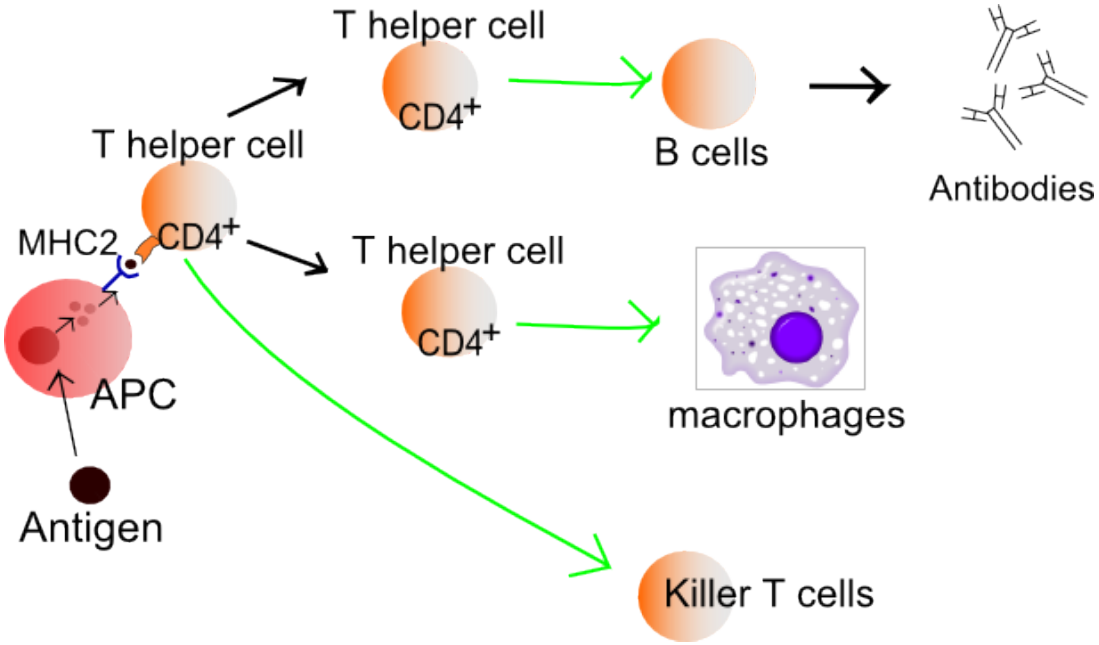
The Immune System, Vaccination and Autoimmune Diseases

See online here

Immunology is concerned with the human immune system. It is about much more than the emergence of colds or infectious diseases. In the course of studies, immunology is one of the interdisciplinary subjects.



Cells of the Immune System

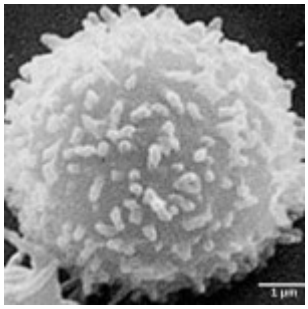


Image: “T lymphocyte” by Philschatz. License: CC BY 4.0

During the early stages of pregnancy, the precursors of T and B cells are detectable in the embryo. They migrate to the liver, thymus, and spleen. The majority of T cells and a portion of the lymphocytes remain in the blood and lymphatic vessels and reach the lymphoid organs this way. Approximately 90% of the lymphocytes detectable in the blood

are **T cells**.

The blood stem cells in the bone marrow are the basis for other cell types with different functions and tasks. The immune defense is mainly performed by the white blood cells (**leukocytes**), which are divided into **granulocytes**, **lymphocytes,** and **monocytes**. Granulocytes account for 50–70%, lymphocytes for 20–40%, and monocytes for 1–6% of WBCs.

Note: The body's defense is the immunological defense. It consists of nonspecific and specific defenses.

The nonspecific defense is fast, innate, and generally non-adaptive. The specific defense is slow in its initial response, but its response adapts to the respective trigger (the pathogen). Thus, this immune response is acquired. The specific defense also leads to immunological memory.

The Immune System Is Complex

The immune system consists of 2 pillars. These include the **acquired specific defense** and **general innate defense**. However, the systems are not independent of each other. Defense cells are located in tissues, blood, and other fluids. The cells that fight and eliminate pathogens are assigned to the **cellular defense system**.

	Cellular	**Humoral**
Non-specific	PHAGOCYTES Granulocytes, mast cells, killer cells	COMPLEMENTS Cytokines (interferons), lysozyme
Specific	T-LYMPHOCYTES Cytolytic and regulatory T cells	ANTIBODIES formed by plasma cells and B-lymphocytes

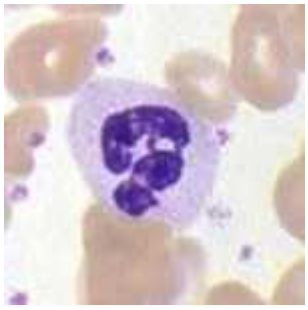
Defense cells in fluids

Defense cells are also found in the blood and other fluids. They are soluble and consist mainly of **proteins** and **antibodies**, as well as **short-chain amino acids**. They serve as the **humoral defense**.

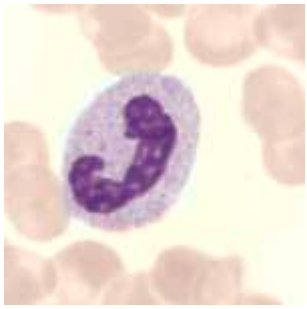
Note: The innate and the acquired immune system include humoral and cellular defenses.

The innate defense is directed against inflammations. Myeloid cells are used for this purpose. **Myeloid cells** are **neutrophils, eosinophils,** and **basophils**. **Monocytes** and **macrophages** are also involved, as well as **natural killer cells** and **cytokines**. These subgroups are also referred to as **phagocytes**.

Neutrophils



Neutrophile segmented Granulocyte



Neutrophile stick-nucleated Granulocyte

Humans produce more than 1,000 neutrophils in the bone marrow in a single day. They result from **CMP (common myeloid progenitor)**, the **oligopotent myeloid stem cells**. Young neutrophils differ from the old as they possess a rod-shaped core. When they mature, 3–5 core segments are visible.

Therefore, they are referred to as neutrophils with segmented nuclei. Neutrophils are mobilized to sites of inflammation by attractants (chemokines). There, they destroy the cellular structure of the microbes that caused the inflammation.

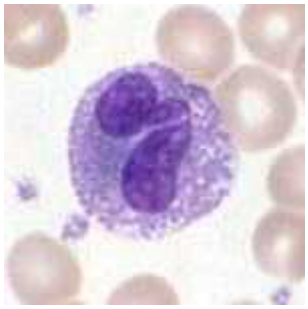
High neutrophil levels are an indication of **different diseases** or **processes**. These include:

- Inflammations
- Sepsis
- Necrosis
- Surgeries
- Abscesses
- Anemia
- Chronic granulocytic leukemia

However, stress or pregnancy can also cause elevated levels. **Low levels (neutropenia)** are a **possible indication of**:

- Damage to the bone marrow (different possible triggers)
- Disturbed formation of neutrophils
- Increased consumption due to inflammation or disease
- Diseases such as Kostmann syndrome

Eosinophils



Eosinophils Granylocyte

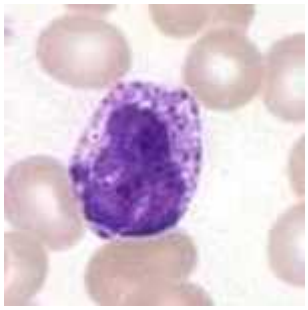
Eosinophils are important in the defense against parasites. However, they also play a role in allergies. **Low levels** are an **indication of**:

- Severe, acute infections
- Stress
- Cushing's syndrome
- Corticotherapy

High levels can occur in:

- Worm infestation (e.g. echinococcosis, ascariasis, etc.)
- Allergies (e.g. asthma, neurodermatitis)
- Some serious skin diseases (e.g. psoriasis)
- Autoimmune processes
- Certain medications (such as penicillin and aspirin)
- Cancers (e.g. CML or Hodgkin's disease)

Basophils



Basophils Granylocyte

Basophils are the smallest group of granulocytes. They transport many messenger substances and can even trigger allergic reactions, e.g. by releasing histamine under the skin. The result is severe itching. Basophils also play important roles in the immune response. **Decreased** levels are indicative of:

- Contact with chemicals
- Some medications
- Radiation exposure
- Some cancers
- Vitamin B12 deficiency
- Folic acid deficiency
- Bacterial infection
- Viral infection

In addition, basophil levels drop after **lupus erythematous**. It is also possible that no granulocytes are detectable in the blood, which is described as **agranulocytosis**.

Monocytes

Monocytes initially move in the blood and migrate from there into the tissue. Here, the **conversion to macrophages** takes place. Their task is **phagocytosis**. Phagocytosis is the seizure of bacteria or tissue debris. Elevated levels after longstanding disease are an important indication that the body is recovering. Low monocyte levels without the general reduction of granulocytes are unusual.

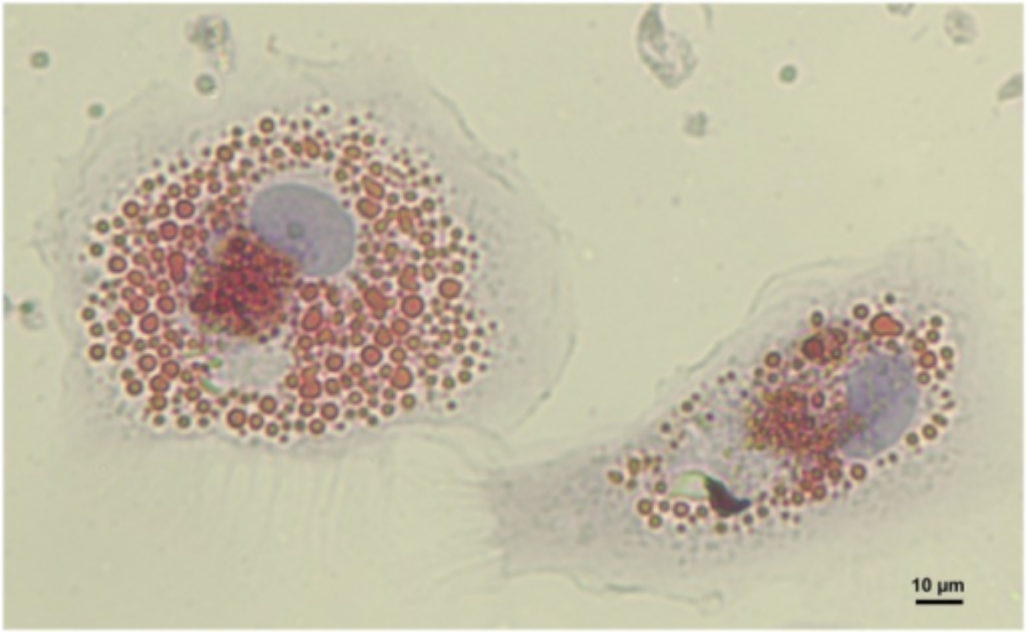


Image: “Human monocyte derived macrophage foam cells.”” by Openi. License: CC BY 4.0

Elevated values can be an indication of:

- Bacterial infections
- Viral infections
- Parasitic infections (e.g. malaria)
- Autoimmune diseases
- Some cancers
- Endocarditis

Cytokines

Cytokines are also important for the immune system. Cytokines are proteins that are formed and released by immune cells. Cytokines are part of the acquired defense and act as messenger substances. They enable the immune cells to facilitate an exchange. Thus, they are able to stimulate or inhibit the immune response.

Note: Cytokines coordinate the immune response by inhibiting or stimulating the defense against pathogens.

The Innate Immune System

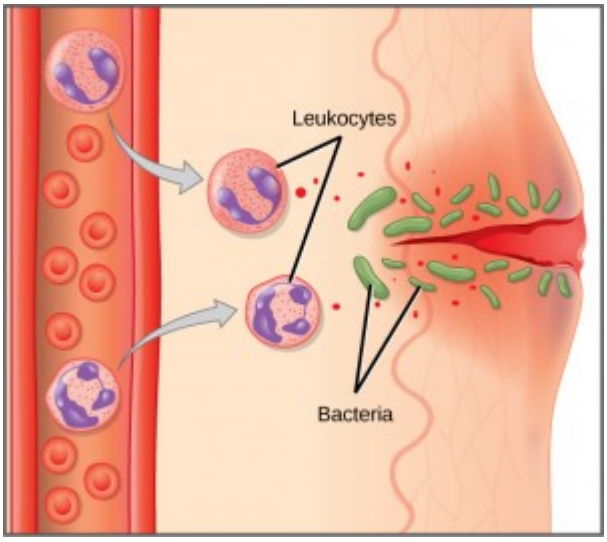


Image: “In response to a cut, mast cells secrete histamines that cause nearby capillaries to dilate.” by Philschatz. License: CC BY 4.0

The innate immune system is characterized by its rapid response. One example is the immediate reaction to a wound with invading bacteria. The effectiveness is widespread but nonspecific, therefore the reaction is possible within only a few hours.

The innate immune system consists of several components, being related to the skin and mucous membranes as the outer barriers, as well as to the orifices. Furthermore, it consists of various immune cells (WBCs) and various substances in the body fluids, such as blood.

Development of innate immunity

The innate immune system is not just an initial defensive measure against pathogens and is not limited to the human body as plants and invertebrates have this immunity for defense purposes.

Innate immunity is genetically fixed and is not adjustable, and this is an important limitation. However, acquired immunity is the improvement and specialization of innate immunity. Nevertheless, innate immunity is able to repel and eliminate the majority of disease-causing substances. The effectiveness of the immune system can be seen in patients with AIDS or in those who require immunosuppressive drugs. Even a cold can become a life-threatening event in this patient group.

Note: The innate immune system reliably defends the body against most infections.

The Acquired Immune Defense

As opposed to innate immunity, the acquired immune defense is **adaptive,** i.e. trainable. It becomes active if the innate immunity appears incapable of eliminating a pathogen. One example is experienced children’s diseases that provide lifelong immunity in many cases. It is believed that this adaptive immune defense was developed in vertebrates only about 500 million years ago. Research into the acquired immune defense is the basis for the development of vaccines.

Note: Knowledge about the adaptive immune defense underpins the research on vaccinations.

The **acquired immune response** is based on the occurrence of pathogens that require different responses. Antibodies attack germs that occur in the blood or other body fluids. Pathogens that reside in the tissue are fought by a **cell-mediated immune response**.

Vaccinations

Vaccination can be divided into active and passive vaccination.

Active immunization

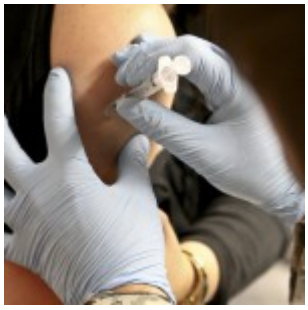


Image: “Flu vaccinations make their way to U.S. Army in Europe” by U.S. Army Corps of Engineers Europe District. License: CC BY 2.0

In active vaccination, **attenuated pathogens** or **proteins** are supplied. These are barely potent but have an activating effect on the specific and nonspecific immune defense. This works because they mimic infection in the body. Thus, the body is able to produce specific antibodies. At the same time, memory cells are formed, which ensure that the vaccination protection remains for a long time. This achieves a crucial goal of vaccination, which is long-term protection.

If the body comes in contact with the pathogen in the future, the immune system is able to respond accordingly. In most cases, a basic immunization is required, consisting of partial vaccinations. Repetitions after a few years (**vaccination schedule**) serve to ensure that the immune system ‘remembers’ the pathogen.

Passive immunization

If the body has already come in contact with the pathogen, passive immunization is possible for some diseases. Thus, protection is quickly available. During passive immunization, concentrates of antibodies are injected. These antibodies are derived from people who are immune to the relevant disease. The downside is that this protection does not last long and is often lost after a few months.

Autoimmune Diseases

In a healthy individual, the immune system can distinguish between the body’s own cells and foreign bodies/cells. If an error in this process occurs, the immune system fights the body’s own cells. The consequences are inflammation and damage to the organs. This is possible because the development of adaptive immunity is complex and prone to failure.

There are more than 80 types of autoimmune diseases.

Typical autoimmune diseases include:

- Rheumatism
- Type 1 diabetes
- Multiple sclerosis
- Vasculitis
- Myasthenia gravis
- Celiac disease
- Graves' disease
- Inflammatory bowel diseases

The mechanisms underlying autoimmune diseases are not fully understood.

Note: It is estimated that 7% of the people living in the USA (about 24 million) are affected by autoimmune diseases. Additionally, women are more affected than men.

Possible mechanisms of autoimmune diseases

One possible explanation identifies the **thymus** as the trigger. The development and maturation of **T lymphocytes** (T stands for the thymus origin) take place in this organ. The processes are dependent on the **transcription factor Foxn1**. It is a regulatory protein. The protein coordinates genes that reside in the epithelial cells of the thymus. These genes attract progenitor cells to the thymus and control the subsequent differentiation into mature T cells.

Defense via MHC (major histocompatibility complex) proteins

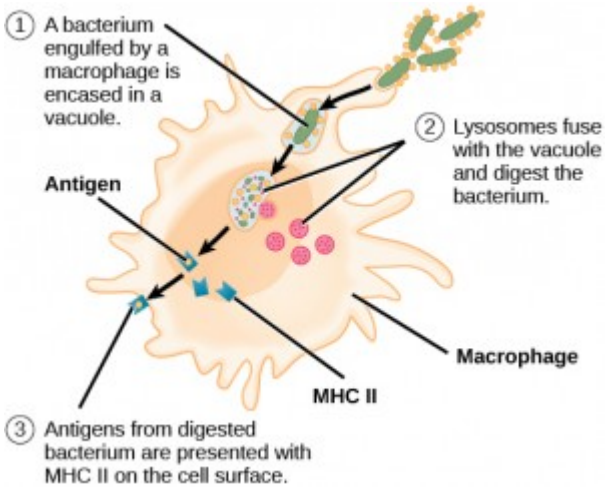


Image: "A macrophage, engulfs and digests a foreign bacterium" by Philschatz. License: CC BY 4.0

The adaptive immune response is dependent on T cells and B cells (produced in the bone marrow). Antibodies are able to recognize antigens. **Antigens** are proteins derived from pathogens that need to be combated in the body. The antibodies attach to the antigens and the pathogens are "marked". Furthermore, it is also possible that they will be directly rendered harmless. T cells, however, only respond after being notified by other body cells (B cells, macrophages, dendritic cells) that fragments of peptides (proteins from pathogens) are present.

They are aided by T cell receptors. From a chemical point of view, this happens via **MHC proteins**. These MHC proteins are able to bind multiple protein fragments. The fragment results from the protein breakdown.

Presentation at the cell surface

On the cell surface, the **peptide-MHC complex** is visible. Once these complexes contain foreign peptide, the T receptors of the T cells can recognize them. The complex is destroyed as an infected cell. However, it is also possible that other immune cells are stimulated initially, which in turn destroy the infected cell.

Occurrence of T receptors

T receptors occur virtually at random. In the thymus, T cells receive different T receptors. The T cells are also trained, so they are able to distinguish foreign substances from their own. They also have to tolerate their own structures.

Note: T cells must first be trained to tolerate endogenous substances.

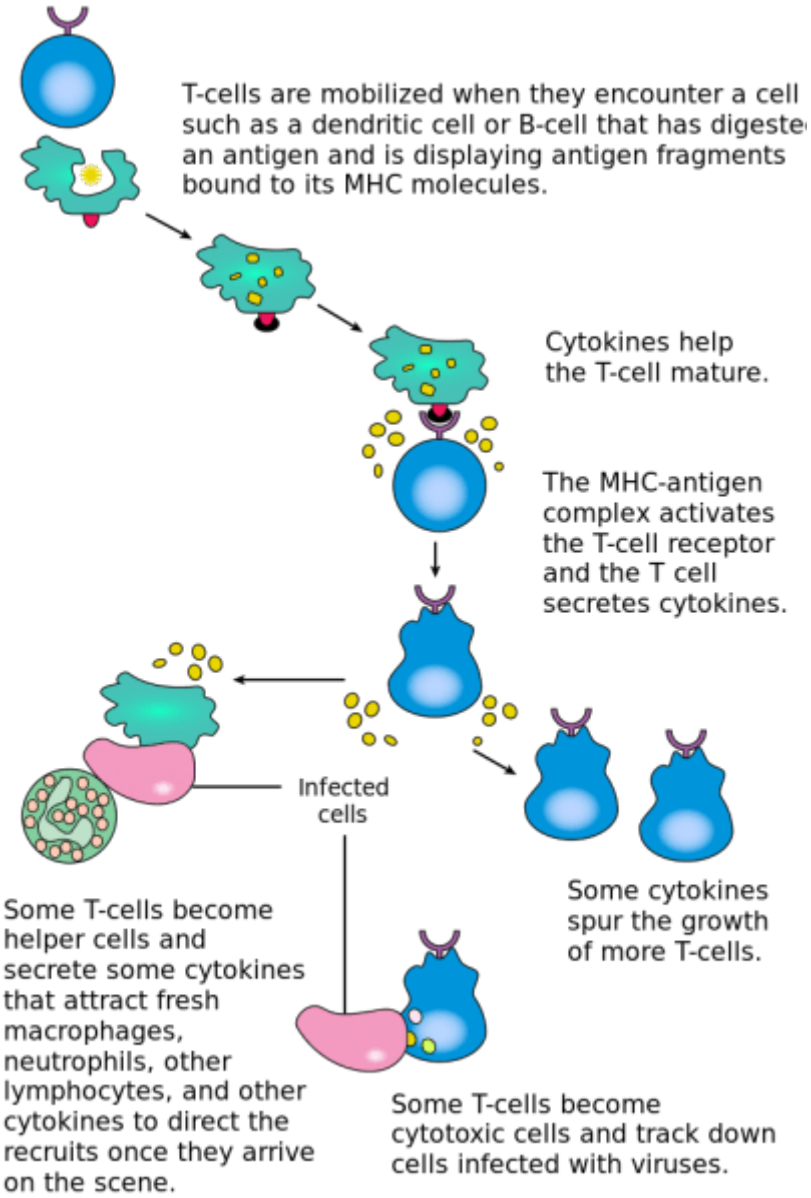


Image: “T-cell activation” by Hazmat2. License: Public domain

The learning process is carried out in several steps

Initially, only the T cells that are able to recognize MHC molecules on the cell membranes

survive. This eliminates initial confounding factors. In the next step, the T cells that react too violently to cells that are marked with the protein fragments must be eliminated. This refers to negative selection where the cell reacts to the foreign material but does not do so appropriately. Negative selection is not yet completely understood.

The process takes place in the thymus. The T cells are ‘shown’ all the proteins present in the body. This may be referred to as a test process. T cells that react here later initiate the autoimmune processes in the body. The aim of the body is to eliminate all the improperly responding cells and to produce only those that are able to distinguish and react exclusively to foreign peptides.

Note: The body’s T cell training aims to prevent the onset of autoimmune diseases.

It is not clear how autoimmune disorders arise. For example, in type 1 diabetes, it is striking that the autoimmune disease often follows acute disease. While the immune system is successful in cases of acute illness, the defense cells subsequently attack the insulin-producing beta cells of the pancreas.

Symptoms of autoimmune diseases include:

- Fatigue
- Low-grade fever
- Hair loss
- Skin rashes
- Numbness of the feet and hands
- Swelling and redness
- Achy muscles

However, it is worth noting that each patient might have his/her own unique symptoms. For instance, a patient with type 1 diabetes may experience weight loss, fatigue, and extreme thirst.

References

Notes