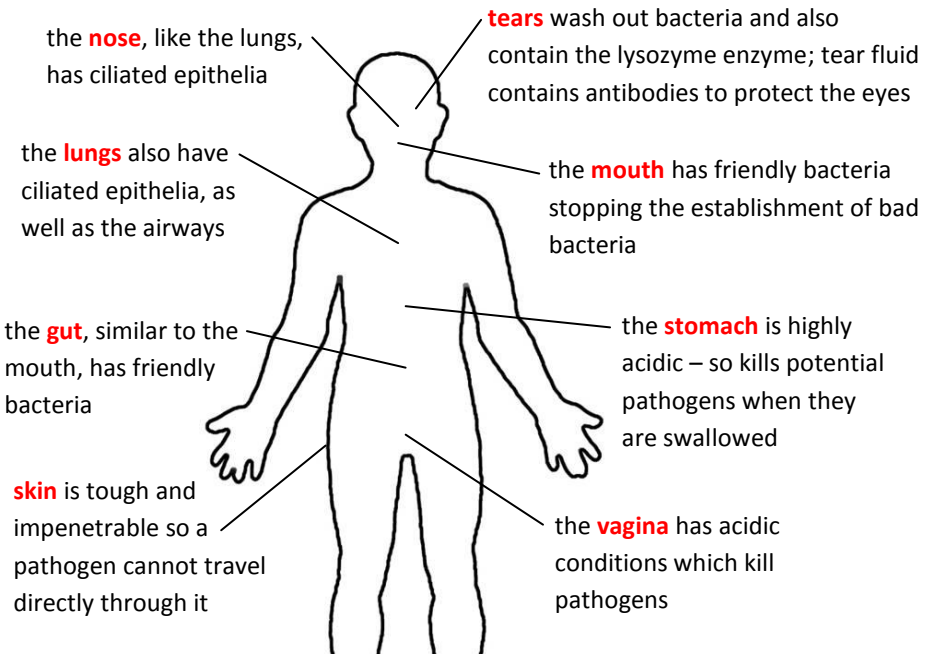
4.5 The Immune Response

How the immune system responds to a pathogenic infection

Barriers to infection

A barrier to infection, also referred to as a **primary defence**, are those defences which set out to prevent pathogenic organisms from entering the body to cause harm. A pathogen cannot cause disease unless it enters the body of their host, and *evolution* has allowed us to adapt to have these following barriers to infection.



The immune response

The term **secondary defence** is used to describe those defences which occur inside the body should a pathogen manage to enter. This will be the **immune response**.

Phagocytes

If the conditions of the body are not sufficient to kill invading pathogens, and they enter the body, the pathogens have to be killed before they can reproduce, spread and cause the symptoms of disease. This can be done by a variety of some non-specific **phagocytes**.

Neutrophils

A **neutrophil** is the most abundant type of phagocyte, most recognisable by their lobed nuclei. They are manufactured in the bone marrow. They move around in the blood and are able to 'crawl' out of capillaries into tissue fluid. Neutrophil cells can be found in high concentrations along epithelial layers, for example, in the lungs. They tend to be short-lived but are released in very large numbers as a response to infection.

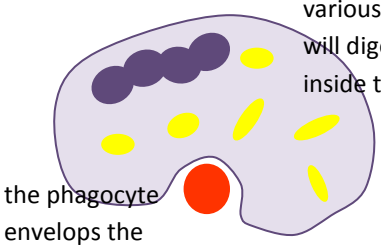
Macrophages

Cells called **monocytes** travel around in the blood, and settle at various organs and tissues, especially the liver, lymph nodes and alveoli. When they settle, they become fixed in that particular place and develop into **macrophages**, which are the other type of phagocyte. Although fixed in place, they are still involved in the non-specific response to infection, and so still undergo phagocytosis just as neutrophils do.

Phagocytosis

This is the process all phagocytes undergo to kill pathogens. It involves engulfing, ingesting and destroying pathogenic cells. When a pathogen invades our bodies, the chemical markers, called **antigens**, on its membrane are identified as foreign. Various proteins which are in the blood, called **antibodies** will attach to the foreign antigens. A phagocyte has membrane-bound proteins which act as receptors, which bind the antibodies to the antigens.

Once attached, the phagocyte folds its own membrane inwards and envelops the pathogen, trapping it inside a vacuole called a **phagosome**. Various **lysosomes** fuse with the phagosome and release lysin enzymes into it which digest the pathogen. The waste products are harmless and can be absorbed into the cytoplasm. Neutrophils die shortly after this process. They may collect in great numbers to form pus.



Lymphocytes

The *immune response* is the initiation of the *specific* response to an infection. Whereas phagocytes are non-specific, the immune response involves the activation of **lymphocytes** in the blood to help fight a disease.

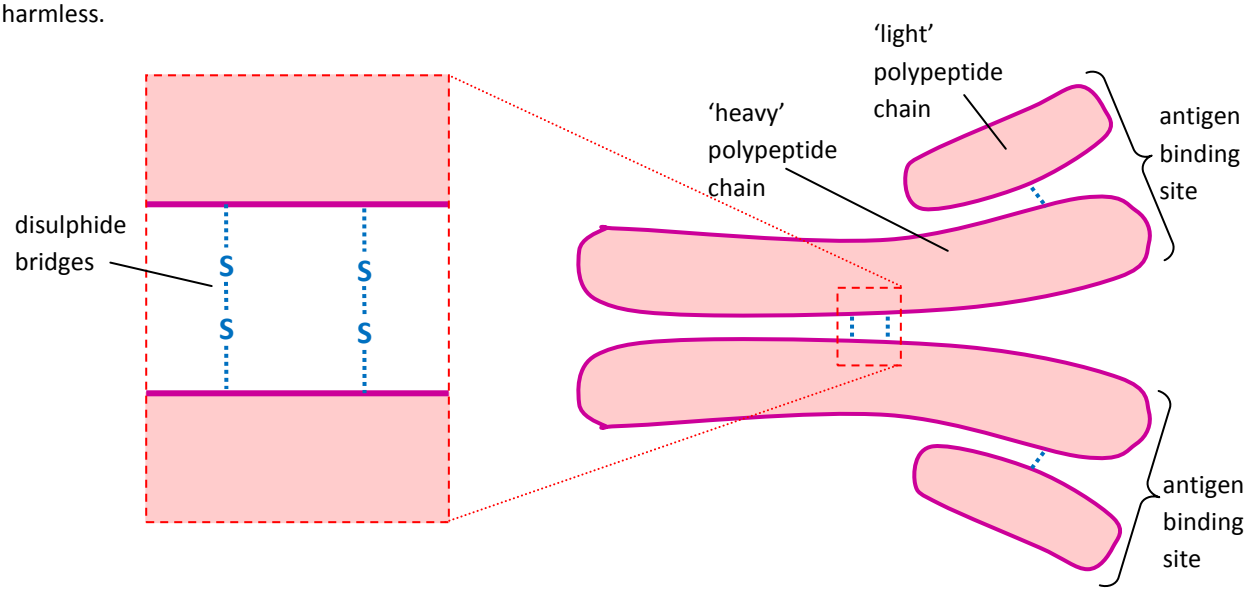
Macrophages actually play an important role in triggering the immune response. When cells are infected, they release chemicals which attract neutrophils to the area. One such chemical is *histamine*, which also makes capillaries more leaky as a result of its release. This means more fluid leaves the capillaries in the area of infection, so more tissue fluid passes into the **lymphatic system**. This leads the pathogens towards macrophages which wait in the lymph nodes.

Lymphocytes also come in two varieties: **B lymphocytes** (B-cells) and **T lymphocytes** (T-cells). B lymphocytes produce antibodies which stick to an antigen.

Antibodies and antigens

Antigens are present on the invading pathogens. They are recognised by our bodies as foreign, and this is what triggers the immune response. Our own 'good' cells have antigens on them, but we can successfully recognise them as our own, so they do not cause an immune response.

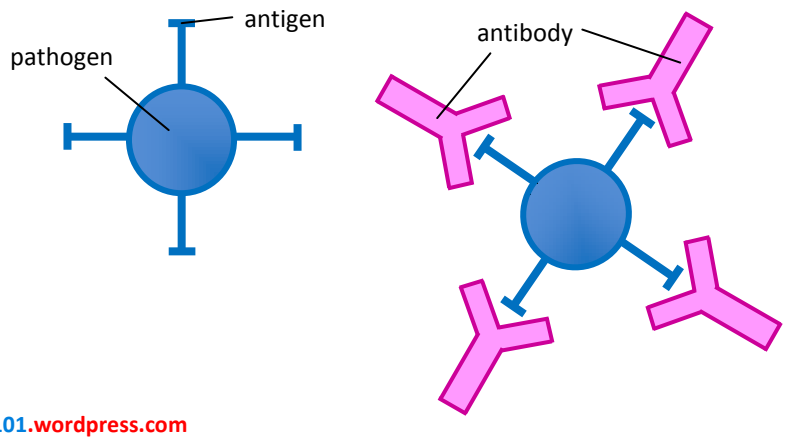
An antigen has a specific shape to the cell it is for. A foreign antigen stimulates the production of *antibodies* from the B lymphocytes. These antibodies are specific to the antigens on the pathogen. An antibody is a **protein** with a quaternary structure and is sometimes referred to as an **immunoglobulin**. The immune system needs to manufacture an antibody for each antigen recognised by the immune system, so the antibodies can attach to the antigen, rendering them harmless.



The diagram above shows the structure of an antibody. It consists of four polypeptide chains, two of which are **light polypeptide chains** and two of which are **heavy polypeptide chains**. Each of the chains is held together by **disulphide bridges**. Every antibody shares the same 'constant' part of the protein, but the 'variable' part is specific for its complementary antigen. This structure of the variable section is dependent upon the amino acid sequence.

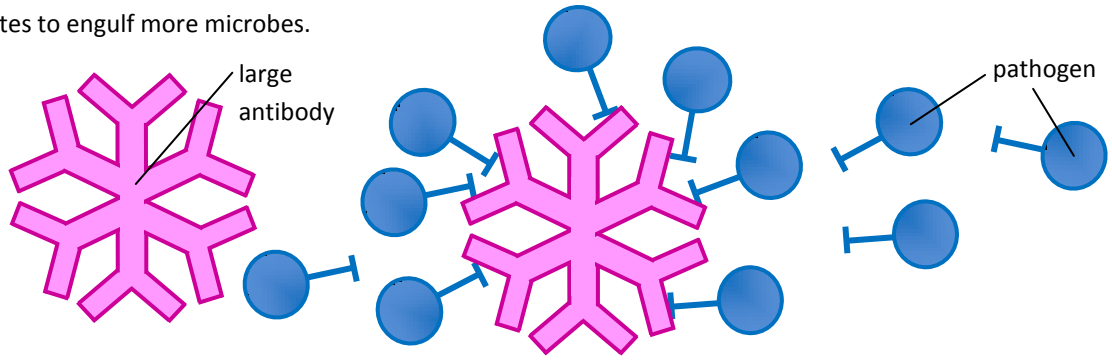
Neutralisation

Antibodies work in three main ways. One way involves the antibody attaching itself to the antigen on a pathogen. The antigen may be a binding site to bind with the host cell to infect it, so if the antibody does this, it renders the pathogen harmless as it cannot attach to a host cell. This is called **neutralisation**.



Agglutination

Some larger antibodies might not have that fixed Y-shape as seen above. They can have the appearance of multiple Y-shaped antibodies glued together, with many specific variable regions. Multiple binding sites can mean that an antibody is able to attach to several pathogens, which brings many pathogens together in clumps. This has two benefits: firstly, the pathogens cannot enter host cells because they are in large clumps and have been effectively 'paralysed' by the antibody; but also it leads to more efficient *phagocytosis*, because when the pathogens are in clumps, it is easier for the phagocytes to engulf more microbes.



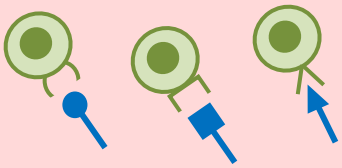
Lysis

The third way in which antibodies can perform their jobs is by binding to antigens whereby the binding action activates proteins in blood plasma which then digest bacterial walls. This will kill the invading cells.

The cell-mediated immune response (what T-cells do)

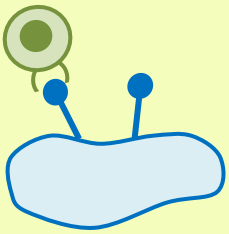
The immune response occurs as a reaction to an invasion of pathogens. The response produces antibodies to fight off the pathogens, but also is designed to provide long-term **immunity**. Immunity is given after becoming infected and the right antibodies being produced, through **immunological memory** (i.e. your immune system remembers those antibodies so future pathogens can be recognised and stopped immediately). The *cell-mediated immune response* is the immune response of the T-cells.

Pre-infection



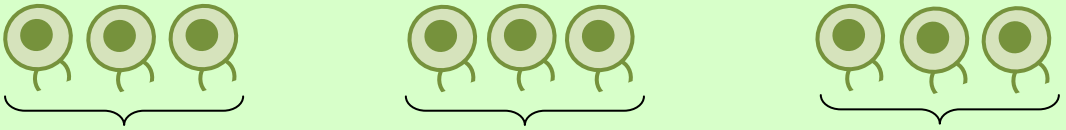
T-cells with various receptors

Clonal selection



T-cell encounters its complementary antigen:
- on a cell infected with a virus
- or on an APC (antigen-presenting cell)
- or actually stuck to the pathogen

Clonal expansion and differentiation — divides by mitosis



T-memory cells
these stay in the body to provide long-term immunity, for any period up to a lifetime

T-helper cells
produce cytokines that stimulate the B-cells to develop and for the phagocytes to undergo phagocytosis (i.e. stimulate the rest of the immune system)

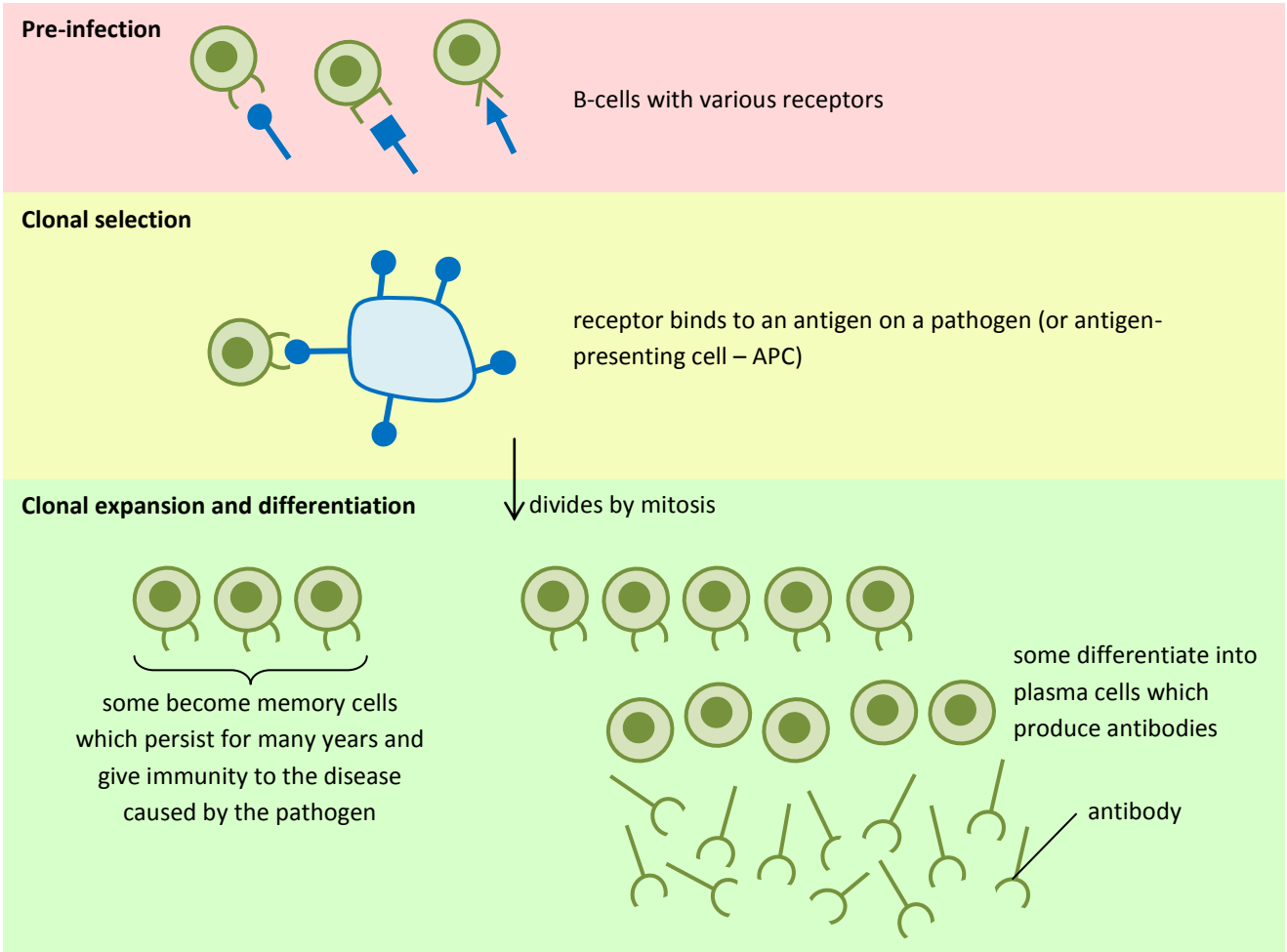
T-killer cells
bind to cells carrying the antigen and produce toxic chemicals (peroxides) which kill the infected body cells

As you can see, the cell-mediated response does not involve antibodies. The process of **clonal selection** is simply the selection of the correct T lymphocytes. But before the T lymphocytes can be effective in fighting the disease, they must increase in their numbers, and so they undergo **clonal expansion** where they divide by mitosis (clone) a number of times. T-cells develop, or **differentiate**, into three different types of cell:

- **T-helper** (T_h) cells release **cytokines**, which are chemical messengers, which stimulate the rest of the immune system – this involves encouraging the B-cells to develop and for phagocytosis to be undergone by phagocytes
- **T-killer** (T_k) cells can bind to the pathogens which have the antigens, and they produce peroxides – toxic chemicals – which will destroy the invading cells and infected body cells
- **T-memory** (T_m) cells, which are one type of **memory cell** which provides long-term immunity (with T-cells, this type of immunity is called **cell-mediated immunity**)

The humoral immune response (what B-cells do)

The *humoral response* is that of the B-cells in the immune system. The diagram below outlines the various stages involved in the humoral response. This response does use antibodies in order to provide immunity. The type of immunity given from this response is called **humoral immunity**.



B-cells undergo the same clonal selection and clonal expansion processed as T-cells do. However, the differentiation stage is different. There are only two types of cell B-cells can differentiate into:

- **plasma cells** which flow around in the blood and can produce the specific antibodies whenever required
- **B-memory cells**, the other type of memory cell to T-memory cells, which provide the humoral immunity

Is it important to understand that both types of lymphocyte (B lymphocyte and T lymphocyte) *differentiate* because they are manufactured originally from stem cells in bone marrow. These cells are unspecialised, which allows them to differentiate to a more specific type of cell to perform a particular function.