Charlotte Jäggi: Introduction to the Immune system

The following list aims to list, explain and relate the most important terms of the immune system.

Basically, the white blood cells, the leucocytes, play an important role.

"Jobs" of leucocytes

non-specific defense cells

Signaling cells mark the antigens

Phagocytes: Monocytes, granulocytes, macrophages

mark and destroy foreign cells and toxins by phagocytosis: they surround the foreign cells and destroy them by lysis, i.e. they cause the cells to burst.

specific defense cells

B- lymphocytes

Plasma cells

- form antibodies specifical to their defined antigens. There are not existing genes for every antibody. The fixe part is the same for every type of antibody. The variable region attaching at the antigen is formed by gene segments. If one or more genes had to be available for each antigen, far too many The m- RNA (copy of the relevant DNA sections, i.e. the genes) is adapted to the corresponding antigen by splicing (removing the pieces that are not needed). genes of the human genome would be needed.

- arise from B-memory cells by enlargement

B- memory cells

- store the information of the antigens during infections

T- lymphocytes mature in the thymus

T- helper cells

- support the immune response
  stimulate B- lymphocytes and T- memory cells by releasing cytkines (interleukins)

T- destroyer cells (cytotoxic T- lymphocytes)

destroy - antigen-antibody complexes
- tumor cells

- transplanted foreign tissues

T- suppressor cells
terminate an immune response

T- memory cells
also store the information of the antigens for the rapid start of the immune response.

Inflammatory reaction

An infection with viruses, bacteria trigger first a non-specific and later often a specific immune reaction.
External signs are
- heating
- reddening
- Swelling of the infected area

There are several possibilities of the immune reaction
Often both, first the non-specific and then the specific reaction take place

Nonspecific defense

mechanical
- skin
- cilia in the respiratory tract
- mucus

chemical
- Lysozymes to dissolve bacteria
- hydrochloric acid in the stomach

granulocytes, monocytes, macrophages
- phagocytose of bacteria, viruses and toxins

complement systems: enzyme proteins
- are located in the blood, i.e., not in the cells
- Are activated by bacteria through substances foreign to the body in the cell membrane of the pathogen → reaction cascade

cytokines
- Are released by secretion from producer cells, primarily in infected tissue, and partly into the blood plasma.
- They can affect several different cell types by docking to the appropriate receptors.
- They have various effects on the target cell, neighboring cells or even on cells further away.

Specific immune response

Humoral immunoreaction takes place in the blood

diversity of antigens

→ diversity of antibodies

Antigens:

- proteins or polysaccharides. Often only no sections act as antigen: epitopes

Antibodies:

- relatively small proteins called immunoglobulins (Ig) with variable epitope binding sites.
- individual building blocks look like a Y.
- they are produced by transformed B- lymphocytes, the plasma cells.

- **they are specific:** key-lock principle

Antibodies have only a limited life span. The information is then stored in the memory cells.

- different types

  - o Ig G: 80%, defense in secondary infections, "late" antibody, monomer (1AK building block)
  - o Ig M: 6%, first defense in case of infection, "immediate" antibody, pentamer (consists of 5 antibodies building blocks)
  - o Ig A: 13%, defense against pathogens in the mucous membranes, dimer (2 AK building blocks)
  - o Ig D 1%, builds up B cell receptors, possibly enhances AK formation
  - o Ig E: 0.002% allergic reactions, defense against toxins and parasitic worms, (1AK- building block)

Origin of antibody diversity

It is impossible to anchor information for all possible antibodies in the genome individually. There are no genes that can be used for each of the variable regions of the antibodies, but only gene segments with the information for the structure of the antibodies. The m- RNA (copy of the relevant DNA sections, i.e. the genes) is adapted to the corresponding antigen by splicing (removal of the pieces that are not needed).

Antigen- antibody reaction

The antibodies block the antigens on the surface of the bacterium, virus, foreign cell. This prevents or at least reduces the penetration of the viruses and certain bacteria into the host cell and/or the multiplication of the bacteria in the blood.
→ No or at most weak infection.

Cellular immune response

It occurs when body cells have already been attacked by viruses or bacteria that can invade the cells. Cancer cells are usually also identified as foreign cells and are destroyed by the same mechanism.

T-helper cells

- activate and support the immune response
- stimulate B- lymphocytes and T- memory cells by releasing cytokines (interleukins)

T- destroyer cells (cytotoxic T- lymphocytes)

- are activated by cytokines
- destroy antigen-antibody complexes
  tumor cells
  transplanted foreign tissues

T- memory cells

- also store the information of the antigens for the rapid start of the immune response at the next identical event with the same pathogen.

T- suppressor cells

- terminate the immune response

Immune memory by the two memory cell types

lymphocytes b and lymphocytes t
Immune memory through the two memory cell types:
B- lymphocytes and T- lymphocytes store the information about the antigens they have repelled.

Distinction " self - foreign"

Normally, the surface proteins on the body's own cells must not be classified as foreign by the defense system. Otherwise, these body cells will be destroyed by the lymphocytes.
During the maturation of lymphocytes t and b in the thymus (lymphocytes t) and bone marrow (lymphocytes b), their antigen receptors are tested to see if they react with the body's own antigens.
If so, they are normally eliminated by programmed cell death. This leaves only those lymphocytes that react with molecules foreign to the body.

Cross-reactions

In addition to the specific reaction to their "own" antigen, antibodies can also at least partially block similar antigens and thus usually do not prevent the infection but attenuate it. *Example: antibodies against the various influenza virus strains.*

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Immunization by Vaccination

active:

This vaccination is preventive. The healthy individual is given pathogens or their antigens so that his immune system actively produces antibodies to them. The information of the pathogen is stored in the memory cells for more or less time. Depending on the pathogen and/or the type of vaccination, boosters become necessary.

- Live vaccine contains attenuated pathogens.
  They trigger the immune response.
  Examples: Measles Rubella.

- Dead vaccine contains killed, inactivated but otherwise intact pathogens.
  They trigger the immune response.
  Examples: Diphtheria, tetanus, pertussis.

- Vaccination with inactivated pathogens:
  The pathogen is intact but no longer able to reproduce.
  Examples: Hepatitis A, rabies, cholera, polio.

- m-RNA vaccine
  contains the m-RNA, i.e. the information for the surface protein, i.e. the antigen of the pathogen. The cells at the vaccination site (mostly muscle cells) first form the corresponding antigen by means of protein synthesis, which then initiates the immune reaction.
  Examples: Covid 19, Ebola

- Gene ferries:
  Harmless DNA viruses contain the genetically engineered DNA, i.e. the information for the antigen. The organism uses this information to synthesize RNA and, through protein synthesis, the surface protein of the pathogen, i.e. the antigen, which then triggers the immune reaction.
  Example: Covid 19

- Injection of toxoids Substances very similar to the toxin of a pathogen, but harmless. This also activates the immune response.
  Examples: Pneumococcus, meningococcus.

Passive:

Antibodies raised in advance against the pathogen are administered to the already ill individual.
Antibodies against the pathogen, which render the pathogen harmless.
Example especially in temperate zones: Snake venom antibodies

However, there is a risk of an antibody-antibody reaction: The foreign antibody becomes an allergen and is fought against accordingly. A 2nd administration of the identical vaccine is therefore practically often ineffective.

Allergies and atopias

Allergen is the trigger of an allergy, but is harmless:
False reaction of the defense system.
Suppressor cells do not suppress the defense reaction.

→ Allergen-antibody reaction.

Sensitization phase:
For an allergy to develop, an initial, usually unnoticed contact with the allergen is usually required. This produces antibodies and then the corresponding memory cells.

Immediate reaction: Ig- E activate the mast cells and a kind of grtnulocytes.
Release of histamine(as in the case of infection).
→ Redness, swelling, water retention, temperature increase, especially local, itching.

Late reaction 2-4 h after the immediate reaction:
The released substances can also damage healthy tissue.

Types of allergies:

- Ig-E dependent reactions (type I)
  mainly on the skin with rash, itching

- Ig-M and IgG dependent reactions (type II)
  Rejection reactions after blood transfusion and organ transplantation.

- Immune complex mediated reactions (type II)
  Inflammatory reactions, especially to skin, kidneys and joints.

- Cell-dependent reactions (type IV)
  A specific type of helper cell is active (CD4), affecting mainly the skin. Reaction occurs 24-72 h after allergen contact.
  Mainly contact allergies

Allergies mostly affect the whole system.
Atopy rather affects single organs, e.g. skin, respiratory tract and/or gastrointestinal tract.

A*llergy ≠ Hypersensitivity!* The transitions are often fluid.

Combat: Avoid allergen
Calcium
Vitamin B2, possibly B1
Antihistaminica (immediate reaction)

Weakness of the immune system

congenital: various degrees and strengths, up to the complete absence of the immune system.
Depending on the type of defect, they must be treated quite differently.

acquired: AIDS (Acquired immunodeficiency syndrome), triggered by the human immunodeficiency virus (HIV).
It is mainly the T-helper cells that are affected. This weakens the immune response and the pathogens can no longer be adequately fought over time.
The disease occurs in several stages.
1st stage: infection with HIV
2nd and 3rd stage: asymptomatic. The virus test is positive. These stages can last for several years. The infected person can infect other persons without treatment.
Stage 4: full-blown disease. The body's defenses collapse and the immune system of the infected person can no longer defend itself even against pathogens that are harmless in themselves.

Autoimmune diseases

Autoimmune reaction:
Immune reaction against the body's own structures (autoantigens).

Autoimmune disease:
The immune reaction leads to tissue and/or organ damage. Several organs may be affected simultaneously.

Antibody-dependent:
The antigens are located on the outside of the cells.
Activation of complement factors and granulocytes or formation of autoantibodies. Autoantibodies destroy the cell connections or are

directed against the body's own structures as antigens (e.g. DNA)
Damage to the tissue.
Example: Lupus erythrematoides (changes in skin, joints and internal organs due to vascular inflammation)

Antibodies against receptor molecules can also be formed.
Example: myasthenia gravis (a chronic neuromuscular disease characterized by weakness and rapid fatigability of skeletal muscles)

T- cell mediated:
Destroyer- T- cells destroy body cells possible (not yet confirmed).
Example: Diabetes mellitus

Other examples of autoimmune reaction: certain forms of rheumatism, psoriasis.
Those mechanisms are suspected in other diseases.
It is noticeable that many (possibly all) of these diseases are multifactorial!

Combat: especially cortisone preparations (late reaction)

Malignant diseases of the immune system

In all these diseases, diseased cells migrate into healthy tissue and multiply there, displacing and/or destroying the healthy cells of the lymphoid organs and/or bone marrow.

Malignant lymphomas

Changes in immune cells, predominantly in lymph nodes.

Non Hodgkin lymphomas

Immigration of malignant leukocytes into lymph nodes, bone marrow, spleen, liver and gastrointestinal tract.
Various forms of the disease

Hodgkin's lymphoma

Malignant tumors of the lymphatic system

Leukemias

heterogeneous group of malignant cells newly formed from precursor cells in the hematopoietic bone marrow.
These enter the blood and later other organs such as lymph nodes, spleen, liver, skin, gastrointestinal tract and central nervous system.

Acute lymphatic leukemias

Acute myeloid leukemias

Chronic lymphocytic leukemia

Chronic myeloid leukemia

Plasma cell neoplasia

Degeneration of antibody-producing B lymphocytes.

Multiple myoma

Immunoglobulin synthesis is unrestrained.
Scattering of the tumor cells, in the bone marrow.
Consequence: susceptibility to bacterial infections, bone "holes" causing severe bone pain.

Blood groups

On the red blood cells (erythrocytes) as on the other body cells there are surface proteins. The blood serum contains antibodies against foreign blood proteins.

ABO- System: Main blood group system

The surface proteins A and B are essential for blood grouping. AB0-system and rhesus factors are genetically determined.
Information/genes for A and B are dominant. If an individual has them, he/she is A or B if he/she has one of them or AB if he/she has both. 0 is therefore recessive.

- Blood type A has protein A on the red blood cells and anti-B in the serum.
- blood group B has protein B on the red blood cells and anti-A in the serum
- Blood group AB has both on the red blood cells and in the serum neither anti-A nor anti-B
- Blood group 0 has neither of them on red blood cells and anti-A and anti-B in serum

Antibodies in serum to own antigen(s) on red blood cells would make embryo survival impossible because blood would clump together.

Rhesus factors

most important secondary blood groups
Proteins: C, c, D, d, E and e.
Genes for C, D, and E are dominant over genes for c, (d, probably a silent gene), and e.
These genes are linked and inherited as a so-called triplet.

Rhesus-positive blood always contains the protein D
About 85% of Central Europeans are rhesus positive, about 15% rhesus negative.

Rhesus negative blood has no D. When it comes into contact with rhesus-positive blood, the immune system forms anti-D, which clumps the blood cells with D.

Incompatibility:

If a woman is rhesus negative and has previously had a rhesus positive child or has had a blood transfusion with D- positive blood and is expecting a rhesus positive child, pregnancy problems may occur. The child may
- be anemic,
- develop severe jaundice due to excessive breakdown of erythrocytes, or
- develop hydrops fetalis (fluid accumulation in the tissues) which may result in stillbirth.

Ant-D, unlike the other antibodies, can diffuse through the placenta. To prevent this, the rhesus-negative woman is sometimes given anti-D prenatally, but usually after the birth of a rhesus-positive child, to prevent the formation of anti-D triggered by blood contact during the birth process.

Other secondary blood groups

There is a whole series of them, which are determined for the diagnosis of various diseases and which were important for paternity determinations in the past.

Determination of blood groups

→ Blood transfusions

Normally, blood of the same blood group and the same rhesus factors is given, if possible.
If this is not possible
- A donates A and AB
- B donates B and AB
- AB donates AB only → universal recipient.
- 0 can donate to all main groups → universal donor

Sources

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