

Immune system.

One of the more complex systems we're looking at.

An immune response (a response to a pathogen) can be of two types:

(pathogen - disease causing organism)

1) Non specific. Anything foreign is attacked.

2) Specific. The immune system attacks only one kind of pathogen.

I. Non-specific defenses (could be labeled innate defenses):

- skin: acts as a barrier, also secretes acids that inhibit bacteria.
- body fluids: sweat, saliva, tears, all contain anti-microbial enzymes
- stomach acid: kills many bacteria
- mucous membranes in nose and trachea trap many pathogens.

If something does get through, the first line of defense is generally an inflammatory response [**Fig. 24.2, p. 487**]:

tissue damage --> histamine is released by damaged cells --> dilates blood vessels
--> blood flow to the damaged area increases --> increasing number of
phagocytes show up.

Phagocytes engulf ("eat") bacteria and damaged cells. They disinfect the area.

In the process, they often die and contribute to the pus found in inflamed areas.

This inflammatory response can be more widespread:

- bacteria in blood stream can cause overall increases in phagocytes.
- fever can sometimes slow bacterial growth, though if too high this is dangerous.
- immune system can be overwhelmed and respond massively, generating septic shock (a common cause of death in hospitals).

Other nonspecific responses include:

- release of interferon (inhibits viral replication)

- a cell infected with a virus makes interferon. This triggers proteins in other cells that slow viral replication [Fig. 24.1B p. 486].

- complement proteins - interact with microbes or the immune system.

- mark surfaces of microbes so that phagocytes can get them easier.

- sometimes cut holes in microbial membranes, killing or weakening the microbes

Lymphatic system [Fig. 24.3, p. 488]

- in addition to moving interstitial fluid back to the heart (& circulatory system), the lymphatic system also helps remove pathogens.

- lymph nodes are packed with lymphocytes & phagocytes

- these can filter the fluid, attack bacteria & viruses.

- attack can be specific or non-specific.

- efficient system since much fluid in the body is filtered this way.

II. Specific defenses (acquired immunity)

Some definitions:

antigen - a molecule (usually on the surface of a bacterium or virus) that causes an immune response.

An antigen may have several different “antigenic determinants”. These are areas that antibodies can bind to. [Fig. 24.6, p. 491]

antibody - a protein that attaches to a specific antigen (antigenic determinant).

Lymphocytes:

Two types (both originate in the bone marrow):

B-cells: continue to develop in bone marrow. They provide immunity within body fluids.

T-cells: continue to develop in the thymus (exact process is not well understood). They provide immunity to infected cells & help B-cells.

Both B & T cells have antigen receptors on their surfaces (think of these as antibodies attached to the cell membrane). When mature, both move to the lymph nodes.

Humans are thought to have over 100 million different antigen receptors. Most are never needed.

- each cell has only one kind of antigen receptor (up to 100,000, all identical).

B-cell defenses:

- B-cells congregate in lymph nodes [**OVERHEAD, fig. 24.7A, p. 492**].

- as an antigen comes along, some of the B-cells may bind to the antigen (only if they have the correct antigen receptor).

- this triggers cell growth & differentiation.

- effector cells are made that start producing large amounts of antibody specific to the antigen. A group of effector cells made like this are referred to as clones. They usually do not survive long.

- some cells are converted into memory cells that can respond much faster should the body be exposed to the same antigen in the future.

- The first time B-cells are exposed, the immune response can be slow and not very strong.

- But memory cells are now in place, and if the same antigen comes along again, they can multiply very quickly and produce large amounts effector cells quickly (a second clone) [**Fig. 24.7B, p. 493**].

Antibodies:

- antibodies have a variable end (specific to antigen determinants) and a constant end (actually, there are about 5 different “constant” ends, each of which specializes the antibody for slightly different functions).

- the variable end binds to the antigen (i.e., virus, bacteria, parasite). This can have four possible consequences [**Fig. 24.9, p. 495**]:

- 1) Virus or bacterium is coated with antibodies. This can prevent

the virus or bacteria from attaching to other cells.

2) Since antibodies are Y-shaped, they can bind to more than one virus or bacterium. This causes them to clump together. This makes it easier for phagocytes to capture them.

3) Antigen molecules can precipitate out. They're no longer dissolved in the body fluids, and so are easier for phagocytes to capture.

4) Antibodies activate complement proteins (from above). These cause holes in the bacterial membrane and kill it.

- also, depending on the type of constant end, the constant end is more easily recognized by phagocytes (so if antibodies are attached to bacteria, these are more easily recognized).

T-cell defenses:

- fight against pathogens that have already entered cells of the body (& help B-cells).

- Two types of T-cells:

- Cytotoxic: attack infected body cells.

- Helper T-cells: activate cytotoxic T-cells, phagocytes, & help stimulate B-cells to make antibodies.

Suppose a phagocyte (macrophage) engulfs a microbe [Fig. 24.11, p. 497].

- It may become an APC (antigen presenting cell).

- exactly what it says. It presents the antigen to the helper T-cell.

- It combines the antigen with its own surface proteins in something known as the self-nonself complex (it's a combination of its own proteins (self) and the antigen (non-self)).

- This is recognized by the helper T-cell. The helper T-cells then does three things:

1) makes more helper T-cells of the same kind.

- including memory T-cells.

2) activates cytotoxic T-cells (for that antigen).

3) activates B-cells (for that specific antigen).

Cytotoxic T-cells [OVERHEAD, fig 24.12, p. 498]:

- attack cells in the body that are infected. An infected cell will have a self-nonsel complex on it's surface.

- This is recognized by the cytotoxic T-cell.

- the cytotoxic T-cell releases perforin, which punctures the infected cell membrane which is then destroyed.

- appear to function against many kinds of cancers as well (cancers are abnormal body cells that keep dividing).

III. Miscellaneous topics:

The immune system recognizes self vs. non-self. Anything that isn't "self" may be attacked.

- this is the problem with many organ transplants.

Even so, the immune system will sometimes run haywire:

Diabetes (type I) results when the immune system destroys insulin producing cells (the beta cells in the pancreas).

Multiple sclerosis results when the myelin sheath of the nervous system is attacked (destroys nerve cell function).

Rheumatoid arthritis - joints are attacked by the immune system.

- the list is endless.

At the other extreme, the immune system can overreact to essentially "harmless" antigens [Fig. 24.17, p. 501].

Allergies are caused by histamines being released in response to things like pollen or dander.

For example, antibodies for pollen attach to mast cells (cells that make histamine). When these cells encounter an antigen (pollen in this case), histamine is released

and can cause symptoms related to allergies (itching, sneezing, etc.).

Anaphylactic shock can result in extreme cases (causes massive dilation of blood vessels, precipitous drop in blood pressure, and even death).

Two diseases that are responsible for more deaths than any other (we won't discuss tuberculosis, the third big killer):

AIDS

Destroys helper T-cells. As such, the body can not defend itself against (usually) quite harmless diseases. Most people with AIDS die from unrelated diseases caused by a breakdown of the immune system.

- don't confuse HIV with AIDS (AIDS is the disease, HIV the virus - people can live with the virus for years before developing AIDS).

- the virus keeps changing until the immune system is overwhelmed.

- drugs can be used to treat (but not cure) AIDS, but they are very expensive and can be more difficult to get in poor parts of the world.

Malaria

Malaria is a single celled parasite. It infects red blood cells. The parasite reproduces inside red blood cells, the red blood cells burst, releasing thousands of new parasites that go on to infect other red blood cells. The cycle repeats, each time destroying more red blood cells.

- the cycle is timed - blood cells rupture periodically, which is why people with malaria get a fever every "x" hours.

- the parasite has thousands of antigens, and as it grows, makes even more antigens. The immune system doesn't know what to do with so many antigens.

- additionally, the parasite spends considerable time inside red blood cells, and for some reason, these do not generate an immune response.

- Malaria is increasingly difficult to treat since it has evolved resistance to many common anti-malaria drugs.

Finally, just a diseases that changes itself:

Sleeping sickness or *Trypanosoma brucei*

- One reason why some parts of Africa are still wild.
- People won't enter areas where sleeping sickness is endemic (kills people and livestock).
- Transmitted by the bite of the tsetse fly.
- Symptoms include high fever, swelling of lymph nodes, headaches, itching (much of this is actually caused by the immune system reaction to the parasite).
 - Eventually, the nervous system becomes more involved - slurred speech, slowing of mental processes, prolonged periods of sitting and staring, sleeping.
- Untreated, usually leads to death.
- Treatments are extreme, and involve administration of various toxic compounds (often containing arsenic) and the hope that the parasite is killed before the patient.

Circumvents immune system as follows:

- Worm presents antigen to immune system
- Immune system reacts normally, and parasite is attacked
- After parasite levels drop, parasite presents a different antigen to the immune system
- Levels of parasite climb again, until immune system responds to this new antigen
- Worms have a repertoire of over 1000 different antigens that they can present to the immune system.