

Immunology in pregnancy

Pregnancy is considered a condition that is one of the proofs of the adaptability of the immune system. For the proper development of the fetus during *pregnancy*, the immune system must **adapt to a state where it is able to tolerate different paternal antigenic structures** that are present in the fetus. This tolerance is due to *the acquired* and *innate* immune systems.

Physiology of immunity in pregnancy

We need the placenta for proper adaptation to different antigens. Functional and morphological changes take place in it, which will ensure fetal tolerance. In total, there are **four main events** that take care of the correct immunology of pregnancy:

- *suppression of cytotoxic reactions*
- *presence of the tissue compatibility molecule HLA-G at the fetomaternal interface*
- *predominance of immune reactions mediated by subpopulations of TH2 lymphocytes*
- *blocking antibodies formed by the mother against allogeneic antigens present on the structures of the developing with the fetus*

Placenta

Syncytiotrophoblast has the greatest contribution to the creation of an immunologically favorable environment in favor of the fetus. It protects the developing fetus from the mother's immunological reactivity. The syncytiotrophoblast contains a membrane that **is impermeable to potentially damaging substances** such as maternal blood. **Villous trophoblast** cells also play an active role. They grow into the uterine arteries and replace the mother's endothelial cells. It participates not only in covering the placenta, but also in the substance exchange between maternal and fetal blood in the intervillous space. Villous trophoblast cells **produce placental hormones**, especially chorionic gonadotropin and prostaglandins, which thus participate in the mutual cooperation of cells of the immune system from the mother's womb.

NK cells

NK cells are the **most abundant leukocyte population** in the endometrium at the time of implantation and early pregnancy. *Their quantity gradually decreases* as the pregnancy progresses. The greatest decrease in NK cells is recorded in the period III. trimester. During pregnancy, there is a proliferation of NK cells, which have an important function in the production of cytokines. They are necessary for angiogenesis, without which the continuation of pregnancy would not be possible. Unfortunately, sometimes NK cells have aggressive cytotoxic properties, which then lead to miscarriage.

HLA-G molecules

During pregnancy, there is a lack of HLA I and II tissue compatibility molecules. classes at the maternal-placental interface. This absence provides the fetus with the main protection against damage by the mother's immune system. Due to the absence of HLA molecules, the abilities of T and B-lymphocytes are blinded, because they lack the effective presentation of antigens through HLA molecules. At the same time, **due to the absence of HLA class I molecules, there are no destructive effects** through cytotoxic T-lymphocytes.

Antibodies

Thanks to the predominance of the TH2 lymphocyte subpopulation, the formation of **antibodies** during pregnancy is supported. These antibodies promote a protective character, therefore they **blind the activated immunocompetent cells of foreign structures** that could lead to a cytotoxic reaction.

Immunopathology in pregnancy

Placenta

Unfortunately, the placental barrier is not completely impermeable. Her tolerance lies in a process that suppresses immune reactions that could lead to rejection of the semi-allogeneic fetus. For example, if there is a mechanical disruption of the placenta and the transfer of fetal erythrocytes into the maternal circulation, then in the case of Rh difference between the fetus and the mother, hemolytic anemia of newborns or otherwise known as fetal erythroblastosis can occur. Simply put, **when the Rh-positive erythrocytes of the fetus penetrate into the Rh-negative blood of the mother, the mother induces the formation of antibodies against the fetal erythrocytes**. This immune response has features of a primary antibody response along with the production of antibodies of the IgM isotype. However, in the case of a first pregnancy, this is not a significant threat to the child. Difficulties arise **in the second pregnancy**, when the mother has **developed antibodies against fetal**

erythrocytes . Here, an immune reaction of the secondary type of immune response takes place and antibodies of the IgG isotype are produced here , they pass through the placental barrier, **bind to fetal erythrocytes and destroy them** . The cytotoxic effect is manifested by hemolysis and fetal erythroblastosis and neonatal jaundice occur.

Allergic diseases in pregnancy

Due to genetic predisposition, the greatest risk for the fetus is allergic diseases of the mother, which cause hypersensitivity through IgE antibodies. It mostly concerns **atopy** , therefore women with this hypersensitivity should limit the possibility of contact with the allergen as much as possible during pregnancy, the second trimester is considered the most important period. After birth , **however, a child whose mother is atopic has a high risk of further sensitization** , especially to food allergens via breast milk. The development of this sensitization also depends on the external environment in which the child grows up

Immunological causes of disorders in pregnancy

There are many immunological causes that affect the course of pregnancy itself. **Repeated miscarriages** are mostly experienced by **women with antiphospholipid syndrome, systemic lupus erythematosus or autoimmune thyroiditis** . Fetal loss in these women usually occurs during the second trimester. Dysregulation of immune reactions with the potential for autoimmune damage can also be an immunological cause of repeated miscarriages or even infertility in women.

Treatment of immunopathological conditions in pregnancy

First of all, it must be said that each cause has a different solution, in the following paragraphs I want to introduce you to the basic ones.

Systemic autoimmune diseases

These diseases can be positively influenced **by administering anti-inflammatory doses of glucocorticoids** . Cytostatic drugs are not administered. In women with allergies with features of asthma bronchiale, therapy with inhaled corticoids can be administered. **Antihistamines are not recommended** .

Organ autoimmune diseases

Hormone replacement therapy is prescribed here. For example, in the case of thyroiditis, in which we do not encounter significant clinical disorders of the thyroid gland, treatment is chosen in the form of isohormonal therapy with small doses of thyroid hormones.

Antibody immunodeficiency

If it is **an antibody immunodeficiency of the CVID type** , we choose a form of **substitution therapy with intravenous preparations of gamma globulin** in the ratio of 400-600 mg/kg/month. It may also happen that only intramuscular preparations of Igamplia in the ratio of 5 ml/week are completely sufficient if we are facing a mild form of the disease.

Immunostimulatory therapy

As for **immunostimulation therapy** , it is **not indicated during pregnancy** due to the possibility of damage to the physiological dysregulation leading to TH2 predominance and fetal tolerance.

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Resources

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References

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- ULČOVÁ-GALLOVÁ, Zdenka and Jindřich MADAR. *Immunology and immunopathology of human reproduction: selected chapters*. 2nd revised and supplemented edition of the edition. Prague. 2016. 152 pp. ISBN 978-80-204-3901-7 .

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