The immune system is a complex network of organs, cells and proteins that defends the body against infection, whilst protecting the body's own cells. The immune system keeps a record of every germ (microbe) it has ever defeated so it can recognise and destroy the microbe quickly if it enters the body again.

1st line of defense

The first line of defense against infection are the surface barriers that prevent the entry of pathogens into the body
Physical and chemical barrier

The Skin Barrier

One of the body's most important physical barriers is the skin barrier, which is composed of three layers. The thin upper layer is called the epidermis. A second, thicker layer, called the dermis, contains hair follicles, sweat glands, nerves, and blood vessels. A layer of fatty tissue called the hypodermis lies beneath the dermis and contains blood and lymph vessels. the epidermis, consists of cells that are packed with keratin. The keratin makes the skin's surface mechanically tough and resistant to degradation by bacterial enzymes. Keratin also helps to make the outer surface of the skin relatively waterproof, this helps keep the surface of the skin dry, which reduces microbial growth.

In addition sebaceous glands and sweat glands in the dermis secrete oily substance called sebum and sweat respectively which act as anticeptic as they contain lactic and fatty acids and the low pH of sebum and sweat inhibits growth of most pathogens.

Mucous Membranes

The mucous membranes lining the nose, mouth, lungs, and urinary and digestive tracts provide nonspecific barrier against potential pathogens. Mucous membranes consist of a layer of epithelial cells bound by tight junctions. The epithelial cells secrete a moist, sticky substance called mucus, which traps debris and particulate matter, including microbes. Mucus secretions also contain antimicrobial peptides.

Cilia

The epidermal cells of the respiratory passage are lined with the cilia. The microorganism trapped in the mucous of the respiratory passage are swept away by the constant movement of these cilia.

Hairs inside the nose may trap larger pathogens and other particles in the air before they can enter the airways of the respiratory system

Secreation of the digestive tract

The high acidity of the stomach has a microbial effect and this is due to the presence of HCl in the gastric juice

. Also, lysozyme found in tears, sweat, and saliva acts as a vital antimicrobial agent to destroy pathogens.

Mechanical barrier

- Mechanical defenses include the flushing action of urine and tears which carry microbes away from the body. The flushing action of urine is largely responsible for the normally sterile environment of the urinary tract, which includes the kidneys, ureters, and urinary bladder.

- The eyelashes and eyelids prevent dust and airborne microorganisms from reaching the surface of the eye.
- Mechanical action of Coughing and sneezing help in driving out the foreign particlesthat enter the respiratory tracts.

2nd line of defense

- The second line of defense are the non-specific phagocytes and other internal mechanisms that comprise innate immunity

- The second line of defense includes the inflammatory response and phagocytosis by nonspecific leukocytes

1. **Inflammation**

   Inflammation is the 1st response of the body to protect tissues from infection, injury or disease. The inflammatory response begins with the production and release of chemical agents by cells in the infected, injured or diseased tissue. These agents cause redness, swelling, pain, heat and loss of function. Inflamed tissues generate additional signals that recruit leukocytes to the site of inflammation. Leukocytes destroy any infective or injurious agent, and remove cellular debris from damaged tissue.

2. Phagocytosis

Phagocytosis is an important feature of innate immunity that is performed by cells classified as phagocytes. In the process of phagocytosis, phagocytes engulf and digest pathogens or other harmful particles. Macrophages, cytotoxic T cell, dendritic cells are example for phagocytes.

3. Neutrophils

Neutrophils are leukocytes that travel throughout the body in the blood. They are the first immune cells to arrive at the site of an infection. They are the types of phagocytes, and they accounting for about 50-60% of the circulating white blood cells. Their primary function is to prevent infections in the body by engulfing and destroying invading pathogens

4. Monocytes

they accounting for about 3-8% of the circulating white blood cells. They are precursors of tissue macrophages and dendritic cells. Before they enter the tissues monocytes circulate in the blood for 1-3days. Monocytes migrate quickly and are usually 2^{nd} cell after neutrophiles arrive at the site of infection

5. **Macrophages**

When monocytes enter the tissues and become macrophages they do not re-enter the circulation. They are the most efficient phagocytes, and they can phagocytize substantial numbers of pathogens or other cells. Macrophages are also versatile cells that produce a wide array of chemicals — including enzymes, complement proteins, and cytokines — in addition to their phagocytic action. As phagocytes, macrophages act as scavengers that rid tissues of worn-out cells and other debris, as well as pathogens. In addition, macrophages act as antigen-presenting cells that activate the adaptive immune system.

6. **Dendritic Cells**

Like macrophages, **dendritic cells** develop from monocytes. They reside in tissues that have contact with the external environment, so they are located mainly in the skin, nose, lungs, stomach, and intestines. Besides engulfing and digesting pathogens, dendritic cells also act as antigen-presenting cells that trigger adaptive immune responses.

7. **Eosinophils**,

Eosinophils so named because of their intense colour when stained with eosin.They specialize in defending against parasites. They are very effective in killing large parasites (such as worms) by secreting a range of highly-toxic substances when activated. Eosinophils may become overactive and cause allergies or asthma.

8. **Basophils**

Basophils are non-phagocytic leukocytes that are related to neutrophils. They are the least numerous of all white blood cells. Basophils secrete two types of chemicals that aid in body defenses: histamines and heparin. Histamines are responsible for dilating blood vessels and increasing their permeability in inflammation. Heparin inhibits blood clotting, and also promotes the movement of leukocytes into an area of infection.

9. **Mast cells**

Mast cells are non-phagocytic leukocytes that help initiate inflammation by secreting histamines. In some people, histamines trigger allergic reactions, as well as inflammation. Mast cells may also secrete chemicals that help defend against parasites.

10. **Natural Killer Cells**

- Natural killer or NK cells are a part of innate immunity and they do not have antigen-specific receptors present on the surface. They play a major role in eliminating tumour cells and infected cells. They distinguish the normal cells from the infected or cancerous cells by MHC class I surface molecules, which is absent in most of the abnormal cells.

- NK cells are also activated by cytokines known as interferons. Activated natural killer cells release cytotoxic granules, which kill infected cells.

Immunity

- Immunity is the ability of the body to defend itself against disease-causing organisms.

Types of Immunity

There are two major types of immunity:

1. Innate Immunity or Natural or Non-specific Immunity.
2. Acquired Immunity or Adaptive Immunity.

Innate Immunity

- This type of immunity is present in an organism by birth.
- Innate immunity is non-specific because it does not depend on previous exposure to foreign substances
- This is activated immediately when the pathogen attacks.

- Innate immunity includes certain barriers and defence mechanisms that keep foreign particles out of the body.

Innate immunity can be categorized based on individual, racial and species

1. Individual Immunity – Sometimes, individuals belonging to the same race and who have been exposed equally to the virus, pathogens or worms can show a different level of immunity to a disease or infection This can be due to health, age and hereditary traits

2. Racial Immunity – When one race is immune to a certain disease, and another race is susceptible to it, it is referred to as racial immunity factors such as genetic make-up, food habits, climate conditions play an essential part in determining racial immunity.

3. Species Immunity – When a disease attacks a species only and another species is entirely immune to it, it is known as species immunity. For example, Birds are resistant to anthrax but Human are susceptible.

Cells involved in innate immunity

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Cells Involved In Innate Immunity

- Phagocytes: These circulate through the body and look for any foreign substance. They engulf and destroy it defending the body against that pathogen.
- Macrophages: These have the ability to move across the walls of the circulatory system. They release certain signals as cytokines to recruit other cells at the site

of infections.

- Mast Cells: These are important for healing wounds and defence against infections.
- Neutrophils: These contain granules that are toxic in nature and kill any pathogen that comes in contact.
- Eosinophils: These contain highly toxic proteins that kill any bacteria or parasite in contact.
- Basophils: These attack multicellular parasites. Like the mast cells, these release histamine.
- Natural Killer Cells: These stop the spread of infections by destroying the infected host cells.
- Dendritic Cells: These are located in the tissues that are the points for initial infections. These cells sense the infection and send the message to the rest of the immune system by antigen presentation.

Acquired immunity

- Acquired immunity or adaptive immunity is the immunity that our body acquires or gains over time. Unlike the innate immunity, this is not present by birth.
- An individual acquires the immunity after the birth, hence is called as the acquired immunity.
- It is specific and mediated by antibodies or lymphocytes

There two types of acquired immunity are active and passive immunity

1. **Active aquired Immunity**

- the immunity which results from the production of antibodies by the immune system in response to the presence of an antigen

- Active immunity can be acquired through natural immunity or artificial immunity.
- **Naturally acquired active immunity** involves the development of an immune response when an individual comes in contact with disease causing pathogens. In this case, the individual's immune system starts producing antibodies For example-children who develop chickenpox and recover from the illness, get better because they have made an effective immune response against the chickenpox
- **Artificial acquired active immunity** is the type of immunity which is acquired artificially by vaccination. Vaccines contain dead or live but attenuated (weakened) pathogens The vaccine is introduced into the body to stimulate the formation of antibodies by the immune system. For example, polio vaccine available which helps to provide protection from poliomyelitis.

2. **passive immunity**

- When ready-made antibodies are directly injected into a person to protect the body against foreign agents, it is called passive immunity. It provides immediate relief. Passive immunity may be natural or artificial.

1. **Naturally acquired passive immunity**

   Natural passive immunity is the resistance passively transferred from the mother to the foetus through placenta. IgG antibodies can cross placental barrier to reach the foetus. After birth, immunoglobulin's are passed to the new-born through the breast milk.

2. **.Artificial acquired passive immunity**

   Artificially acquired passive immunity results when antibodies or lymphocytes produced outside the host are introduced into a infected host. example of artificial passive immunity is an injection such as snake anti-venom.

Primary and secondary immune response

- A primary Immune Response occurs when the body's immune response encounters an antigen for the first time.
- During this immune response, the body learns to recognize the antigen, produce antibodies against the antigen, and induce a long-term memory response against the antigen.
- This response involved the activation of naive B-cells and naive T-cells.
- The response lasts about 14 days to resolve.
- There are four phases of immune response that take place when the body responds to an antigen for the first time.

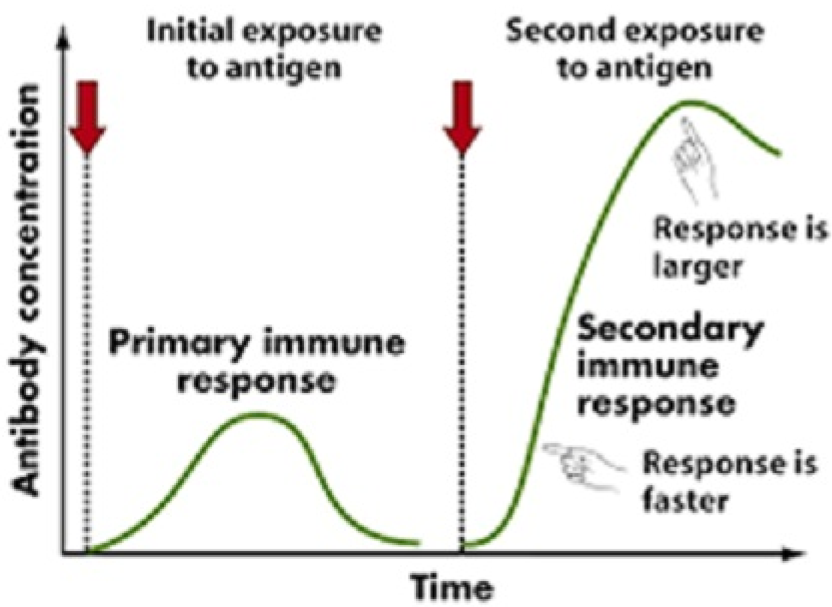
1. The lag (latent) phase
2. The exponential phase
3. steady state phase (plateau phase
4. declining phase

1. The lag (latent) phase- is the period from the initial exposure of immunogen to the time of detection of antibodies (In humans the average time of lag phase is about one week). During this lag phase specific T cells and B cells are activated by their contact with immunogen.
2. The exponential phase- is the period during which there is a rapid increase in antibody levels due to secretion of antibodies by many plasma cells.
3. steady state phase (plateau phase)- The antibody level remains relatively at a constant level because the secretion and degradation of antibodies occur almost at equal rates.
4. declining phase- The antibody level gradually declines because new plasma cells are no longer produced and the existing plasma cells are dying. This generally indicates that the immunogen has been eliminated from the body and consequently there is no stimulus for continued antibody production.

Secondary response-

- Secondary response occur when a similar antigen enters the host for the second and subsequent times, the immune responses induced are called secondary immune responses.

- This response is mediated by the memory lymphocytes that were produced during the primary response. Immediately after the same antigen is encountered the memory lymphocytes induce the production of antibodies.
- The lag phase is usually very short (e.g. 3 or 4 days) due to the presence of memory cells. and The antibody production levels increase rapidly within a short period, normally within a few days This is because of the antigen-specific memory T and B-cells produced during the primary response.
- During this response the antibodies remain in circulation for a longer period.
- Because of the rapidity of the secondary response, the antigen gets eliminated as soon as it encounters the memory cells and before it can cause disease.



Antigen presenting cells (APC)

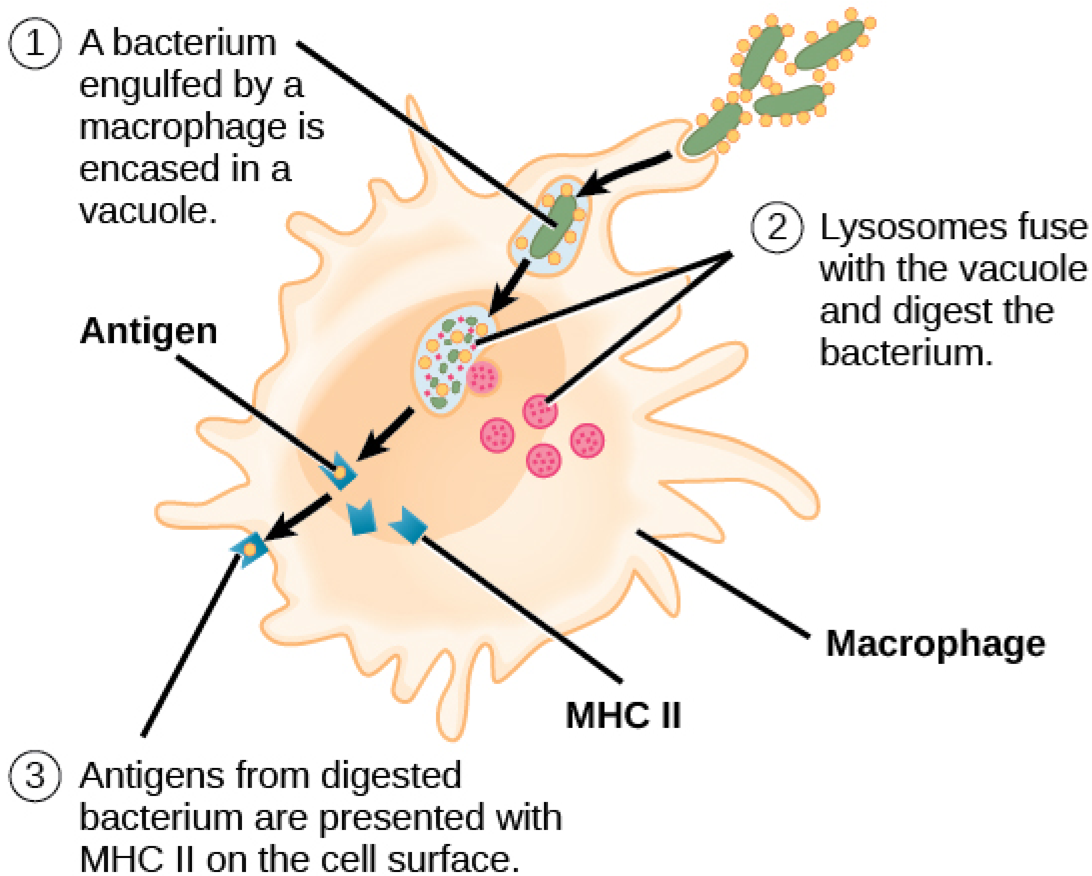
- Antigen presenting cells are a group of immune cells that are capable of processing and presenting antigens for recognition by T cells to initiate the adaptive immune responses.

- T cells cannot recognize antigens on its own. They can only recognize and respond to antigen that has been processed and presented by APC cells

- B-lymphocytes, macrophages, and dendritic cells are the three primary antigen-presenting cells.
- They constitutively express class II MHC comlex on their surface and they activate helper T cells.

Mechanism

  - when a pathogen such as a bacteria, virus are enter to the body the APC cells engulf the pathogen . Once inside the APC Cells, the pathogen becomes enclosed within an intracellular vesicle called a phagosome. The phagosome then fuses with another vesicle called a lysosome, forming a phagolysosome. in which it is degraded into antigen fragments then this ultimately associate with class II MHC molecules transported to surface of the cell then this MHCII-peptide complex is recognized by helpet T cells which induce adaptive immune response



B lymphocytes

- B lymphocytes or B cell is a type of lymphocytes
- In humans and some other mammals, the main site of B lymphocytes development and maturation is the bone marrow.
- Once B cell encounter antigen it multiply rapidly and differentiates to become either memory B cells or plasma cells.

- Plasma cells: Plasma cells produce antibodies in response to antigens , hence they are known to trigger the humoral immune response Once a B-cell becomes a mature plasma cell, it can release up to 2,000 antibodies per second. Plasma cells are also called plasmacytes or effector cells. They have a shorter lifespan than memory cells.

- Memory cells: Memory B cells are formed after primary infection and they remain in the blood for decades. They circulate in the blood, identify and act against previously infected antigens. Memory cells remember particular antigens so, if they appear in the body in the future they differentiated into plasma cells and produce antibodies . For example, most vaccines work because they expose immune system to antigens that the memory cells remember. If an invader appears, body can mount an attack quickly.

T Lymphocytes

- T cells get their name from the site of maturation, i.e. thymus.
- T cells also have surface receptors to recognize antigens but they do not directly bind to the antigens like surface receptors on B cells.
- It recognize an antigen when they bind with major histocompatibility complex (MHC) molecules on the surface of the APC cells.

T lymphocytes differentiate into three main subtypes:

1. **T helper (T_H) cells-**
    - They generally contain CD4 membrane glycoprotein on their surface and recognise antigens with class II MHC.
    - The major function of Helper T-cells is stimulate the B-cells to make antibodies
    - T helper cells also trigger different types of immune cells to act against the antigens like macrophages, B lymphocytes and cytotoxic T cells.
    - They also secrete different types of cytokines, which mediate inflammation and regulate other types of immune cells.
2. **T cytotoxic (T_C) cells-**

- They generally contain CD8 membrane glycoprotein on their surface and recognise antigens with class I MHC.

- cytotoxic T lymphocytes eliminates virus-infected cells, tumour or cancerous cells and also foreign grafts, etc.

3. **regulatory T cell-**

   - it is a type of immune cell that blocks the actions of some other types of lymphocytes, to keep the immune system from becoming over-active. thereby maintaining the homeostasis and self-tolerance.

   - regulatory T cell are able to inhibit T cell proliferation and cytokine production and play a critical role in preventing autoimmunity.

4. **The memory T cells** are antigen-specific T cells which have a longer life span. They play a key role in rapid immune response on the re-exposure of a pathogen. They are responsible for the secondary response.

cell mediated immunity

- cell-mediated immunity does not depend on antibodies for its adaptive immune functions.

- Cell-mediated immunity is primarily driven by mature T cells, macrophages, and the release of cytokines in response to an antigen.

mechanism

- it begins when an invading bacteria is engulfed by an antigen presenting cells inside the APC Cells, the pathogen becomes enclosed within an intracellular vesicle called a phagosome a lysosome containg digestive enzymes combines with the phagosome to process the antigen

- the processed antigens combine with the MHCII molecules and are presented on the surface of the APC

- Helper T cells (CD4+) recognize the displayed antigen on the APC with the help of CD4 receptor and bind to the MHC class II- antigenic peptide complex

- The activated helper T cell releases the cytokine which stimulates the cytotoxic T cell which kill the infected cells it also attract other immune cells to the site of infection.
- The cytotoxic T cell releases perforine molecule which makes hole in the cell membrane pathogen resulting in the lysis of bacterial cell.

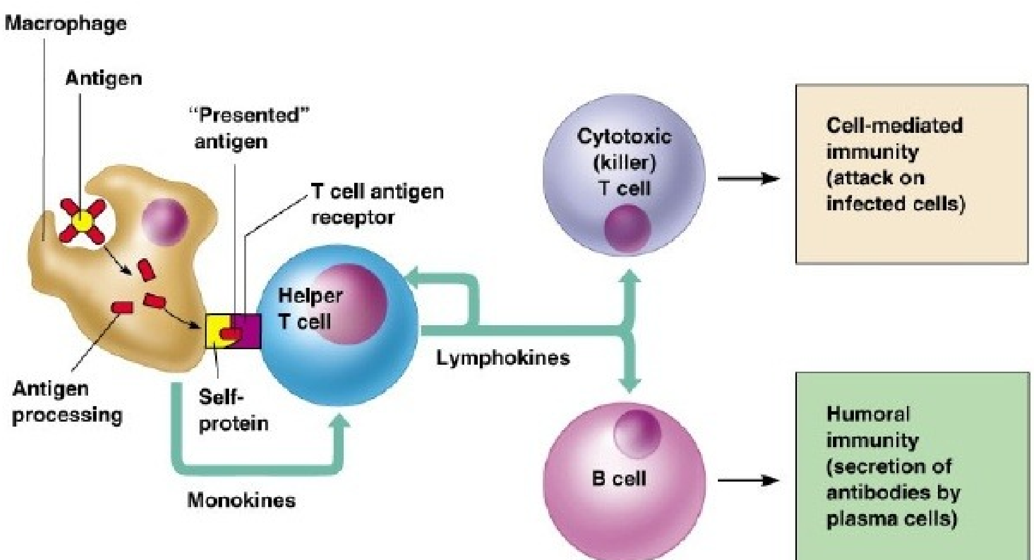


Figure 12.15

humoral mediated immunity

- Humoral immunity is an antibody-mediated response that occurs when foreign material – antigens - are detected in the body.

- This mechanism is primarily driven by B cell lymphocytes a type of immune cell that produces antibodies after the detection of a specific antigen.
- It's also called *"antibody-mediated immunity"* as antibody production is one of the notable features of this immunity

mechanism

- it begins when an invading bacteria is engulfed by an antigen presenting cells inside the APC Cells, the pathogen becomes enclosed within an intracellular vesicle called a phagosome a lysosome containg digestive enzymes combines with the phagosome to process the antigen
- the processed antigens combine with the MHCII molecules and are presented on the surface of the APC
- Helper T cells (CD4+) recognize the displayed antigen on the APC with the help of CD4 receptor and bind to the MHC class II- antigenic peptide complex
- The activated helper T cell releases the cytokine which stimulates the B cell to divide and differentiated into antibody producing plasma cells and memory cells
- The plasma cells produces antibodies. These antibodies binds to the antigen in a lock and key fashion. This makes easier for killer cells to attack and destroy the bacteria by phagocytosis
- The activated B cells and T cells differentiated into memory cell this brings secondary immune response when the same antigen enters the body for the second time

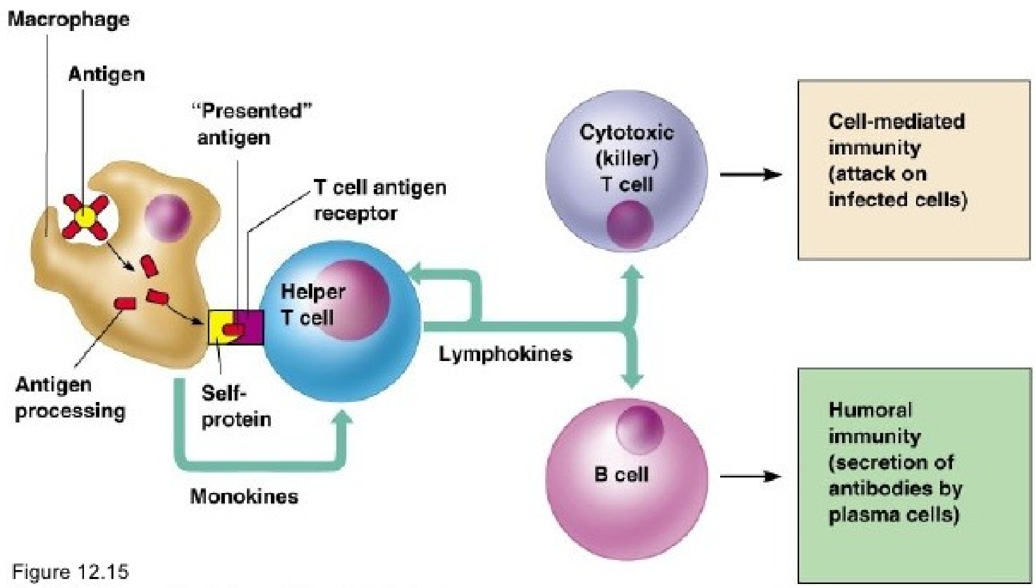


Figure 12.15

Hapten

A hapten is a substance that can combine with a specific antibody but lacks antigenicity of its own. Many small molecules of Mr < 1000 such as toxins, drugs and hormones are not capable of invoking immune response when injected directly into animals. They are thus not immunogenic by themselves, and are called haptens.

they stimulates the production of antibody only when conjugated to a larger molecule, called a carrier molecule.