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**STUDY OF MODERN  
PROBLEMS OF  
CIVILIZATION**

**V**

**SCIENTIFIC AND PRACTICAL  
CONFERENCE**

**19-23 October**

**Oslo, Norway**

**DOI 10.46299/ISG.2020.II.V**

**ISBN 978-1-63649-940-6**

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Abstracts of V International Scientific and Practical Conference

Oslo, Norway  
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Library of Congress Cataloging-in-Publication Data

UDC 01.1

The V th International scientific and practical conference «STUDY OF MODERN PROBLEMS OF CIVILIZATION» (October 19-23, 2020 Oslo, Norway 2020. 516 p.

ISBN - 978-1-63649-940-6`

DOI - 10.46299/ISG.2020.II.V

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**INTRANATAL ANTIGEN INJECTION AS AN  
EXPERIMENTAL MODEL OF UNDIFFERENTIATED  
CONNECTIVE TISSUE DYSPLASIA SYNDROME**

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The role of connective tissue in the functioning of organs and systems of the body is undeniable, because it performs many functions, participates in maintaining homeostasis, so disorders of connective tissue metabolism lead to a variety of structural changes in organs, contribute to the formation of secondary (associated) pathologies of internal organs and systems. Connective tissue dysplasia is a group of genetically heterogeneous and clinically polymorphic pathological conditions characterized by impaired connective tissue formation in the embryonic and postnatal periods, and also combines a number of genetic syndromes (Marfan, Ehlers-Danlos) and undifferentiated (non-syndromic) forms with multifactorial development mechanisms. In contrast to the syndromic forms, the manifestations of undifferentiated forms of connective tissue dysplasia are not so pronounced and often pass unnoticed. However, the universality of the connective tissue defect in undifferentiated forms of connective tissue dysplasia causes a variety of visceral changes, some of which can have serious clinical consequences. The variety of clinical manifestations of undifferentiated connective tissue dysplasia complicates its diagnosis. Connective tissue dysplasia is based on a violation of collagen synthesis, which is manifested in the insufficiency or defect of fiber formation, which is associated with a decrease and / or violation of the metabolic activity of fibroblasts. Systematic lesions in connective tissue dysplasia is confirmed by the presence of pathology of the cardiovascular system, musculoskeletal system, various parts of the

gastrointestinal tract, including reactive changes in the pancreas, primary caries, impaired intestinal motor function etc.

In the modern literature there is enough data on the clinical manifestations of connective tissue dysplasia, its diagnosis, principles of correction, but work on the factors leading to dysplasia and morphological manifestations of this condition, as well as data reflecting the patterns of connective tissue morphogenesis in normal and after modeling changes in the mother-placenta-fetus system in the early periods of ontogenesis is not enough.

**Purpose:** to establish systemic reactive morphological changes of the knee joint, heart, organs of digestive system after intranatal injections of antigens.

**Materials and methods.** To study the features of reactivity, morphogenesis and systemic reactions of connective tissue, the knee joint, heart, pharynx, duodenum, pancreas, ileum, cecum and ascending colon of white laboratory rats from birth to the ninetieth day of postnatal life were selected. All animals were kept according to the relevant recommendations. The studied animals were divided into three groups: the first group - intact rats; the second - control rats, which were injected with saline solution; the third - rats, which obtained on the 17<sup>th</sup> day of the dated pregnancy was antigen according to the method of Voloshin MA. When working with experimental animals, it was guided by the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 18.03.86), the Law of Ukraine № 1759-VI (15.12.2009) On the Protection of Animals from Cruelty. To study the peculiarities of the distribution and structure of fibers, histological samples were stained according to Mallory, Van Gieson, orcein-fuchsin, and the Laidlow silver carbonate impregnation reaction was performed.

Analysis of the obtained results was conducted by means of statistical methods with the use of computer license program «Statistica for Windows 13» (StatSoft Inc., № JPZ804I382130ARCN10-J). The compared results considered such, that for certain differ at  $p < 0,05$ , that is generally accepted for biological and medical researches.

**The results and discussions.** It is found that in the capsule of the knee joint and ventricular myocardium of rats after intrauterine administration of immunoglobulin slows down the process of fiber formation in comparison with control and intact animals, increases the relative area occupied by extracellular matrix compared to control. In rats after intranatal injection of immunoglobulin it is revealed a significantly thickens of the synovial layer of the joint capsule visceral part, associated with the acceleration of differentiation of articular cartilage and with compensation of functional immaturity of the extracellular matrix of articular cartilage, which is not able to provide adequate resistance to pressure with increasing load. Thinning of the intima-media complex of the arteries of the heart ventricles is also observed in experimental animals after intranatal injection of immunoglobulin. In the pancreas of animals after intrauterine administration of antigen from the 1<sup>st</sup> up to the 14<sup>th</sup> day of life significantly increases the relative area of the organ occupied by connective tissue, that is especially pronounced in newborns:  $12.35 \pm 0.21\%$ , compared to the control group ( $9.15 \pm 0.28\%$ ). The relative area occupied by the

exocrine part was reduced by 4% in newborn rats in the experimental group compared to the control group. In the duodenum, ileum and colon, there is a thickening of the mucous membrane on the background of thinning of the muscular layer, mainly due to the longitudinal layer. There is an elongation of the tubular organs of the intestinal tract. Also, in experimental rats after intranatal injection of immunoglobulin there is a disproportionate formation of the membranes of the proximal and distal parts of the duodenum. In all studied organs of laboratory animals in comparison with the control ones there is an increase in the absolute number of lymphocytes, including cytotoxic, CD 16<sup>+</sup>, CD 8<sup>+</sup> and PNA<sup>+</sup> lymphocytes.

Thus, experimentally established changes in rats after intranatal injection of immunoglobulin in the form of impaired fiber distribution in the joint capsule, thickening of articular cartilage on the 14<sup>th</sup> day and its progressive further thinning up to the 60<sup>th</sup> day; earlier appearance of subchondral bone with subsequent limb bone formation process of fiber formation in the myocardium of the ventricles of the heart; thinning of the intima-media complex of the heart arteries; elongation of the tubular organs of the intestinal tract on the background of thinning of the muscular layer mainly due to the longitudinal layer; increasing the relative area of connective tissue of the pancreas, - approve an intranatal injection of antigen as an experimental model of the syndrome of undifferentiated connective tissue dysplasia.