Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 12, pp.63042-63046, December, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

INFECTIONS IMMUNOLOGY OF THE PRESENT TIME PREGNANCY IMMUNOLOGY

[1]Andrey M. Zemskov, [1]Veronika A. Zemskova, [*,2]Vladimir M. Zemskov, [1]Elena V. Enkova, [1]ZoyaA. Vorontsova and [1]Natalia I. Ponomareva

[1]Department of Microbiology of Burdenko Voronezh State Medical University, Voronezh, Russia
[2]Clinical Immunology Group, Vishnevsky Institute of Surgery, Moscow, Russia

ARTICLE INFO

Article History:
Received 28th September, 2017
Received in revised form
06th October, 2017
Accepted 11th November, 2017
Published online 31st December, 2017

Key words:
Pregnancy, Fetal,
Infections, Immunity.

ABSTRACT

Was studed and analized the changes in immune reactivity during pregnancy, the mechanisms of fetal rejection inhibition, immune infertility formation, toxicosis, the peculiarities of bacterial, viral, protozoal infections in pregnant women and puerperas and the principles of their treatment

Citation: Andrey M. Zemskov, Veronika A. Zemskova, Vladimir M. Zemskov, Elena V. Enkova, ZoyaA. Vorontsova and Natalia I. Ponomareva, 2017. "Infections immunology of the present time pregnancy immunology", *International Journal of Current Research*, 9, (12), 63042-63046.

INTRODUCTION

Immune reactivity in pregnancy

Immune mechanisms are at the heart of the birth of life, since the interaction of parents' gametes is due to an immune response reminiscent of the compound AG (antigen) with AB (antibody), - fertilizine located on the surface of the egg, and antifertilizine found on spermatozoa. During the formation of a fetal egg, immunosuppressive reactions are formed that prevent rejection reactions. In a follow-up, the immune relationship between the maternal and fetal organism is characterized by a dynamic equilibrium in which the fetus receives passive immunity from the mother and simultaneously develops its own immune competence. At the same time mother sustains her own immune potency without rejecting the trophoblast and the fetus. Generally, the normal duration of pregnancy in most mammals is much longer than the time required for the rejection of allografts. Therefore, a normal pregnancy is a kind of immune "paradox" (Zemskov *et al.,* 2015). During the course of pregnancy mother is sensitized to alloantigens of erythrocytes, serum proteins, platelets, and leukocytes of the fetus. The organ that determines the formation of a biological barrier between the mother and the fetus is the placenta. In it, the trophoblast, a tissue of fetal origin, functions as an immune buffer zone: where the fetal alloantigens are masked by mucoproteins (seromucoid, fibrinoid, sialomucine), maternal immune responses are inhibited by placental hormones (estrogen, progesterone), and trophoblast specific antigens, albumin, α-, β- and γ-globulins, α-1-fetoprotein, α-2-glycoprotein. By the end of the pregnancy, every day about 100,000 trophoblast cells enter mother's bloodstream, performing the function of remote antibody sorbents against fetal cells (Zemskov *et al.,* 2016). There are other mechanisms of tolerance of the immune system of the mother. This is the inability of her macrophages to present fetal antigens, the lack of lymphocytes responsible for immune interaction with fetal antigens - a deficit of lymphocyte repertoire, the presence of serum factors blocking cellular immune responses against fetal lymphocytes and the child's father. T-lymphocytes-suppressors, antigen-antibody complexes, whose content also increases by the end of pregnancy, participate in a specific suppression of rejection. All these changes develop against the background of a significant increase in the concentration of free and protein-bound corticosteroids, allotted with immunosuppressive action. In addition, embryonic and placental antigens, entering the maternal bloodstream in excess, neutralize the antibody produced by the body of the pregnant woman, causing a specific suppression of the immune response. The immune suppressor mechanism in pregnancy is supplemented by the induction of the immune response by Type 2 helper cells that direct the immune response along the humoral pathway, synthesize interleukin-10, which inhibits anti-inflammatory cytokines-IL-1, IL-2, TNF-α (Novikov and Novikov, 2009).

Corresponding author: **Vladimir M. Zemskov,**
Clinical Immunology Group, Vishnevsky Institute of Surgery, Moscow, Russia.

Despite the above mechanisms, the overall immune reactivity of a pregnant woman practically does not suffer. It is able to adequately respond to immunization with vaccines, actively fight infections. However, certain phase changes in immune reactivity do occur. Thus, in the first trimester, there is a decrease in the relative number of T cells, and in III trimester - B-lymphocytes. In different periods of pregnancy, the woman has a change in the content of the main populations and subpopulations of lymphocytes, an increase in the spontaneous migration of macrophages, an increase in the level of the C3 complement component, activation of the lymphocyte blast-transformation reaction by T- but not B-mitogens, variations in the expression of IL-2 receptors on mononuclear cells, an increase in the formation of IL-1, a decrease in the immunosuppressive effect of blood serum. During pregnancy, there is some suppression of the ability to reject the cutaneous graft and respond to stimulation with mitogens of T cells. Disorders of normal fetal development occur with a certain similarity of the HLA genotype of the father and mother, which causes the isosensibilization of the pregnant to the male haplotype, and this prevents the development of the physiological humoral and cellular suppressor mechanisms necessary for bearing the fetus. Besides, there are immune conflicts between the mother and the fetus on Rh Factor and antigens of ABO factor or system, when the red blood cells of the fetus induce the formation of class G cytotoxic anti-group antibodies that cause the development of hemolytic disease especially often when the mother's blood group is 0 (I) and the fetus has a blood group of A (II).

Immune infertility formation mechanisms

It is believed that 75% of infertility in marriage is due to chronic inflammatory processes in the reproductive organs caused by protozoa (trichomonads), bacterial microflora (streptococci, staphylococcus, E. coli), chlamydia, gardnerella, ineffective treatment of venereal diseases (gonorrhea, syphilis, etc.). In addition to these factors in the pathogenesis of infertility the changes in local and systemic immunity with the emergence of a vicious circle: inflammation → disorders of the immune-endocrine mechanisms→secondary immunodeficiency play an important role. The cause of pathology can also be significant acquired immune deficiency without inflammation, increased antispermal immunity (10-15%), the formation of antibodies against sperm in the secretion of the cervical canal, ejaculate, serum, against the egg, increased histocompatibility of spouses gametes. Secondary immunodeficiency can be the cause of infertility II, which is manifested by habitual miscarriage of the fetus (miscarriage in the first trimester of pregnancy) or infertility I - the absence of conception.

Phospholipid syndrome

It is based on the development of an autoimmune reaction to phospholipid determinants found on platelet membranes, vascular endothelial cells, and neural tissue, which is accompanied by the development of various diseases. Relative immune infertility or infertility of an unknown genesis develops at a certain similarity of the HLA genotype of the father and mother, which causes the insensitivity of the pregnant to the male haplotype, which prevents the development of the physiological humoral and cellular suppressor mechanisms necessary for bearing the fetus. If an immune conflict occurs in the body of a woman, then it has an adverse effect not only on the fetus, but also on the mother. So, late toxicosis occurs more frequently in women with 0 (I) blood group, carry a fetus with A (II) or B (III) markers. In severe forms of late toxicosis, there is incompatibility in the HLA leukocyte antigen system. Whereas, antigenic differences between the mother's organism and the embryo are very important, because the higher the degree of genetic alienation, the more viable the fetus is.

Peculiarities of infections in pregnancy

In general, the frequency of cytomegalovirus infection in pregnant women is 13 to 91%, herpetic - from 7 to 47%, chlamydial - from 25 to 40%, mycoplasma - from 17 to 50%, ureaplasma - from 25 to 75%. The frequency of infection of the fetus is from 5 to 60%, depending on the timing of pregnancy, the nature of the pathogen, the state of immune reactivity. With intrauterine infection, almost 50% of patients die in the first 6 months, and 88% die before the age of 1 year (Pokrovsky, 2012; Pokrovsky *et al.,* 2013).

Infectious and inflammatory diseases in pregnant women

Against the background of immunodeficiencies, they are a threat to the fetus, during the latent infection of the fetus. Viral infections – poliomyelitis, hepatitis A and B, influenza can cause pregnant fatty liver dystrophy, acute pancreatitis, disrupt the formation of bones and teeth in the fetus. Bacterial infections cause an increased risk of infection in pregnant women with typhoid fever, gonorrhea, listeriosis, streptococcus, tuberculosis, a more severe course of toxoplasmosis, amoebiasis, giardiasis. In the period of pregnancy, acute, subacute, chronic forms of vaginitis, cervicitis, parametritis, pelvioperitonitis, pyosalpingitis caused by staphylococcus, anaerobic bacterial and fungal infections develop in women due to a deficiency of local and general immunity factors (secretory immune globulin of class A, absorption, metabolic, chemotactic ability of phagocytes). Abdominal typhoid, gonorrhea, tuberculosis, listeriosis, amoebiosis, giardiasis, toxoplasmosis resistant to antibacterial therapy and viral lesions caused by genital herpes, cytomegalovirus, Epstein-Barr virus, influenza, poliomyelitis, hepatitis A and B, etc., can develop which induce severe diseases. In connection with viral cell damage, autoantibodies accumulate to the body's antigens of the ovaries, tubes, and uterus, which serves as an additional factor of inflammation, autoimmune processes and allergization.

General principles of pregnant women treatment

In the presence of infection, antibacterial and antiviral therapy is performed, which often depresses phagocytosis, promotes allergization, imbalance of immune reactivity. Therefore, antibiotics with immunostimulating properties are preferred, local antiseptics with desensitizing and modulating action, vitamins, microelements that enhance the regeneration of the epithelium, cytokines that suppress viruses and possess an anti-inflammatory effect; corticosteroids, antihistamines, depressing allergic reactions. Antimicrobial therapy of infections during pregnancy should take into account the probability of toxic effects on the fetus, increased volume of circulating blood, renal blood flow, etc., which requires increasing the doses of drugs, excluding the prescription of fluoroquinolones (ciprofloxacin, ofloxacin, metronidazole) tetracyclines to women. Antiviral treatment should include early diagnosis of infections, assessment of immune status,

prompt administration of antiviral treatment, assessment of the form, stage, localization and prevalence of the process, the presence and severity of bacterial complications. It is necessary to implement a differentiated mono, combined, complex immunotherapy with sodium nucleate, neovir, lycopide, myelopid, polyoxidonium, suppositories-kipferon, viferon, superlimph, adaptogens, biostimulants, eubiotics, physiotherapy with immunocorrecting effect (ultrasonic radiation, quasi-high frequency radiation), substitution therapy with lactobacilli preparations and others (Zemskov *et al.,* 1996, 2007; Pokrovsky, 2005; Khaitov, Ataullakhanov, 2012).

Postinfectious complications in pregnant women

Influenza

In pregnant women, the frequency of miscarriages in the first trimester is up to 50% with the increase in the probability of congenital malformations. It is permissible to vaccinate pregnant women during the epidemics by the inactivated vaccine A and B.

Herpes virus infection

In women in the first half of pregnancy increases the frequency of miscarriages, in the second - of premature births, forms immunodeficiency in T-cells, their regulatory subpopulations, dysfunction of the mononuclear phagocyte system. Herpes simplex viruses in women with habitual miscarriage are defined in 55% without clinical manifestation, in 10% periodic exacerbations with rashes and skin itching are possible. Usually the causative agent is associated with cytomegalovirus, chlamydia, mycoplasma with a probable outcome in chronic endometritis. Transplant transfer is not infrequent. However, congenital syndrome is possible - with microcephaly, intracranial calcifications, chorioretinitis. A child is usually infected in the process of childbirth in the presence of rashes in the birth canal. The disease manifests itself in disseminated or localized forms. Symptoms of lesions are manifested as early as 4-5 days. The liver, brain, adrenals, lungs and other organs are affected. Children die from pneumonia, coagulopathy, encephalitis.

Chicken pox virus

May cause encephalitis in children.

Poliomyelitis

In 25% is transferred in-utero to the fetuses with the development of paralysis. The virus is not teratogenic. During epidemics, the pregnant women can be vaccinated by inactive vaccine.

Rubella virus

During the primary disease in the first trimester determines a high percentage of miscarriages and congenital malformations-retinopathy, cataracts, open arterial ducts, pulmonary artery stenosis, deafness, thrombocytopenia, CNS damage. In case of absence of antiviral specific IgG in the blood of not pregnant woman the vaccination by live attenuated vaccine is possible. It is not allowed to vaccinate pregnant women.

Measles

In acute illness, it can interrupt pregnancy in seronegative women. The virus is not teratogenic. For the prevention of severe disease in the first 6 hours after contact with the patient, it is desirable to administer human immunoglobulin normal for intravenous administration (octagam, sandoglobulin) at a dose of 0.25 mg / kg body weight. Out of pregnancy, immunization with live attenuated vaccine is carried out.

Acute hepatitis A virus

It is relatively easy for pregnant women. It is diagnosed by a high level of hepatic transaminases and specific anti-viral IgM antibodies in serum. If the mother has suffered the disease during pregnancy, immunization of the newborn is not required, since IgG passes through the placenta. If the pregnant woman was seronegative and in contact with the patient, passive immunoprophylaxis is allowed in the first 14 days by normal human immunoglobulin.

Acute hepatitis B virus

In pregnant women causes fetal death, miscarriages, premature birth. In 60-80% newborns become chronic carriers with a remote risk of developing hepatocellular carcinoma. Therefore, all children born from HBs-positive mothers are injected intravenously with an immunoglobulin of a normal or specific hyperimmune right after birth, and on the first day of life, the child is given active vaccination.

Acute hepatitis C virus

Has a low probability of transmission from the infected mother to the fetus. In combination with HIV, the risk of disease increases.

Acute hepatitis E virus

It is dangerous for women in the third trimester of pregnancy, and etiotropic treatment and immune prevention of infection is absent.

Cytomegalovirus infection

It is dangerous for intrauterine infection in 1% of women, and in women with infection with cytomegalovirus, abortion is most often observed. Congenital pathology manifests itself in the form of mental retardation, meningoencephalitis, pneumonia, hepatitis, retinal lesions, up to blindness, calcification of the brain, thrombocytopenia. When infected, passive vaccination of pregnant and newborns with Cytotect, which contains elevated titers of specific IgG to the cytomegalovirus, is possible.

Epstein-Barr virus

In pregnancy, it can induce anemia, encephalitis, myocarditis, nephritis, liver failure.

Chlamydia in pregnant women

Primary infection caused by this pathogen in pregnant women can cause premature birth, postpartum endometritis. Intrauterine infection of the fetus is extremely rare, but the infection rate during childbirth is up to 40%. In newborns, the disease manifests itself in the form of conjunctivitis, ophthalmochlamydiosis, pneumonia. Less common generalized infections with lung, kidney, heart, digestive tract,

liver, and encephalopathy with seizures develop. Symptoms of intrauterine chlamydial pneumonia appear already on the 4th-5th day of life.

Parasitic infections in pregnant women

Congenital toxoplasmosis can occur only if a woman first becomes infected during pregnancy and does not have specific IgG antibodies. In this case, intrauterine infection of the fetus may occur. There are 4 forms of congenital toxoplasmosis: (a) neonatal, clinically manifested; (b) manifest, in the first months of life; (c) residual manifestations in children and adolescents of previously undiagnosed toxoplasmosis; (d) asymptomatic. Immunotherapy of parasitic infections should be complex, it is necessary to include stimulants of T-dependent protective reactions, interferons, interferonogens, metabolites and antioxidants.

Peculiarities of infections in puerperas

Postpartum infectious-inflammatory diseases

They occur in 13.3-54.3% of cases and occupy 2-4 place among the causes of maternal mortality. The majority of postpartum purulent-septic diseases is endometritis. Its frequency after spontaneous delivery ranges from 6.3 to 49.5%, the operation of cesarean section increases the risk of this complication by 5-10 times. Another representative of infectious and inflammatory complications of puerperia is wound infection, which accounts for between 3 and 20% of all postpartum purulent-septic morbidity. Despite the advances in modern medicine, the risk of severe forms of purulent-septic diseases, such as peritonitis and sepsis, which develop in 0.47-2% of puerperas, remains large, and lethality reaches 32.9%. These diseases continue to occupy a leading place in the structure of maternal mortality. A high level of postpartum infection is due to a number of factors, one of which is the state of the macroorganism, namely, adaptation possibilities, including immune, endocrine, biochemical reactions that provide homeostasis. There is a clear tendency for the growth of postpartum infectious-inflammatory diseases in connection with the increase in the incidence of maternal morbidity. Recently, the number of women with severe extragenital and urogenital pathology has increased significantly. An increase in the incidence in women causes a complicated course of pregnancy and childbirth, which significantly contributes to a decrease of immune tolerance, and this, along with the virulence of the pathogen, the massive infection, the state of the entrance gates and the primary focus of infection leads to the development of the inflammatory process.

Studies of recent years indicate that in the early stages of the postpartum period, transient partial immunodeficiency is observed, which is characterized by a combined deficiency of T- and B-systems of immunity and causes an increased sensitivity of puerperas to bacterial infection. The growth of postpartum purulent-inflammatory diseases is possibly associated with an increase in the proportion of pregnant women with induced pregnancy, accompanied by a decrease in the body's immune reactivity. Complications of the postpartum period may also be caused by a change in the nature of the microflora due to the widespread and not always sufficiently valid application of broad-spectrum antibiotics before and during pregnancy. It is significant that 60% of the women with postoperative endometritis have the same microorganisms from the vagina and uterine cavity. In childbirth there are additional factors that contribute to the development of postpartum infectious diseases. In particular, premature rupture of amniotic fluid, prolonged labor, unreasonable early amniotomy, multiple vaginal examinations, invasive methods of examination of the fetal condition in childbirth, disturbance of the sanitary-epidemiological regime in the obstetric hospital significantly increase the risk of purulent-inflammatory complications in the postpartum period. In addition, in connection with the departure of the mucous plug, which is a mechanical and immune obstacle (due to the secretory IgA), one of the physiological anti-infective barriers of the female genital tract is lost for microorganisms. The outflow of amniotic fluid causes an increase in the pH (a decrease in acidity) of the vaginal contents, and the study of vaginal contents after the outflow of water has revealed an important circumstance consisting in the complete absence of secretory IgA. The reason for this phenomenon is a purely mechanical removal of protein-containing substrates from the surface of mucous membranes of the birth canal, which sharply reduces local secretory protection. It was established that in 6 hours after the outpouring of amniotic fluid, there is practically no anti-infective barrier of the female genital tract, and the degree of dissemination and the nature of the microflora depend on the duration of the anhydrous gap (Zemskov *et al.,* 2008).

Etiology, pathogenesis and clinic of postpartum infectious-inflammatory diseases

At present, microbial associations that have more pathogenic properties than monocultures play a leading role in the etiology of postpartum infectious diseases (more than 80%). Thus, non-spore-forming anaerobic bacteria in association with aerobic species cause the development of severe forms of postpartum endometritis. In the last 10-15 years there is an obvious change in the pathogens of obstetric infection, which is associated with the expansion of the possibilities of specific diagnosis of infection. This applies to various microorganisms, including chlamydia, cytomegalovirus, group B streptococci. Non-spore-forming anaerobic microorganisms have become a real clinical significance. Infringement under the influence of antibiotic therapy of evolutionary-ecological balance between representatives of competitive saprophyte flora and pathogenic microorganisms caused significant changes in the biological properties of some microbes and the growth of their virulence. In this case, the conditionally pathogenic flora acquires pathogenic properties with synergistic action of bacteria in the microbial association, there is a mixed infection, which causes severe inflammatory processes, difficult to treat by traditional methods. In connection with this, a discrepancy appeared between local manifestations of suppuration and the general status of patients, it became more difficult to diagnose the initial stages of the disease. A mixed microflora with low virulence normally colonizes the vagina. Postpartum infections are usually polyethiologic and are associated with the ingestion of intestinal microflora on the perineum and into the vagina. According to one of the studies, in women with endometritis developing within 48 hours after birth, more than 60% of cases showed 2 or more microorganisms. Usually, opportunistic gram-positive cocci are sown (especially Group B streptococci), often in combination with mycoplasma. After birth, the natural barriers to ascending infection disappear for some time, and therefore potentially pathogenic microorganisms are able to penetrate from the vagina into the uterine cavity. After opening the placenta, the wall of the

uterine cavity is a vast wound surface, and the remaining parts of the fetal egg and blood clots in the uterus create an excellent nutrient medium for the growth of bacteria. In addition, births through natural birth canals are accompanied by ruptures of the soft tissues of the birth canal (uterus, cervix and vagina), and although not all of them need to be sutured, they can nevertheless become a gateway to infection. The same danger threatens postoperative wounds (after cesarean section or episiotomy). Severe postpartum infections are caused by hemolytic group A streptococcus (Lansfield classification) and Staphylococcus aureus. An essential role in the origin and flow of the infectious process in the postpartum period belongs to protective mechanisms and, in particular, to the state of immunity. It has been established that even transient partial immunodeficiency is observed in healthy women during pregnancy and in the early stages of the postpartum period (a decrease in the absolute number of B-lymphocytes and "zero" cells-large granular lymphocytes, proliferative activity of lymphocytes, IgG concentration in blood serum). With the development of inflammatory complications after birth, lymphopenia and a significant decrease in the absolute number of T and B lymphocytes, an imbalance of regulatory subpopulations, a deficit in IgG and IgM concentration, IgA, complement, an excess of circulating immune complexes, inhibition of the absorption capacity of phagocytes, and CIC are observed after delivery.

REFERENCES

Khaitov, RM. And Ataullakhanov RI. 2012. Immunotherapy. Manual for doctors. Moscow. Publishing house: GEOTAR-Media. 669 p.

Novikov, DK. and Novikov PD. 2009. Clinical Immunopathology. Moscow. Publishing House: Medical Literature. 449 p. Russia.

Pokrovsky, VI. 2012. National conception of prevention of infections associated with first aid rendering and informational material based on its provisions. Nizhny Novgorod. Publishing House: Remedium Privolzhye. 84 p.Russia.

Pokrovsky, VI. (Ed.). 2005. Handbook of Clinical immunology, Allergology, Immunogenetics and Immunopharmacology for general practitioners. Part 1 and Part 2. Moscow. 517 p. Russia.

Pokrovsky, VI. *et al.* 2013. Infectious diseases and epidemiology.Textbook. 3rd revised edition. Moscow: 1008 p. Russia.

Zemskov, AM. *et al.* 2007. Immune disorders and their correction at pyo-inflammatory processes. Moscow. Publishing House:Triada-X.160 p. Russia.

Zemskov, AM. *et al.* 2015. Handbook of a Clinical Immunologist. Theoretical, Practical and Applied Aspects of Clinical Immunology at the Present Stage. Moscow. Publishing House: Triada-X.704 p. Russia.

Zemskov, AM. *et al.* 1996. Principles of Prescription of Immunocorrective Medicines.*Russian Medical Journal.*№ 6.p.44- 47. Russia.

Zemskov, AM. *et al.* 2016. Immunology. Electronic Textbook with applications. Approved by FIRO. Moscow. Publishing House: GEOTAR-Media. 127 author lists. Russia. http:// www.studentlibrary.ru/ru/book/01-GEO-201601.html.

Zemskov, AM. *et al.* 2008. New principles evaluation and correction of immunological disorders. Publishing House: Triada-X. 336 p. Russia.

****