Higher Human Biology

Unit 4: Immunology and Public Health

Course Notes

Name:
The Immune system

The human body has the capacity to protect itself against pathogens (disease causing organisms), some toxins (poisons produced by living things) and cancer cells through the immune system.

There are three lines of defence used by the body. The first two are non-specific which means that they work against any type of disease-causing agent. The third line of defence is specific. This means that it works against one particular pathogen.

The first line defence mechanisms which are non-specific include:

- **Physical and chemical defences.**
  - Skin (epithelial cells) is a physical barrier to keep pathogens out.
  - Secretion of acid by the internal lining in the stomach to kill microbes.
  - Secretion of mucus by epithelial lining of trachea to trap microbes.

The second line of defence mechanisms which are also non-specific include:

- **Inflammatory response**
  - When the body suffers a physical injury such as a cut, it responds with a localised defence mechanism called the inflammatory response at the affected site.
  - Mast cells are present in the connective tissue throughout the body. The mast cells possess many granules containing histamine. Histamine is a chemical that causes blood vessels to dilate and capillaries to become more permeable.

Website

http://www.youtube.com/watch?feature=player_detailpage&v=_bNN95sA6-8
Following injury, the damaged mast cells become activated and release large quantities of histamine. This results in vasodilatation where the capillaries become swollen with blood. The additional blood supply makes the area become red and inflamed. It swells up because the stretched capillary walls become more permeable and leak fluid into the neighbouring tissues.

Cytokines are cell signalling protein molecules secreted by many types of cells, including white blood cells that have arrived at the site of injury. The increased flow of blood and permeability of capillary walls brings about the following effects.

1. The arrival of phagocytes which are attracted by the cytokines. These phagocytes recognise the surface antigen molecules on pathogens and destroy them by phagocytosis.

2. Delivery of antimicrobial proteins to the infected site. These proteins amplify the immune response.

Web site
http://www.bbc.co.uk/learningzone/clips/white-blood-cells/1838.html
3. Rapid delivery of blood-clotting chemicals to the injured area stops blood loss. This helps to prevent further infection of the wound and marks the start of the tissue repair process.

Natural Killer (NK) cells also play a non-specific role in defence. NK cells release protein molecules which cause pores to form in the target pathogen's cell membrane. Signal molecules from the NK cells enter the target cell which switches on a 'suicide gene' within the pathogen. The suicide proteins produced from these genes function as self-destructive enzymes which results in the pathogen cell's DNA and viral coat (if the pathogen is a virus) being broken down into useless fragments. The cell then shrinks and dies. This process of programmed death is called apoptosis.
In addition to their role in no-specific immunity, phagocytes and NK cells release cytokines which then stimulate the specific immune response by activating lymphocytes.

The third line of defence - the specific immune response - is brought about by lymphocytes produced from stem cells in the bone marrow. Specific cellular defences include:

- Immune surveillance
- Clonal selection theory
- T and B lymphocytes

Immune surveillance

A range of white blood cells constantly circulate the body in the circulatory system monitoring the tissues. If tissues become damaged or invaded, cells release cytokines which increases blood flow resulting in specific white blood cells accumulating at the site of infection or tissue damage. White blood cells will often squeeze through tiny spaces in the capillary wall to gain access to the surrounding infected or damaged tissue.

Website

http://www.youtube.com/watch?v=y1-KcQx4Gaw
Clonal Selection Theory

A foreign protein (on the surface of pathogen) that is recognised in the body and causes a response from a lymphocyte (a type of white blood cell) is called and antigen.

The body has a large number of lymphocytes each with a single type of membrane receptor specific for one antigen. The diagram below shows a pool of lymphocytes with several antigen receptors.

The antigen receptors on the surface of lymphocytes are specific to one type of antigen. When a receptor is activated by the binding of an antigen, the lymphocyte repeatedly divides resulting in a clonal population of lymphocytes.

website

http://www.youtube.com/watch?v=ua2Fz4hV5xs

B and T Lymphocytes

There are two distinct groups of lymphocytes:

- The B lymphocytes that secrete antibodies.
- The T lymphocytes that have a variety of jobs including attacking infected or defective cells. They do not produce antibodies.

All lymphocytes originate from bone marrow and initially they are all alike. They then specialise into B or T cells. Lymphocytes that move to the thymus (a gland in the upper chest region) develop into T cells (hence ‘T’ stands for ‘thymus’). Lymphocytes that remain in the bone marrow become B cells (‘B’ stands for bone).

As the T cells and B cells mature in the thymus or the bone they develop immuno competence which means that they recognise one specific type of antigen on foreign cells, cells infected by pathogens and toxins released by pathogens.

Recognition of self and non self

Each person’s body cells are different because they possess a combination of cell surface proteins that is unique to them. It is important that the persons own lymphocytes don’t regard their own body cells surface proteins as antigens and attack them.

T lymphocytes have specific surface proteins that allow them to distinguish between:

1. the surface proteins of the body’s own cells AND
2. cells with foreign proteins (antigens) on their surface.

If the immune system is not regulated, this leads to a T lymphocyte immune response to self cells. In other words our T lymphocytes fail to recognise our own cells and start to attack them. This results in an auto immune disease such as rheumatoid arthritis or multiple sclerosis. An allergy is a hypersensitive B lymphocyte response to an antigen that is normally harmless.
Among the body’s vast pool of T lymphocytes there are two main types in the human body:

- One group destroys infected cells by **apoptosis**.
- The other secretes **cytokines** that activates B lymphocytes and phagocytes.

When a phagocyte engulfs a pathogen, it displays fragments of the pathogen’s **antigens** on its surface. These phagocytes are now called **antigen-presenting cells**. A T lymphocyte that carries antigen **receptors** is able to recognise and bind with these foreign antigens on the surface of the **antigen presenting cell** (phagocyte). When this happens, the T lymphocytes make **identical** copies of themselves (clones). When they then multiply, the T lymphocytes release chemicals called **cytokines** signalling other immune cells to the scene – in particular “**killer**” T lymphocytes. The **phagocyte** **activates** only those “killer” T lymphocytes that have **matching receptors** to the **antigens** on their surface. These “killer” T lymphocytes are also **cloned**. This army of “killer” T lymphocytes then move towards the infected phagocytes and bind to them. They then **release toxins** into the phagocyte which **destroys** it. T lymphocytes also activate B lymphocytes when they secrete cytokines.

http://www.youtube.com/watch?v=ouqVI6CpW-U
**B lymphocytes**

B lymphocytes produce antibodies, and each B lymphocyte produces a **specific antibody** that will recognise a **specific antigen** molecule on the surface of a pathogen or a toxin. An antibody is a Y-shaped protein molecule.

![Antibody Diagram](image)

Each of the arms of an antibody bears a **receptor** site (binding site) that is specific to a particular **antigen**.

The antigen-antibody complexes that result may **inactivate** a pathogen or toxin or render it more susceptible to **phagocytosis**.

In other cases the antigen-antibody complex stimulates a response which results in **cell lysis (death)**.

![Antigen-B-Lymphocyte Diagram](image)
B lymphocytes are activated by antigen presenting cells (phagocytes) with the help of T lymphocytes. When the T lymphocytes release cytokines (after being released from the antigen presenting cells), this stimulates the B lymphocytes to multiply and produce:

- a clone of activated B cells which make antibodies for immediate use OR
- a clone of memory B cells capable of making antibodies in the future if required.

The B lymphocytes secrete their antibodies into the lymph and blood where they make their way to an infected area.

**Memory cells**

Some T and B lymphocytes produced (in response to antigens) by clonal selection survive as long term memory cells.

When a person is infected by a disease causing organism (pathogen), one of the ways that the body responds is to produce antibodies. This is called the primary response.

Due to the latent period elapsing before the production of the antibodies, this primary response is often unable to prevent the person from becoming ill.
A secondary exposure to the same antigen rapidly gives rise to a new clone of lymphocytes producing a rapid and a greater immunological response.

**Infectious diseases and Immunity**

Due to its role in maintaining health and combating infectious diseases on a global level, the immune system is at the centre of much of the research in public health.

**The transmission of infectious diseases**

Infectious diseases are caused by pathogens such as viruses, bacteria, fungi, protozoa and multicellular parasites.

Infectious diseases are transmitted by:

- direct physical **contact** e.g. shaking hands
- contaminated **water**
- food contaminated with pathogens
- body **fluids** e.g. exchanging saliva
- inhaled air contaminated with microbes from infected person sneezing
- a **vector** (person, animal or micro-organism) organisms e.g. being bitten by a mosquito.
The transmission of infectious diseases can be controlled by:

1. Quarantine
   This is a period of compulsory isolation of a person suffering a contagious disease or a person who has been in contact with an infected person.

   [Provide a link to a relevant source on quarantine, e.g., BBC Learning Zone clips]

2. Antisepsis
   Asepsis is a state of being completely free of micro-organisms. Antisepsis is the destruction of micro-organisms that cause disease. Examples would include using sterile equipment, using antiseptic cream and wearing sterile gloves.

3. Individual responsibility (good hygiene, care in sexual health and food storage)
   Hygienic practices such as hand-washing, brushing teeth daily and showering to control population of microbes.

   [Provide a link to a relevant source on individual responsibility, e.g., BBC Learning Zone clips]

   Using condoms gives protection against sexually transmitted diseases (STDs) such as HIV.

   Handling food with clean hands, storing uncooked meats separately from cooked meats and sterilising knives and work surfaces to prevent transmission of microbes.

   [Provide a link to a relevant source on food hygiene, e.g., BBC Learning Zone clips]
4. **Community responsibility**

Examples include the quality of the water supply. Human drinking water goes through a series of treatments including filtration and **chlorination** to ensure water is free of pathogens.

We have safe food webs. UK manufacturers are obliged to ensure that micro-organisms do not enter the food chain. Milk is pasteurised (heated to 72°C for 15 seconds) to kill the harmful micro-organisms.

Dry refuse is collected on a **regular basis** and **recycled**, incinerated or buried.

There are many methods used to eradicate animals that transmit pathogens. Millions of people die every year of **malaria**. It is caused by a **parasite** which is carried and therefore **spread** by mosquitoes (the **vector**). Control of mosquitoes can be achieved by:

- Draining **stagnant** water to remove breeding sites.
- Introducing **sterile** male mosquitoes to reduce breeding rate.
- Using chemicals like **insecticides** to kill the mosquitoes.

http://www.bbc.co.uk/learningzone/clips/the-malaria-cycle/6989.html

**Epidemiology of infectious diseases**

The epidemiology of an infectious disease is the study of its characteristics such as:

- **Location** of initial outbreak.
- Pattern and **speed** of spread.
- Its geographical **distribution**.

The work is done by epidemiologists who can determine the factors that affect the **spread** of the disease.

The spread of infectious diseases are classified in the table below.

<table>
<thead>
<tr>
<th>Spread pattern of disease</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporadic</td>
<td>An <strong>occasional</strong> occurrence. Scattered or isolated instances no connection between them.</td>
</tr>
<tr>
<td><strong>Endemic</strong></td>
<td><strong>Regular</strong> cases occurring in a particular area.</td>
</tr>
<tr>
<td><strong>Epidemic</strong></td>
<td>Unusually <strong>high</strong> number of cases in a particular area.</td>
</tr>
<tr>
<td><strong>Pandemic</strong></td>
<td>A series of epidemics that spreads across whole continents or even throughout the <strong>world</strong>.</td>
</tr>
</tbody>
</table>
Based on the epidemiological studies control measures can be considered that include:

- Preventing transmission
- Drug therapy
- Immunisation for people not yet affected.

http://www.bbc.co.uk/learningzone/clips/how-the-source-of-cholera-was-discovered-in-victorian-times-drama/13648.html

**Active immunisation and vaccination**

**Immunity** is the process by which a person develops immunity to a disease-causing organism. **Active immunity** is gained as a result of a person’s body producing its own antibodies in response to antigens (foreign proteins).

Active immunity can be developed by vaccination with antigens from an infectious pathogen which is usually mixed with an adjuvant. An adjuvant is a substance that is formulated as part of a vaccine to enhance its ability to induce protection against infection. Adjuvants help to activate the immune system, allowing the antigens to elicit an immune response— in vaccines this helps to stimulate a response that leads to long-term protection.

**Vaccination** is the method of immunisation by which a weakened or altered form of the pathogen (inactivated pathogen toxins, dead pathogens, parts of pathogens or weakened pathogens) is deliberately introduced into the body by injection, ingestion or nasal spray in order to act as an antigen and initiate an immune response.

The antigens induce a primary immune response, which is the production of B and T cells and the formation of antibodies. Some of these B and T cells persist in the body as memory cells. These cells will then initiate a secondary response if the person is exposed to the disease causing antigen at a later date. People can therefore acquire active immunity by an artificial means (vaccination), but not have disease symptoms.

http://www.bbc.co.uk/learningzone/clips/what-are-vaccines-and-how-quickly-can-they-be-made/7134.html
Vaccine clinical trials

Vaccines must be subject to clinical trials in the same way as other pharmaceutical medicines to establish their safety and efficacy (produces the correct result) before being licensed for use.

Before a clinical trial is carried out, the potential treatment undergoes extensive testing on cells and on animals in the laboratory. If the new treatment works then permission from the regulatory authority is sought to start clinical trials.

Clinical trials are:

- Randomised
- Double-blind - the patient and the doctor do not know who is receiving what.
- Placebo-controlled protocols - control group patients are given a fake treatment that takes the same form as the real treatment except it lacks the active ingredient.

The subjects are split into groups in a randomised way in which neither the subjects nor the researchers know which group they are in, in order to eliminate bias. One group receives the vaccine, while the second group receives a placebo control to ensure a valid comparison.

At the end of the trial, results from the two groups, which must be of suitable size to reduce the magnitude of experimental error, are compared to determine whether there are any statistically significant differences between the two groups.

Herd immunity

If a large percentage of a population are immunised, non-immune individuals are protected as there is a lower probability that they will come into contact with infected individuals. This herd immunity is important in reducing the spread of disease and in protecting vulnerable and non-vaccinated individuals. The herd immunity threshold depends on the disease, the efficacy of the vaccine and the contact parameters for the population.
The herd immunity **threshold** is the percentage of **immune** individuals in a population **above which** a disease no longer manages to **spread**. The table below shows the herd immunity for some common diseases - DO NOT LEARN.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Herd immunity threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>83% - 94%</td>
</tr>
<tr>
<td>Mumps</td>
<td>75% - 86%</td>
</tr>
<tr>
<td>Rubella (german measles)</td>
<td>83% - 85%</td>
</tr>
</tbody>
</table>

**Public health medicine**

In most countries, the public health policy for combating a number of common diseases is due to **mass vaccination programmes** that create **herd** immunity to them. In the UK a person's immunity vaccination programme normally begins around the age of 12 months and continues for many years.

Difficulties can arise when widespread vaccination is not possible due to malnutrition and poverty (the **developing** world), or, when vaccines are **rejected** by a percentage of the population (the **developed** world).

http://www.bbc.co.uk/learningzone/clips/measles/7149.html
Evasion of specific immune responses by pathogens

Many pathogens have evolved mechanisms that allow them to evade specific immune responses made by the human body. This makes it possible for a new version of a pathogen to appear that is resistant to the current vaccination program which is intended to give immunity against the original pathogen.

Antigenic variation

Some pathogens can change their antigens. These changes are brought about by mutations. The changes to the pathogen’s antigens avoids the effect of immunological memory, and so the immune system is no longer able to recognise the pathogen as it has been genetically altered. This antigenic variation occurs in diseases like malaria and trypanosomiasis (sleeping sickness) and is one the reasons why it is still common in many parts of the world.

Antigenic variation also occurs in the influenza virus explaining why it is still a major public health problem and why at risk individuals need to be vaccinated every year.

Direct attack on immune system

Pathogenic bacteria have often evolved a means of producing a direct attack on the host’s immune system.

Micro-organisms that invade the body soon come into contact with phagocytes. The bacteria that causes tuberculosis (TB) survives within phagocytes and avoids immune detection. When the phagocyte engulfs the tuberculosis bacterium and then isolates it in a vesicle, the microbes prevent the lysosomes (containing the digestive enzymes) from fusing with the vesicle. Therefore that pathogen remains alive within the phagocyte and avoids immune detection.

HIV (human immunodeficiency virus)

HIV is a virus that attacks lymphocytes and is the major cause of acquired immunodeficiency syndrome (AIDS) in adults. The HIV has glycoproteins attached onto its surface.
These glycoproteins then bind with receptors found on the surface of the T lymphocytes. The HIV virus fuses with the lymphocyte and the virus' nucleic acid is injected into the host cell. The virus is then able to replicate (copy) itself using resources (e.g. free nucleotides and ATP) supplied by the host cell. The replicated virus is then able to escape from the infected lymphocyte and move off to infect other cells.

Web site (up to 1min 25 secs)
http://www.google.co.uk/url?sa=t&rct=j&q=how+HIV+replicates&source=video&cd=2&cad=rja&uact=8&ved=0CCgQtwIwAQ&url=http%3A%2F%2Fwww.youtube.com%2Fwatch%3Fv%3DodRyv7V8LAE&ei=nlCaVLyPFaHbH7AbH5AY&usg=AFQjCNEnqOoKXk488eTskC4wNxFxBVuvCyg
Human African trypanosomiasis or sleeping sickness is a widespread tropical disease that can be fatal if not treated. It is spread by the bite of an infected tsetse fly (Glossina Genus).

The tsetse fly bite erupts into a red sore and within a few weeks the person can experience fever, swollen lymph glands, aching muscles and joints, headaches and irritability.

In advanced stages, the disease attacks the central nervous system, causing changes in personality, alteration of the biological clock (the circadian rhythm), confusion, slurred speech, seizures, and difficulty walking and talking. These problems can develop over many years in the Gambiense form and some months in the Rhodesiense form; if not treated, the person will die.

Control of sleeping sickness is based on reduction of the reservoirs of infection by early diagnosis and control of tsetse flies.