Immune system.

This is one of the more complex systems we're looking at, mostly because we need to look at the cellular level to really understand what's going on.

First some definitions:

Immune response is a response by your immune system to some type of pathogen.

A *pathogen* is a disease causing organism.

An immune response can also occur when you are exposed to things like toxins.

Immune responses can be divided into two broad groups:

1) Non specific. Anything foreign is attacked.

Generally provides a good initial defense, but often isn't terribly powerful.

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

This can be a much stronger response; generally occurs after the pathogen gets into your body.

I. Non-specific defenses (sometimes called *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: these trap many pathogens and other debris in such areas as the nose, mouth and lungs.

Acidity in the vagina and in the urethral tract (of both sexes): kills many potentially harmful bacteria and viruses.

Openings to the body are protected by some type of barrier.

However, despite all this, pathogens do occasionally get through

For example, you cut yourself.

This triggers and *inflammatory response* **[Fig. 24.2, p. 487]**:

tissue damage → histamine is released by damaged cells → dilates blood vessels
↓
allows the number of ← blood flow to the damaged areas increases
phagocytes in the area
to increase.

Phagocytes are “eating cells” and 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 the blood stream can cause an overall increases in phagocytes.

The inflammatory response can also trigger fevers, which are thought to slow bacterial growth.

Obviously this can also be dangerous.

Sometimes the immune system can be overwhelmed and/or respond massively

This can lead to septic shock (a common cause of death in hospitals).

Other nonspecific responses include:

Release of *interferon* (this inhibits viral replication)

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

Interferon can be used to cure the common cold, but it has very nasty side effects and is very expensive (we need a practical cure!).

Complement proteins - these interact with microbes or the immune system.

Mark the surfaces of microbes so that phagocytes can find them easier.

Sometimes cut holes in microbial membranes, killing or weakening the microbes

Have a variety of functions and can also work with the specific defenses.

. 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.

The lymph nodes are packed with lymphocytes & phagocytes.

These filter the fluid.

The lymphocytes and phagocytes can attack bacteria & viruses (and other pathogens or toxins).

The attack can be specific or non-specific.

It's an efficient system since much of the fluid in the body is filtered this way.

II. Specific defenses (sometimes termed *acquired immunity*)

Some definitions:

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

An antigen may have several different "antigenic determinants". These are areas that antibodies actually bind to. **[Fig. 24.6, p. 491]**.

Note: we won't worry too much about the difference between antigens and antigenic determinants (we'll just refer to everything as an antigen).

Comment: all cells (including our own) have molecules on the surface that perform various important functions.

One of the jobs of the immune system is to figure out which "molecules" belong to our bodies, and which belong to pathogens.

antibody - a protein that attaches to a specific antigen (technically the antigenic determinant, but see note just above).

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.

T-cells in particular are important in recognizing the body's own cells; the idea is that they will attack anything they don't recognize.

Once mature, both types congregate in the lymph nodes.

Both B & T cells have *antigen receptors* on their surfaces

Antigen receptors are very similar to antibodies. Think of them as antibodies that stay attached to the cell membrane.

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

Important: Each individual cell has only *one kind* of antigen receptor

Each cell may have up to 100,000 antigen receptors, but they're all identical.

B-cell defenses:

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

Suppose an antigen comes along

Some of the B-cells may have the correct antigen receptor to bind with this antigen.

If they do, this this triggers cell growth & differentiation. Two things happen.

Effector cells are made

These start producing large amounts of antibody specific to the antigen.

A group of effector cells like this are referred to as *clones*. They usually do not survive long.

Some cells are converted into *memory cells*.

Memory cells can respond much faster should the body be exposed to the same antigen in the future.

The first time B-cells are exposed to a particular antigen, the immune response can be slow and take a while to build up strength.

But if memory cells are in place, and if the same antigen comes along again, the response is much quicker and much stronger.

Memory cells can multiply very quickly and produce large amounts of effector cells (a second clone) **[Fig. 24.7B, p. 493]**.

This, incidentally, is the basic idea behind immunizations.

You get an injection with something that triggers this particular immune response without making you sick

Now you have memory cells, and if you're exposed to the actual pathogen, your immune system responds almost instantly.

Bottom line - you don't get sick (if everything works as it should).

Antibodies:

Antibodies have a variable end (specific to a particular antigen) 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., the virus, bacteria, parasite, toxin, etc.). This can have four possible consequences **[Fig. 24.9, p. 495]**:

1) The virus or bacterium is coated with antibodies. This can prevent the virus or bacteria from attaching to other cells.

2) Since many 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) Antibodies can bind to antigens that are dissolved blood/fluid. This causes the antigens to precipitate out. They're no longer dissolved in the body fluids, and so are easier for phagocytes to capture.

The first three responses all help phagocytes find the pathogen or toxin.

The variable end acts as a "sign post" to phagocytes.

Phagocytes then come along and eat the virus/bacterium/parasite/toxin, etc.

4) Antibodies activate complement proteins (see above). These can cut holes into membranes and kill pathogens.

T-cell defenses:

Cells in the body can be infected with viruses and other pathogens that actually move inside the cell.

Somehow the body needs to recognize infected cells and deal with them.

T-cells fight against pathogens that have already entered cells of the body

They also help B-cells.

There are two types of T-cells that we will be concerned with:

Cytotoxic: these are the ones that actually attack infected body cells.

Helper T-cells: perform several functions:

They activate cytotoxic T-cells.

Stimulate the appropriate B-cells to make antibodies.

Make memory T-cells.

Suppose a phagocyte or macrophage engulfs a microbe **[Fig. 24.11, p. 497]**.

This phagocyte may then an APC (**a**ntigen **p**resenting **c**ell).

This is exactly what it says. It takes surface molecules from the pathogen and presents these "antigens" to the helper T-cell.

The APC combines the antigen with some of it's own surface proteins in something known as the self-nonself complex

This is a combination of its own proteins (self) and the antigen (non-self).

This self-nonself complex 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 (specific for that antigen).

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

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

Cytotoxic T-cells attack cells in the body that are infected.

An infected cell will have a self-nonself complex on it's surface.

This complex is recognized by the cytotoxic T-cell.

Once the cytotoxic T-cell recognizes/attaches to an infected cell it does two things:

1) releases perforin, which punctures the infected cell membrane; this can destroy the infected cell.

2) releases enzymes that promote *apoptosis*

This literally causes cells to self-destruct.

Cytotoxic T-cells are also very important in fighting off 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.

Foreign organs have surface markers (antigens) that are not recognized, so they're attacked by the immune system.

Auto-immune diseases: the immune system will sometimes attack cells in the body:

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 (this destroys nerve cell function).

Rheumatoid arthritis - joints (particularly the cartilage) are attacked by the immune system.

The list of auto-immune diseases is endless.

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

Despite the fact that the immune system often attacks anything foreign, there seems to be a way it can recognize harmless substances like pollen, dander, etc.

If the immune system overreacts to these "harmless" substances (antigens), we get an allergic reaction.

For example:

The body is exposed to pollen, and starts making antibodies for them.

Some antibodies attach to mast cells.

When mast cells come in contact with the pollen that they recognize, they release histamine.

Histamine, as mentioned, causes swelling, itching, etc.

Allergies can be treated in a variety of ways (steroids, antihistamine, allergy shots, others)

(Note that the old-fashioned antihistamines may cause drowsiness, but are generally more powerful than the newer ones).

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

IV. Some examples of diseases and how they interact with the immune system:

HIV/AIDS

Destroys helper T-cells.

Without helper T-cells 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.

(Incidentally, HIV refers to the virus, AIDS is the actual disease - 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.

AIDS is a serious problem in Africa and some other areas.

Some countries in Africa have infections rates higher the 30%.

Malaria

Malaria is caused by a single celled parasite.

It infects red blood cells.

The parasite enters a red blood cell, reproduces, and then "bursts" the red blood cell.

This releases thousands of new parasites, each of which then goes on to infect a new red blood cell.

This cycle repeats, each time destroying more red blood cells.

Often this 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, it makes even more antigens. The immune system has a hard time figuring out 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.

(There are some vaccine trials, but we're probably years away from anything really effective).

Finally, a rather odd disease: Sleeping sickness or *Trypanosoma brucei*

Caused by a single celled parasite.

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).

Initially, if caught early, the disease is not difficult to cure.

Unfortunately, the parasite can cross the “blood-brain barrier”.

This involves the nervous system becomes.

The result is slurred speech, slowing of mental processes, prolonged periods of sitting and staring, and just sleeping.

At this point it is very difficult to treat.

Treatments are extreme, and usually involve administration of various toxic compounds (often containing arsenic)

Generally the hope is that the parasite is killed before the patient.

Untreated, sleeping sickness almost always leads to death.

The parasite can circumvent the immune system:

The parasite presents an antigen to the immune system.

The immune system reacts normally, makes antibodies, and the parasite is attacked

The parasite levels drop, the parasite can change it's antigens and present a different to the immune system.

As a result, the levels of parasite climb again, until immune system responds to the new antigen.

The parasite then picks another antigen and the cycle starts over. The parasites have a repertoire of over 1,000 different antigens that they can present to the immune system.

Eventually the immune system looses (particularly once the parasite crosses the blood-brain barrier)

One minor point:

Sleeping sickness is one of the reasons why some parts of Africa are still wild.

People won't enter areas where sleeping sickness is endemic (it kills people and livestock).