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MODULATION OF IMMUNITY AND BARRIER FUNCTION IN PRE- AND POSTNATAL ANIMAL ONTOGENESIS. MECHANISMS OF NATURAL RESISTANCE IN NEWBORN PIGLETS

Masiuk D. M., Nedzvetsky V. S., Kokariev A. V.

INTRODUCTION

Non-specific protection of the animal body are represented by various proteins and peptides[1]. They are present in the various biological fluids and circulate in the blood of animals in the significant amount to maintain the homeostasis[2]. These factors have antimicrobial properties or have the ability to activate other humoral and cellular immune defense mechanisms[3].

Immunoglobulins, namely antibodies, are the group of soluble glycoproteins that persist in peripheral blood and biological fluids[4]. They have the ability to interact with antigens and thus cause neutralization of the latter[56]. This specific recognizing is accompanied by the antigen-antibody immune complex formation, which circulate in the blood for a while[7].

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The main source of immunoglobulins in newborn piglets is the colostrum[89]. Colostrum is the main factor in the newborn piglet protection, as it contains a large number of immune and biologically active substances that maintain piglet health beginning with the first colostrum consuming[10]. This result in the formation of both general and local colostral immunity, which level depends on the immune proteins concentration in colostrum[11]. Colostral immunity has an important impact to maintain the health, the viability, as well as the safety of piglets first week of life[12,13].

1. Physiological aspects of humoral immunity mechanisms mounting in early ontogenesis piglets

After birth, piglet has the potential ability for the functional restructuring of various systems and organs[14]. This period is called the neonatal period. For pigs, it lasts about three weeks. Its end coincides with the ability to secrete hydrochloric acid by the glandular cells of the piglet's stomach[1516]. At the same time, the newborn organism's physiological systems are in a state of

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unstable equilibrium. Its violation can lead to various diseases[17]. A certain dependence of piglet safety in the suckling period on the total protein and immunoglobulin levels in their blood serum has been determined[18][19].

The weight of piglets after birth is related to the mortality rate in the neonatal period[20][21]. The piglets with a body weight of 1.4 kg on average during the suckling period have a mortality rate of 8 %. Whereas the mortality rate of piglets with a body weight of 1.0 kg reaches 20%[22]. This dependency is associated with differences in viability and with varying placental nutrient supply or endocrine differences in uterine conditions[23]. Therefore, the neonatal period is essential for the postnatal formation and animal development. Immediately after birth, newborn animals remain in the late fetal period for some time. During the same period, which coincides with the neonatal period and lasts 12–14-day, prenatal structures of the body, including components of the immune system, are transformed into newborns. This is indicated by dynamic changes in the haematopoiesis and immunopoiesis

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structures and blood components[24][25][26]. Leukocyte number, their phagocytic activity and the content of protein fractions in piglets before colostrum consumption are similar to the values of these parameters in pig fetuses of the late fetal period. In 4–6 hours after birth, the piglets' blood shows an increase of active microphages, phagocytic number, phagocytic capacity, albumin and γ-globulin content by more than 50%[27][28].

Biochemical blood characteristics in piglets before colostrum consumption differ in the large range from those in animals on the first day of life[29]. The level of total protein, including the fraction of γ-globulins, glucose, bilirubin, increases, the activity of the enzymes ALT, GGT and LDH increases, and the amount of albumin, urea and alkaline phosphatase activity decreases.

Another factor indicating the immaturity of the newborn piglet immune system is the low bactericidal and lysozyme activity level in the blood serum[30][31].

The early piglet development period is characterized by low natural resistance levels of the organism. Under these conditions, the blood serum bactericidal activity is in the range of 40.9±1.90%, the neutrophil phagocytic

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activity is 21.0±0.84 %, and the phagocytic index is up to 1.0±0.09 %[32]. This is due to the haemopoietic organs immaturity. They produce young forms of leukocytes with a low phagocytosis capacity.

2. Physiological aspects of cellular immunity mechanisms mounting in early ontogenesis piglets

Morphological changes in the tissue structure of the spleen and thymus in early postnatal piglets are associated with their adaptive functional adaptiveness rate during the first three weeks of piglet life. They are characterized by an increase in the lymphoid tissue percentage[33][34]. Before birth, the piglet lymph nodes only form a full range of morphological markers of immunocompetence at the tissue and cellular levels. Their functional development begins after birth and continues until the end of the lactation period[35]. In the late fetal and early neonatal periods, there is an increase in the absolute weight of the thymus, including its cortical zone, and an increase in the number of thymic bodies in the cerebral zone[36]. At the moment of birth, the thymus cortical zone occupies about 80% of the whole organ weight and contains about 95% of all thymocytes. Meanwhile, in the cerebral thymus layer, single T-lymphocytes and Hassel bodies are detected. Their number increases rapidly in piglets on the second day of life. This is associated with the newborn immune system's response to antigens. Thymus involution in piglets begins during puberty[37]. In one-day-old piglets, the number of T-lymphocytes in the thymus is about 78%, on day 5 of life its level decreases to 55% and remains at this level for 2 months. The newborn piglet thymus

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also contains B lymphocytes, but their number does not exceed 4%[38][39]. Also, in the lymph nodes and spleen, many lymphoid nodules with proliferation foci are created. It indicates the body's ability to respond to antigens. This is confirmed by the intensive lymphoid tissue development in the tonsils, spleen, feather plaques, etc. In piglets of 2-week-old, secondary follicles appear in many lymph nodes. Starting from 3–4-week, plasma cells are found in the bone marrow[40].

The spleen parenchyma which is represented by red and white pulp, is not clearly demarcated in newborn piglets[41]. White pulp makes up about 7% of the organ parenchyma. During 7 days of life, the organ weight increases almost 3 times. This leads to an increase in white pulp by 16%. The white pulp is composed of lymphoid cells, including lymphocytes, lymphoblasts, reticulocytes and macrophages. It indicates the active immune system of newborn piglets' development during the first week of life. Newborn animals have an unformed immune system during the first days of life, as indicated by the lymphoid tissue development state at the fetal level[42]. This is also facilitated by the morphological structure peculiarity of the placental barrier between the sow and the fetus. The pig's placenta is of a diffuse, epithelia-choroidal type. The placenta is impervious to macromolecules, including antibodies. This leads to the creation of an immune balance between the embryo or fetus and the mother's body[43].

The fetal immune system is formed in the late fetal period due to the genetic potential realization and the placental barrier presence[44]. The immune

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system's central organs in piglets are formed at the end of prenatal development. Their maturation occurs after birth, directly under the antigenic load influence[45]. It is accompanied by an increase in the number of T-lymphocytes in piglets up to 2 months of age[46].

Piglets' first two weeks of life are typified by a decrease in the number of phagocytic cells. It is associated with the colostrum immune defense in newborns formation. At the end of the first month of life, this indicator increases, which is associated with the formation of their own immune system[47]. At the same time, during the first month of life, a gradual increase in the number of T-lymphocytes occurs in the piglet's blood[48]. By the end of the second month of life, their number in the piglet's blood reaches the adult pig level. It should be noted that the number of leukocytes in the newborn piglets' blood increases by more than 50 % during the first day of life, mainly due to T-lymphocytes. Whereas the B-lymphocyte level is several times lower than in 4–6-month-old pigs, and after 4 weeks their number doubles[49,50].

Antibodies are detected in the blood of piglets before birth. This indicates a placental barrier violation by antigenic structures and the unborn organism's

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contact with them. This is because the first immunoglobulins synthesis is possible in pig fetuses from the early fetal period[51][52].

The development and growth of immunocompetent structures is autonomous in accordance with the genetic potential due to the placental barrier[53]. It is determined by their ability to respond to the antigen action entering the body immediately after birth. Colostrum proteins are such an antigen, which activate the immunocompetent newborn organs[54][55].

Under the colostrum proteins influence, lymphocytes rapidly colonise the mucous membranes and lymph nodes. As a result, prenatal lymphoid structures change into competent ones. This is confirmed by the inhibition of the immunocompetent structure's formation for 20-30 days with late colostrum feeding. Thus, at the time of birth, piglets form a complex of immunocompetence morphological markers at the tissue and cellular levels. After birth, their functional development is activated[56][57].

The immune components activity in piglets during the first weeks of life has a downward trend. At the end of the suckling period, it changes to an

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upward trend due to the activation and intensification of their own immune system components[58][59].

CONCLUSIONS

Thus, at the time of birth, piglets form a complex of immunocompetence morphological markers at the tissue and cellular levels. After birth, their functional development is activated. The immune components activity in piglets during the first weeks of life has a downward trend. At the end of the suckling period, it changes to an upward trend due to the activation and intensification of their own immune system components.

SUMMARY

The number of studies related to investigation of development of immune system at early stages of ontogenesis are directed to expansion of concepts of mechanisms of inherent and adaptive immunity in premature newborns. However, discrepancy in publication data and absence of accurate conceptions about unique features of immune system in newborn piglets of various gestation age determine actuality of further investigation of this problem. The study was carried out to establish characteristics of phenotypic and functional characteristics of the immune cells and establishment of adaptive immunity in piglets.

The antibody repertoire of sow has interested immunologists for decades, in part because of the ease with which large quantities of high affinity antibodies can be observed in serum, and into other fluids because of the presence of genetic variants for both light and heavy chain of all known immunoglobulin types.

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Information about the authors:
Masiuk Dmytro Mykolayovych,
Doctor of Veterinary Sciences, Professor
Head of the Department of Physiology,
Animal Biochemistry and Laboratory Diagnostics,
Dnipro State Agrarian and Economic University,
25, Serhiia Yefremova str., Dnipro, 49600, Ukraine

Nedzvetsky Victor Stanislavovych,
Doctor of Biological Sciences, professor
Vice-director of Scientific Research Center of Biosafety
and Environmental Control Agro-Industrial Complex,
Dnipro State Agrarian and Economic University,
25, Serhiia Yefremova str., Dnipro, 49600, Ukraine

Kokariev Andrii Viktorovych,
Candidate of Veterinary Sciences, Associate Professor,
Head of the Department of Immunochemical
and Molecular Genetic Analysis,
Scientific Research Center of Biosafety
and Environmental Control Agro-Industrial Complex,
Dnipro State Agrarian and Economic University,
25, Serhiia Yefremova str., Dnipro, 49600, Ukraine