Immunodeficiency

Immunodeficiencies are immunopathological conditions in which **the body's overall reactivity to antigenic and other stimuli**, causing a specific or non-specific immune response, is reduced. The main clinical manifestation is **an increased susceptibility to infections**.

Types of immunodeficiencies

1. **Congenital** (primary) – rarer, but more serious and even life-threatening.
2. **Acquired** (secondary) – common but mostly less severe (except AIDS and acquired agranulocytosis).

According to the affected process

1. Defects of **specific immunity** – disorders of T-lymphocytes and B-lymphocytes (disorder of antibody production).
2. Defects of **non-specific immunity** – disorders of phagocytosis, complement, NK cells.
3. Immunodeficiency associated with other **congenital syndromes**.

Congenital immunodeficiency

🔎 *For more information see Primary Immunodeficiency.*

Disorders of B-lymphocytes and antibody production

The clinical symptom is an increased susceptibility to infections by extracellular bacteria, as the response of immune cells to structures specific to pathogens significantly helps to destroy them.

Changes in antibodies in the blood are divided into:

- **agammaglobulinemia** – the total Ig concentration is below 2 g/l;
- **hypogammaglobulinemia** – the total Ig concentration is above 2 g/l, but less than in the general population (9–17 g/l);
- **dysgammaglobulinemia** – a decrease in the concentration of only one class of Ig, the others have conc. normal or elevated.

They manifest in 6-12 months after delivery, when the level of maternal, transplacentally transferred immunoglobulins.

Selective IgA deficiency

Disruption of the mucosal defense mechanisms (GIT, urogenital and respiratory tract infections), but sometimes does not manifest itself clinically at all.

🔎 *For more information see IgA.*

Bruton's agammaglobulinemia

Gonosomal recessive disease linked to the X-chromosome (defect of the B-cell-specific Atk tyrosine kinase gene). It only affects boys. Immunoglobulins and B-lymphocytes are always completely missing in the **peripheral blood**. However, their precursors are present in the bone marrow, as it is a disorder of B-cell differentiation and maturation.

It is often manifested by purulent and parasitic infections and a tendency to autoimmune diseases.

CVID (common variable immunodeficiency)

Hypogammaglobulinemia, B-lymphocytes in the normal amount, but is defective their maturation in plasmocytes. They recur clinically with **recurrent infections and diarrhea** and a tendency to autoimmune diseases and lymphoproliferative diseases.

T-cell disorders

The symptom is **an increased susceptibility to infections by fungi, viruses and intracellular bacteria**. Their antigens are not derived from cells, but affect the configuration on HLA I. These are recognized and evaluated by T-cell receptors.

SCID (severe combined immunodeficiency)

A deadly disease in which the development of B and T lymphocytes is impaired. In 40%, it is based on a **defect in the enzyme ADA** (adenosine deaminase). The affected child does not thrive, suffers from severe watery diarrhea, bronchopneumonia, meningitis, no lymph nodes or tonsils are developed.

This is the first disease successfully treated with gene therapy.

Bare lymphocyte syndrome

Disorder of MHC II production. This leads to a worsening or even impossibility of presenting the antigen to the lymphocytes.

Reticular dysgenesis

The most severe immunodeficiency, in which there is a defect in the precursor of leukocytes of lymphoid and myeloid lineage and platelets.

Disorders of non-specific immunity cells

The symptom is an increased susceptibility to infections by bacteria and fungi. The immune system is not able to respond quickly and effectively to the so-called **general pathogenic patterns** PAMP (Pathogen-Associated Molecular Pattern).

Chronic granulomatosis

Phagocytosis disorder in neutrophilic granulocytes and macrophages. It is caused by a **congenital enzymatic defect (enzymopathy)** of one of the mechanisms of intracellular killing. Commonly disrupted enzymes include myeloperoxidase or glucose-6-phosphate dehydrogenase.

Chediak-Higashi syndrome

Disorder of **intracellular granules release**. In granulocytes, phagosomes do not fuse with lysosome.

The disease is associated with albinism.

LAD syndrome (*leukocyte adhesion deficiency*)

Leukocyte **integrins** deficiency. Cells of the immune system are not able to interact with stimuli from the environment (tissue ligands, signaling molecules ...). Failure to interact leads to impaired **adhesion, chemotaxis and bactericidal abilities**.

Primary immunodeficiencies associated with congenital malformations

Di-George's syndrome

Hypoplasia or thymic agenesis, which leads to a decrease in the number of T-lymphocytes. Affected individuals have low resistance to viral and fungal infections.

It is usually a developmental defect of the 3rd and 4th pharyngeal pouch, associated with the absence of parathyroid glands (→tetany) and the occurrence of congenital heart defects.

Ataxia teleangiectasia

The cause is a **mutation in the reparator genes**, their products correct DNA breaks arising, among other things, when reorganizing genes for TcR and immunoglobulin chains.

The disorder affects both cellular and humoral immunity.

Other symptoms: cerebellar ataxia (disorders of balance and coordination of movements), telangiectasia (dilation of blood vessels in the skin and mucous membranes), muscle atrophy, cancer.

Wiskott-Aldrich syndrome

GR X-linked disease. The cause is a **defect in the membrane glycoprotein on the surface of T-cells and platelets**, which are increasingly caught up in the spleen.

T-cells and platelets gradually decrease (→thrombocytopenia), disease manifests itself in a trias:

- **recurrent infections**;
- **bleeding** – some patients die within one year of bleeding into the brain;
- eczema.

One of the therapeutic options is splenectomy, which leads to alleviation of thrombocytopenia.

Acquired immunodeficiencies

Secondary antibody immunodeficiencies

Immunoglobulins are lost from plasma. The escape route may be:

- kidneys in **nephrotic syndrome** – mainly IgG loss,
- stomach and intestines – **exsudative gastroenteropathy** (loss of all three plasma antibodies), **Menerier's**

disease (IgM, IgG) and **intestinal lymphangiectasia**.

Decreased immunoglobulin production occurs in **B-lymphomas**, **CLL**, **multiple myeloma**. Decreased synthesis may also be due to malabsorption syndrome with insufficient amino acid absorption.

Acquired granulocytopenia to agranulocytosis

Idiopathic or **medullary depression** after drug damage, poisons, aplastic anemia...

Immunodeficiency after splenectomy

Patients after splenectomy are at high risk of pneumococcal infection (Str. pneumoniae), which can lead to life-threatening meningitis and sepsis.

Immunosuppressive action

Some **drugs** induce targeted immunosuppression (cytostatics, corticoids), other times it is a **side effect of drugs**. Stress, clinical conditions disrupting homeostasis (uremia, diabetes, sepsis, malignancies), deficiencies – vitamins B, C, D, metals (Fe, Cu, Zn, Se, proteins) can also manifest themselves in a severe reduction in the immune response.

🔎 *For more information see Immunosuppressants.*

HIV infection

🔎 *For more information see HIV, AIDS.*

Links

Related articles

- Primary immunodeficiency
- Defects in cellular immunity
- Immunological development of the child

External links

- Immunology department of 3. LF UK – Immune disorders (http://old.lf3.cuni.cz/studium/materialy/imunologie/souhrn_2c.pdf)

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