The immune system distinguishes “self” from “non-self”

When we think of the immune system, we often only think that it protects us from pathogens (bacteria, viruses, fungi, parasites)

But, the immune system also removes dead or damaged cells (“housekeeping”)

Works to recognize and destroy abnormally functioning cells (i.e. protect us from cancer)

What is a pathogen?

In developed countries (like the U.S.) we really only have to worry about viruses and bacteria

Worldwide, parasites can be a major concern

Malaria is transmitted by mosquitoes (~100 million infected worldwide)

Others enter via the digestive tract, or are inhaled

Red blood cells infected with malaria

One method to cure them all? - sort of.

Some methods of keeping us well are not “immune responses” at all, but simply physical or chemical barriers

Our skin, mucus, and stomach acid are examples of these barriers (lysozyme, etc)

However, if a pathogen does get into the body, the same set of steps is followed to remove it:

Detection and identification of the substance
Communication between immune system cells
Recruitment and coordination
Destruction or suppression of the invader
We have evolved both acquired and innate immunity

By definition, barriers are innate (we are born with these), but this “branch” of immunity also includes:

**Natural Killer Cells (NK Cells)** respond to viral infections quickly
- They attack cells infected by virus and induce them to self-destruct (apoptosis), ceasing replication of the virus
- Release cytokines, including interferons (which interfere with viral replication)
- Interferons can target host cells or activate macrophages

**Cytokines** are released by activated macrophages and initiate the inflammation response:
- Immune cells are attracted to the site of damage
- A physical barrier is put in place to prevent the spread of infection
- Promotes tissue repair
We have evolved both acquired and innate immunity.

Many other types of cytokines are released as well:

- Acute Phase Proteins following injury
- Histamine, a powerful vasodilator, opens pores in capillaries to encourage inflammation
- Interleukins play several roles in the body, mostly mediating the immune response by acting as a liaison between tissues
- Bradykinin vasodilates and simulates pain receptors
- Complement is a large collective of proteins (about 25 different ones) that work to form a membrane attack complex.

Our immune system has the capability of responding to specific antigens.

Innate immune responses are evolutionarily very old; all classes of animals and plants have some sort of innate immunity, as do most prokaryotic organisms.

**Acquired immunity** comprises antigen-specific responses and is mediated primarily by lymphocytes (at least in jawed vertebrates...in other animal classes, other molecules are common).

There is overlap between innate and acquired immunity.

Acquired immunity can be **active** or **passive**.

**Active** immunity occurs when we are exposed to a pathogen and make our own antibodies. When you get a cold, you make antibodies to the virus.

**Passive** immunity occurs when we receive antibodies from other animals (maternal-fetal exchange of antibodies, gamma globulins, etc); not long-lasting.
We have millions of types of lymphocytes

Lymphocytes are the mediators of acquired immunity, and are differentiated into clones (based on membrane-bound proteins)

Upon exposure to an antigen, naive lymphocytes expand via a process called clonal expansion; they then differentiate into effector cells (which only live a few days), and memory cells (which are long-lived, and maintain a “memory” of the antigen in the body)
In humoral immunity, B cells secrete antibodies

B cells (a type of lymphocyte) undergo clonal selection and secrete antibodies into our body fluids.

An antibody molecule is composed of two identical light chains and two identical heavy chains, linked by disulfide bonds.

Antibodies are divided into five functional classes (G, A, E, M, & D) and have several functions.
Once pathogens infect cells, they are invisible to the humoral immune system

Infected cells display fragments of foreign antigens on their surface as part of the major histocompatibility complex (MHC) (has huge genetic variation between individuals)

T cells (T lymphocytes) can bind to MHC-antigen complexes on the surface of a target cell

MHC Class I molecules are found on nucleated host cells; cytotoxic T cells can recognize invaders on these "platforms" and destroy them to prevent them from replicating

MHC Class II molecules are found primarily on macrophages, B lymphocytes, etc, and helper T cells can recognize these platforms, and secrete cytokines that enhance the immune response

Cytotoxic T cells prevent replication of infected cells

The easiest way to prevent replication of a cell infected with viruses, parasites, or some bacteria is to kill it; this is the job of cytotoxic T cells

They release perforin, a cytotoxic molecule that literally perforates cells; granzymes are enzymes that digest protein and enter through the pores created by perforin

Cells undergo apoptosis as a result

Cytotoxic T cells also activate Fas, a protein on the target cell membrane that speeds up apoptosis
**Helper T cells secrete cytokines that influence other cells**

Interferon-gamma (IFN-γ) activates macrophages

Interleukins activate antibody production and cytotoxic T cells

Colony-stimulating factors enhance leukocyte production

Interleukins support mast cells and eosinophils

Also...

Bind to B lymphocytes and promote their differentiation into plasma cells or memory cells.

The main target of HIV (the virus that causes AIDS) is helper T cells

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**Allergens are nonpathogenic antigens**

Some are not harmful, but individuals can be hypersensitive to them, which results in an inflammatory response.

Reactions can be mediated by antibodies (immediate) or helper T cells & macrophages (delayed)

Allergies have a strong genetic component, and development of allergies can be affected by geographic, cultural, and social conditions

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**Autoimmune diseases result when our immune system fails to recognize “self”**

During development, some clones develop that can combine with MHC-self-antigen complexes; these must be eliminated by clonal deletion

Reasons why self-tolerance may suddenly fail are unclear
Elevated levels of cortisol are a good indicator of long-term or repetitive stress.

Elevated levels of cortisol also are known to suppress the immune system.

The exact mechanisms behind this suppression are unclear due to the fact that ‘stress’ is difficult to study in non-human models.

When we are burdened, we often compensate for a lack of time by giving up sleep.

Over the last 25 years, our society has become chronically sleep-deprived; a common perception is that this leads to a higher susceptibility to viral illnesses.

Is there any evidence to suggest this?

The circadian rhythms of cortisol and ACTH remain unchanged in response to sleep deprivation.