The analysis of published and original data demonstrates that prenatal stress induced by viral and bacterial infection, or changes in the physiological concentrations of neurohormones in early ontogeny can cause unfavorable impacts on the development of neuroendocrine and immune systems. In early pregnancy bacterial infection simulated by lipopolysaccharide in an experiment activates the maternal immune system, which enhances the synthesis of pro- and anti-inflammatory cytokines in both maternal and fetal organisms. Consequently, cytokines promote the secretion of a hormonal cascade in the hypothalamic-pituitary-adrenal system, thus eliciting the hormonal response to stress. Various stress factors during critical periods of neuroendocrine and immune system development modulate the epigenetic mechanisms controlling specific genes, which can affect the structure and function of these systems and increase the risk of various pathologies in the offspring.

Keywords: prenatal programming; proinflammatory cytokines; neurohormones; neuroendocrine and immune systems; long-term effects.

Various stress factors including viral and bacterial infection and changes in the physiological concentrations of neurohormones in early ontogeny can affect the molecular mechanisms controlling the formation and functioning of neuroendocrine and immune systems. The induced modifications can disturb programming of these systems’ development that increase the risk of various pathologies in offspring [1]. The purpose of this study was to analyze original and published data of the reciprocal influence of neuroendocrine and immune systems on their development and functioning in normal physiological and pathological states. Experimental studies often use bacterial lipopolysaccharide (LPS), which is one of the most potent natural inducers of inflammation. LPS activates the maternal immune system, which enhances the synthesis of pro- and anti-inflammatory cytokines in both maternal and fetal organisms. Consequently, cytokines promote the secretion of a hormonal cascade in the hypothalamic-pituitary-adrenal system, thus eliciting the hormonal response to stress [2]. The excessive production of proinflammatory cytokines leads to premature labor, various bone malformations, thymus atrophy, and impaired development of bone marrow. After maternal LPS exposure in early pregnancy the expression of factors involved in neurogenesis, neuronal migration, and axonal cone growth is suppressed [3]. The white matter injury increases the risk of cerebral palsy in newborns and typical manifestations of schizophrenia in adulthood [4]. The degradation of serotonergic neurons induced by LPS in the fetus is attributed to the increased levels of IL-6 and TNFα as well as to anxiety and depression in children. Dopamine deficiency leads to the development of dysthymia, Parkinson’s disease, impairs learning [2, 5].

According to our data, the increased levels of IL-6, LIF and MCP-1 in rat maternal-fetal system after prenatal LPS exposure affect the development and functions of hypothalamic-pituitary-gonadal system [6]. Prenatal deficiency of serotonin causes
the increase of cellular and humoral immune response, while the deficiency of dopamine and gonadotropin releasing-hormone (GnRH) causes the suppression of cellular immune response in adult offspring [7]. The expression of different types of serotonin, dopamine and GnRH receptors in thymus is identified from the 16th day of embryonic development. The inhibition of monoamine and GnRH synthesis or blockades of their receptors by antagonists in fetuses change the pattern of T lymphocyte maturation in the thymus of adult rats. Regulatory cytokines, which synthesis is increased in the fetal thymus under neurohormonal influence, are involved in the realization of these effects. Thus, early development is the period in which the epigenetic mechanisms providing for the adaptive plasticity of physiological systems are realized. Disruption of molecular mechanisms controlling the development during this period can induce long-term or irreversible changes in their functions.

References