Disease and Defence

This Factsheet summarises:

1. The immunological response in humans and the structure of antigens and antibodies.
2. T-lymphocytes and cell mediated immunity.
3. B-lymphocytes and humoral immunity.
4. Active and passive immunity and vaccination.
5. Other natural defence mechanisms.

Basic definitions

**Immunity:** The ability to be resistant to injury, particularly by poisons, foreign proteins and invading parasites, due to the presence of antibodies.

**Antigen:** A substance, that when introduced into the tissues or blood activates the immune system which is induced to form antibodies. The antibodies are specific to the antigen and react with it to make it harmless.

**Antibody:** A protein produced by certain cells in the body in the presence of a specific antigen. The antibody combines with that antigen to neutralise, inhibit or destroy it.

**Immunoglobulin:** An antibody synthesised by plasma cells derived from B-lymphocytes in response to the presence of a specific antigen. Immunoglobulins are of five kinds (IgG, IgM, IgA, IgD, IgE).

**The immune system:** This consists of a number of lymphoid organs linked by lymphatic vessels and capillaries. Examples of lymphoid organs are the thymus gland (found above and behind the heart in children), spleen, tonsils, bone marrow and the lymph nodes (found extensively around the body e.g. in the armpit, groin, neck, near the lungs, in the gut and urinogenital system). The lymphoid organs house billions of lymphocytes which are responsible for identifying and eliminating infectious parasites.

**Lymphocytes:** Large lymphocytes are formed from stem cells in the bone marrow. The B-lymphocytes make antibodies (humoral response) and are found in the lymphoid organs (except thymus). The T-lymphocytes develop in the thymus, and are concerned not only with cellular immunity but also with the regulation of the humoral response by the B-lymphocytes.

**Phagocytes:** Cells e.g. neutrophils and eosinophils which carry out phagocytosis (the ingestion and destruction of microbes and other particulate matter). The cells can wander around the body by amoeboid action and will congregate in huge numbers at a site of infection in order to engulf any microbial material. Phagocytes are attracted to sites of infection by chemotaxis.

The clonal selection theory: At birth the lymphoid system is thought to contain as many as one hundred million (10⁸) different clones of small lymphocytes, each one committed by the shape of its antigen receptors to recognise just one antigen grouping. Each clone consists of less than a hundred cells but there are more than enough clones to recognise all the different antigen groupings that might be encountered throughout life. (A clone is a population of genetically identical cells formed by mitosis.) Thus if the lymphocytes encounter a particular antigen only a few cells (one clone) will recognise it and respond.

**T-cells and cellular immunity**

The invading pathogen, for instance *Staphylococcal bacteria* are initially phagocytosed by macrophages. Some of the macrophages only partially digest the pathogen and then display the antigen on their cell surfaces, together with one of the body’s own antigenic recognition factors, called HLA (human leukocyte associated antigen). These two antigens are then presented to and activate the T-lymphocytes. Such activated cells are said to be **sensitised**, and will increase in size and divide many times to form a clone of genetically identical cells. These cells then **differeniate** to form clones of killer, memory, amplifier, helper, suppressor and delayed hypersensitivity T-cells, which all have particular roles to play in immunity (Table 1).

**Table 1. Roles of activated T-cells in cellular immunity**

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Major roles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Killer/cytotoxic T-cells</td>
<td>1. Leave lymphoid tissue and attach to and destroy invading cells.</td>
</tr>
<tr>
<td></td>
<td>2. Secrete lymphokines which:</td>
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<tr>
<td></td>
<td>(a) stimulate T-cell growth, division and differentiation.</td>
</tr>
<tr>
<td></td>
<td>(b) cause non-sensitised lymphocytes nearby to become killer T-cells.</td>
</tr>
<tr>
<td></td>
<td>(c) attract macrophages to the area and also stimulate them to increase activity.</td>
</tr>
<tr>
<td>Memory</td>
<td>Are programmed to remember the original invading antigen. They remain stored in the lymphoid tissue and if the same antigen is encountered again it is destroyed before disease symptoms occur.</td>
</tr>
<tr>
<td>Amplifier T-cells</td>
<td>Stimulate helper T-cells, suppressor T-cells and B-cells.</td>
</tr>
<tr>
<td>Helper T-cells</td>
<td>1. Co-operate with B-cells to induce and amplify antibody production.</td>
</tr>
<tr>
<td></td>
<td>2. Secrete interleukin 2, a lymphokine that stimulates multiplication of killer T-cells, thus enhancing the immune response.</td>
</tr>
<tr>
<td>Suppressor T-cells</td>
<td>Reduce the immune response by damping down some activities e.g. production of antibodies by B-cells.</td>
</tr>
<tr>
<td>Delayed hypersensitivity</td>
<td>Produce several lymphokines that promote macrophage activity and the development of immune allergic responses.</td>
</tr>
</tbody>
</table>

**Exam Hint** - Different syllabuses require different degrees of detail - check what you need to know before you start memorising all of this.
Only the memory cells remain in the lymphoid tissues, the other cells migrate out into other tissues and organs. During the processing and presentation of antigens, macrophages secrete lymphokines such as interleukin 1 and interferons, which stimulate T-cell growth, division and differentiation. The T-cell response is illustrated in Fig 1.

Fig 1. The T-cell response

**Exam Hint** - Although there is a lot of detail, remember the underlying principle. A foreign invader (antigen) has now resulted in the production of T cells which are going to kill the invader!

**B-cells and humoral immunity**

Unlike T-cells, B-cells do not attack pathogens directly. Instead, they remain in the lymphoid tissues (spleen, lymph nodes) and produce antibodies. The functions of the two types of B-cells are summarised in Table 2.

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**Table 2. Roles of activated B-cells in humoral immunity**

<table>
<thead>
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<th>Major roles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma B-cells</td>
<td>Secrete antibodies into the circulation. The antibodies are specific to the pathogenic antigen, which is destroyed. The rate of antigen secretion can be as high as 2000 molecules per second per cell and the active plasma cell will live for 4 - 5 days.</td>
</tr>
<tr>
<td>Memory B-cells</td>
<td>These are programmed to remember the specific antigen and to respond very rapidly should the body be challenged by that antigen on a subsequent occasion, thus preventing further infection.</td>
</tr>
</tbody>
</table>

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**The nature of antigens**

An antigen has two important characteristics
1. immunogenicity - ability to stimulate the formation of specific antibodies
2. reactivity - ability of the antigen to react specifically with the antibodies.

Antigens usually have molecular weights in excess of 10,000 and may be protein, lipoprotein, nucleoprotein, glycoprotein or sometimes large polysaccharides. They may be components of bacteria, viruses, pollen, egg white, incompatible blood cells or transplanted organs. Toxins released by some bacteria and viruses may also act as antigens.

**The nature of antibodies**

Most antibodies contain two pairs of polypeptide chains. Two of the chains are identical to each other and are referred to as heavy (H) chains. The other two chains are also identical to each other and are referred to as light (L) chains. The antibody consists of two identical halves held together by disulphide (S-S) bonds. Each half consists of a heavy chain and a light chain, also joined together by a disulphide bond. Under the electron microscope they appear T shaped before combination with antigen and become Y shaped on combination with the antigen.

There are two distinct regions within the light and heavy chains. The tops of the chains are called the variable portions and are the sites which bind to the antigen. The variable portion is different for each kind of antibody and allows the antibody to recognise and attach specifically to a particular antigen. The remainder of each polypeptide chain is called the constant portion. The structure and action of antibody molecules is shown in Fig 2.
Immunoglobulins

Immunoglobulins are antibodies which are synthesised in response to the presence of a specific antigen. Their functions are summarised in Table 3.

Table 3. Function of immunoglobulins

<table>
<thead>
<tr>
<th>Immunoglobulin</th>
<th>Site</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>Blood, lymph, intestines</td>
<td>Protect against bacteria and viruses by enhancing phagocytosis and neutralising toxins. Can cross placenta to take immunity to foetus</td>
</tr>
<tr>
<td>IgA</td>
<td>Tears, saliva, mucus, milk, gastrointestinal secretions, blood and lymph</td>
<td>Localised protection on mucous membranes</td>
</tr>
<tr>
<td>IgM</td>
<td>Blood, lymph, surface of B-cells</td>
<td>First antibody to appear after a first exposure to an antigen. Causes agglutination and lysis of microbes</td>
</tr>
<tr>
<td>IgD</td>
<td>Blood, lymph, surface of B-cells</td>
<td>Involved in stimulating antibody-producing cells into activity</td>
</tr>
<tr>
<td>IgE</td>
<td>Most cells and basophils</td>
<td>Involved in allergic response</td>
</tr>
</tbody>
</table>

Immunological memory and vaccination

**Actively acquired immunity** is when an individual develops immunity to a specific antigen due to exposure to it. Memory cells are formed which provide long term immunity to that antigen. This type of immunity may develop as a result of accidental exposure to the antigen during infection, or by deliberate exposure to the antigen during vaccination. Because second and even third exposures to antigens will cause even larger populations of memory cells to form and much higher levels of circulating antibodies to be produced, vaccinations are often repeated (booster vaccinations). The time scale for vaccinations and for the persistence of immunity varies according to the antigen involved. Babies are vaccinated against the bacterial diseases of diphtheria, pertussis (whooping cough) and tetanus, and against the viral diseases of measles and polio. With the exception of tetanus which requires 5 or 10 year booster immunisations, these childhood vaccinations will give lifelong protection. Vaccinations are also available against the bacterial diseases of meningitis and tuberculosis, and against viral diseases of hepatitis, Rubella (German measles) and influenza.

**Passively acquired immunity** is when an individual becomes immune to an antigen due to receiving ready-made antibodies against the antigen or an infusion of actual activated immune cells from a compatible donor. For instance, antibodies from the mother may pass to the foetus via the placenta or to the baby in the colostrum and milk whilst suckling. The antibodies will only persist in the baby for a few weeks and so this type of immunity is short term. People who have possibly been exposed to tetanus spores are given antibodies to protect them in case their own acquired immunity has weakened if booster immunisations have been missed. Passive immunity in the form of antibodies is also given to people who have been bitten by rabid dogs, to prevent the development of rabies.

**Other natural defence mechanisms/non-specific resistance**

Unlike the development of immunity, which is specific to particular antigens, non-specific resistance is inherited and consists of a wide variety of body reactions which provide a general response against invasion. These are summarised in Table 4.

Table 4. Summary of specific resistance mechanisms

<table>
<thead>
<tr>
<th>Component</th>
<th>Functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Skin and mucous membranes</td>
<td>Form a physical barrier to the entry of microbes. Traps microbes in respiratory and gastrointestinal tracts. With mucus trap and remove microbes and dust from upper respiratory tract. Prevent dust and microbes entering nose. Prevents dust, microbes or food from entering trachea. Secretes tears which dilute and wash away irritating chemicals and microbes from the eye. Washes chemicals and microbes away from teeth and mucous membranes of buccal cavity and pharynx. Washes microbes out of urethra. Inhibits microbial growth on skin. Contains unsaturated fatty acids which have an antimicrobial action. An antimicrobial substance in tears, sweat, saliva, nasal secretions and tissue fluids. Contains hydrochloric acid at pH 1.5 - 2.5 which has a disinfecting action on the stomach wall and contents.</td>
</tr>
<tr>
<td>2. Phagocytosis</td>
<td>Ingestion and digestion of foreign particles/microbes by neutrophils, eosinophils, monocytes and macrophages.</td>
</tr>
<tr>
<td>3. Fever</td>
<td>Raised body temperature inhibits microbial enzymes and growth, and speeds up the processes of repair.</td>
</tr>
<tr>
<td>4. Inflammation</td>
<td>Inflammatory response initiated by histamine and serotonin release from basophils/mast cells attracts phagocytes to infected region. Reduces spread of infection throughout organism.</td>
</tr>
<tr>
<td>5. Antimicrobial chemicals</td>
<td>Protects uninfected host cells from viral infection. A group of plasma proteins which promote antibody action and phagocytosis, and also enhance the inflammatory reaction. A trio of plasma proteins that can destroy certain bacteria by cytolysis. They also enhance phagocytosis and the inflammatory response.</td>
</tr>
<tr>
<td>Interferon</td>
<td>Complement</td>
</tr>
</tbody>
</table>
**Monoclonal antibodies**

When antibodies are produced against specific antigens, although they are similar, they are not exactly the same since they are produced by very many different plasma cells. Scientists can now isolate a single B-cell and fuse it with a tumour cell to produce a hybrid cell called a **hybridoma**. This will multiply endlessly by mitosis to produce a clone of genetically identical cells. The antibodies made by such clone cells are called *monoclonal antibodies*; they are highly specific to one particular antigen, and are produced in large quantities. Monoclonal antibodies are used in pregnancy testing, to measure the levels of a drug in a patient’s blood, and in the diagnosis of such diseases as hepatitis, rabies and cancer. They can also be directed against cancerous cells and so are of use in cancer therapy.

**Some problems of immunity**

1. **Acquired Immune Deficiency Syndrome (AIDS)** is caused by the Human Immunodeficiency Virus (HIV). The HIV virus binds to special receptors, called CD4 receptors, which are on the surfaces of T-helper cells. These are killed by the virus and thus the immune response is impaired. This immunodeficiency exposes the infected person to infection by other pathogenic organisms which will eventually result in death.

2. **Autoimmune disease** is where the body produces antibodies against some of its own tissues and thus these tissues are destroyed, resulting in disease. For instance, in Diabetes mellitus (juvenile type), the beta cells of the islets of Langerhans are destroyed and so insulin secretion fails. The onset of this disease often follows a Streptococcal infection (sore throat) and possibly the Streptococcal antigens resemble antigenic groupings on the beta cells. If this situation is coupled with inadequate Suppressor-T cells then the immune response against Streptococci may continue against the beta cells.

Other examples of autoimmune disease are Rheumatoid arthritis, thyroiditis, rheumatic fever, pernicious anaemia, haemolytic anaemia, Addison’s disease, myasthenia gravis and multiple sclerosis.

3. **Tissue rejection** is a problem in treating patients by transplantation. The implanted organs are recognised as foreign and thus antibodies are produced which may damage or destroy them. This is known as tissue rejection. The problems may be reduced by transplanting closely matching tissues (with same or similar surface/HLA antigens) and by using drugs which suppress the immune response, such as cyclosporine.

4. **Incompatible blood transfusion** with either ABO groups or Rhesus groups will cause a problem if the immune system has previously been challenged by the wrong blood and thus has an immunological memory. The antibodies produced will clump the red cells together and these clumps can block capillaries and small arterioles in the kidneys, heart, brain or anywhere in the body. This could result in death.

**Practice Questions**

1. Which of the following alternatives are correct? A man was inoculated with a particular antigen. Four weeks later the inoculation was repeated. It was expected that after the second inoculation antibodies specific to the antigen would be

   A. produced in greater quantities but more slowly than after the first.
   B. not produced any more due to persistent antibodies from the first inoculation.
   C. produced in greater quantity and more rapidly than after the first.
   D. produced more quickly but in smaller amount than after the first.

   (1 mark)

2. Suggest explanations for each of the following.

   (a) Immunisation against measles virus will last for a lifetime but annual immunisations are necessary to give protection against influenza.

   (3 marks)

   (b) Because the baby’s immune system is not fully competent at birth it is advisable to breast feed the baby for at least several weeks.

   (3 marks)

   (c) If a rhesus negative mother bears a rhesus positive baby there are serious immunological problems in the case of a second such pregnancy.

   (3 marks)

3. Distinguish between each of the following pairs.

   (a) Lysozyme and interferon.

   (3 marks)

   (b) Killer T-cells and plasma cells.

   (3 marks)

   (c) Active and passive immunity.

   (3 marks)

4. Read through the following passage about monoclonal antibodies and then fill in the spaces with the most appropriate word or words.

   During the production of monoclonal antibodies, scientists isolate a single ................. and fuse it with a ................. to form a special cell known as a ................. . This can be kept in tissue culture and will divide many times by ................. to form a ................. which will produce large quantities of the specific monoclonal antibody. Such antibodies have many uses, for example, l. .................................. and 2. ................................................. .

   (7 marks)

5. The following table relates to some features of T and B cells. If a feature is correct put a tick (√) in the box and if it is incorrect put a cross (×) in the box.

   (5 marks)

<table>
<thead>
<tr>
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<td></td>
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<td>Develop in the thymus</td>
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<td>Give passive immunity to the organism</td>
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Answers
Semicolons indicate marking points.

1. A;

2. (a) Measles viruses are stable and rarely mutate into new antigenic forms;
   Influenza viruses are constantly mutating into new antigenic forms
   so that new strains of the virus appear every few months;
   thus memory cells for measles can be effective throughout life but
   memory cells for influenza may not recognise the 3 new strains;

   (b) Colostrum/breast milk contains many antibodies produced in
   mother;
   these can be absorbed into the baby via the stomach from the milk;
   they will persist in the baby’s body for several weeks and thus
   give passive immunity against many diseases;

   (c) In first pregnancy mother produces Rhesus antigen/antiD against
   fetal red cells;
   but baby is born before antibody can destroy many fetal cells;
   but memory cells are retained which will cause a large rapid secretion
   of rhesus antibody in the second pregnancy which will destroy the
   fetal red cells, possibly causing death;

3. (a) Lysozyme is a protein splitting enzyme secreted by lysosomes;
   has antimicrobial activity in tears/saliva/sweat etc;
   interferons are proteins secreted by killer-T cells which inhibit
   viral growth;

   (b) Killer T-cells enter tissues and aggregate around invading organisms;
   produce cytotoxic chemicals to destroy pathogens;
   plasma cells are B-cells which remain in lymphoid tissue and secrete
   antibodies into circulation;

   (c) Active immunity is when the body has memory cells to remember
   an invading or inoculated pathogen;
   this enables rapid production of killer T-cells/plasma cells/antibody
   if the same antigen is encountered again;
   in passive immunity the antibody itself is received, either across
   the placenta or in milk or via injection

4. B-cell/plasma cell;
   tumour cell/myeloma cell;
   hybridoma;
   mitosis;
   clone (of genetically identical cells);
   pregnancy testing/drug monitoring/cancer therapy/disease diagnosis (eg.
   hepatitis/rabies);

5.

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(1 mark per correct line)