right) shows a factory used for the industrial production of monoclonal antibodies. There are many ways in which monoclonal antibodies can be used. Two examples are described here.



Treatment of rabies

Rabies usually causes death in humans before antibodies produced by the immune system controls it. If a person becomes infected, an effective strategy is to vaccinate against rabies and at the same time inject monoclonal antibodies. These control the rabies virus until antibodies are produced as a result of the vaccination.

Diagnosis of malaria

Tests using monoclonal antibodies have been developed for many diseases, including malaria. Monoclonal antibodies are produced that bind to antigens in malarial parasites. A test plate is coated with the antibodies. A sample is left in the plate long enough for malaria antigens in the sample to bind to the antibodies. The sample is then rinsed off the plate. Any bound antigens are detected using more monoclonal antibodies with enzymes attached that cause a colour change. This is called an ELISA test. It can be used to measure the level of infection and to distinguish between different strains of malaria, either in humans or in mosquitoes.