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THE IMPACT OF SYNTHETIC DYE TARTRAZINE (E102) ON THE THYMU MORPHOFUNCTIONAL STATE IN PREGNANT RATS

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Introduction. It is known that even within the permissible daily doses, namely no more than 7.5 mg/kg of body weight per day, regular use of tartrazine (E102) can cause pathological changes in the human body. Tartrazine crosses the placental barrier; therefore, it can be toxic to both the mother and the fetus. Analysis of modern scientific literature indicates that information on the features of immune homeostasis of both pregnant and fetuses under the influence of tartrazine is extremely limited. **Objective.** To identify the morphofunctional features of the thymus in pregnant rats induced by exposure to the synthetic dye tartrazine (E102). **Materials and Methods.** The experiment was conducted on female WAG rats divided into two groups: a control group (Group C, $n = 7$) and an experimental group (Group T, $n = 7$). Beginning at the age of 2 months, the experimental animals received 1 mL of a 0.1% solution of tartrazine (synthetic food dye E102) daily for one month, initially by intragastric gavage and subsequently as a dietary supplement. Animals in the control group received 1 mL of physiological saline. At the age of 3 months, all females were mated with males. Following fertilization and throughout the lactation period, females in Group C continued to receive saline, whereas animals in Group T continued to receive the tartrazine solution. At the age of 8 months, the animals were euthanized by decapitation. Thymic tissue specimens were stained with hematoxylin and eosin, Van Gieson's picrofuchsin, and Mallory staining methods. Immune cell populations were identified using monoclonal antibodies produced by Serotec (Bio-Rad). The following markers were used: CD8, CD4, CD45RA, Thy-1, and ED1. Statistical analysis included comparison of mean values between groups using Student's *t*-test and the Mann-Whitney U-test. Differences were considered statistically significant at $p < 0.05$. Statistical calculations were performed using Statistica Soft 6.0 software. **Results.** Tartrazine intoxication led to the thymus cortex hyperplasia in pregnant rats (cortex to medulla ratio 2.22:1.0) due to proliferation of the lymphoid component and enhanced migration of T-progenitors into the subcapsular zone, while thymocyte differentiation was disrupted, immature forms that express Thy-1 accumulated and the number of mature CD4⁺ cells was significantly reduced, which resulted in a decrease in the immunoregulatory index and selective suppression of the helper component of immunity. The population of B-lymphocytes (CD45RA⁺) in the medulla and perivascular spaces increased; the ED1⁺ macrophage component was activated. **Conclusion.** Exposure to tartrazine during gestation induces morphofunctional alterations in the thymus of pregnant rats that are opposite in direction to the physiological thymic changes observed during uncomplicated pregnancy. Follicular hyperplasia, stage I accidental transformation, accumulation of immature T lymphocytes, and activation of humoral and macrophage components indicate pronounced antigenic stimulation and toxic stress. These changes contribute to impaired thymocyte selection and the development of marked immunoregulatory imbalance, characterized by reduced helper T-cell activity accompanied by a tendency toward increased suppressor activity.

Keywords: pregnant rats, thymus, morphofunctional features, immunomorphology, tartrazine.

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Introduction

The most common synthetic food dye, tartrazine (E102), belongs to azo compounds. In addition to the food industry, tartrazine has long been widely used in the cosmetic and pharmacological industries. The use of food additives is regulated by international legislative documents [1, 2]. The order of the Ministry of Health of Ukraine dated 08.01.2024 regulates the requirements for food additives in Ukraine [3]. The current literature data indicate that even within the permissible daily doses, namely no more than 7.5 mg/kg of body weight [2], regular use can cause pathological changes in the human body. Even low doses of tartrazine can change the configuration of genes, without changing the DNA sequence itself, which can lead to microdamage to chromosomes [4]. Under the influ-

ence of tartrazine, the levels of AST, ALT and AP increase significantly, and moderately pronounced alterative changes are observed in hepatocytes [5]. The toxic effect of tartrazine on the nervous system and liver function is associated with oxidative stress, when the production of reactive oxygen species (ROS) is enhanced, which contributes to alterative changes in the cells, and stimulates the inflammatory response [6]. Oxidative stress, which accompanies tartrazine intoxication, has a detrimental effect on the cardiovascular system and, as a result, leads to damage to cardiomyocytes and impaired vessel formation with damage to the endothelial lining. The lipid profile also changes, namely the accumulation of free radicals leads to lipid peroxidation in the myocardium [6]. It is also known that tartrazine may play a role in carcinogenesis and the occurrence of epigenetic modifications.

This is evidenced by an increase in the expression of DNA methyltransferases (DNMTs) and histone deacetylases (HDACs) in combination with DNA damage intensification [4]. The literature data on the effect of tartrazine on the immune system of both humans and experimental animals are scarce. Increased activity of HDACs (Histone Deacetylases) proteins modulates the density of DNA packaging, which affects the stability of the immune cell genome [4]. Under the influence of tartrazine, hypersensitivity and pseudoallergic reactions may develop. These reactions are not IgE-mediated but are associated with direct mast cell degranulation and disturbances in arachidonic acid metabolism [6].

Studies investigating the effects of tartrazine on pregnant females and the fetus indicate that this compound is capable of crossing the placental barrier. Tartrazine has been shown to induce disturbances in nervous system development in *Danio rerio* embryos through mitochondria-mediated apoptosis [7]. Studies on human umbilical vein endothelial cells demonstrated that tartrazine inhibits endothelial cell proliferation [8]. Oral administration of tartrazine to rats at a dose of 7.5 mg/kg throughout gestation results in visceral and skeletal abnormalities in the offspring, accompanied by pronounced hemorrhagic changes, inflammatory cell infiltration, and degenerative alterations. In the skeletal system, these effects include reduced trabecular thickness, decreased bone volume, significant changes in bone matrix composition and quality, and a marked reduction in fracture strength [9].

Tartrazine exerts embryotoxic effects in pregnant Wistar rats. Although administration of tartrazine does not significantly affect the adjusted body weight of pregnant females, it leads to delayed fetal development, the appearance of morphological abnormalities, embryonic resorption, and delayed skeletal ossification. In addition, morphological alterations have been identified in the placenta, liver, and kidneys of both maternal and fetal organisms [10]. It has also been demonstrated that fetuses exposed to tartrazine via transplacental transfer exhibit signs of chronic glomerulonephritis and tubulointerstitial nephritis during the early stages of postnatal development [11]. However, analysis of contemporary scientific literature indicates that data regarding the effects of tartrazine on immune homeostasis in both pregnant females and fetuses remain extremely limited.

Objectives

To identify the morphofunctional features of the thymus in pregnant rats induced by exposure to the synthetic dye tartrazine (E102).

Material and Methods

The experiment was conducted on female WAG rats. Prior to the study, following transportation, the animals underwent a 10-day adaptation period un-

der barrier-system conditions with group housing. All rats were maintained under identical environmental conditions, received a standard balanced diet consisting of compound feed supplemented with iodized premix, and had body temperatures ranging from 38.5°C to 39.5°C at the time of examination. The animals meeting the inclusion criteria were randomly assigned to two groups: a control group (Group C, $n = 7$) and an experimental group (Group T, $n = 7$). Beginning at 2 months of age (adolescent period) [10], rats in the experimental group received 1 mL of a 0.1% tartrazine solution (synthetic food dye E102) daily for one month, initially via intragastric gavage and subsequently as a dietary supplement. Control animals received 1 mL of physiological saline. At the age of 3 months, females from both groups were mated with males. Following fertilization and throughout lactation, females in Group C continued to receive saline, whereas animals in Group T continued to receive tartrazine solution. All animals were maintained under standard vivarium conditions. At 8 months of age, the rats were euthanized by decapitation.

Thymic tissue was collected for morphological analysis. After fixation in 10% formalin, the thymuses were embedded in paraffin, and 5–6 μm sections were prepared. Histological sections were stained with hematoxylin and eosin, Van Gieson's picrofuchsin, and Mallory staining methods. Microscopic examination was performed using an Olympus BX-41 microscope, followed by morphometric analysis using Olympus DP-Soft version 3.1 software. Thymocyte density per 1 mm^2 was determined at $\times 400$ magnification, whereas the relative volumes of the cortex and medulla were assessed at $\times 200$ magnification.

Immunohistochemical analysis was performed on paraffin sections using primary (direct) immunofluorescence according to Coons and the technique of M. Brosman. Immune cell populations were identified using monoclonal antibodies (MAbs) produced by Serotec (Bio-Rad). The following markers were applied: CD8, CD4, CD45RA, Thy-1, and ED1. The helper/suppressor ratio was subsequently calculated. Fluorescent preparations were examined using an Axioskop 40 FL fluorescence microscope (Carl Zeiss) and documented with a Canon A520 digital camera.

Statistical analysis included Student's t-test and the Mann-Whitney U-test. Differences were considered statistically significant at $p < 0.05$. Statistical calculations were performed using Statistica Soft 6.0 software. Data are presented as mean $\pm$ standard deviation ($M \pm SD$).

The study was conducted in accordance with EU Directive 2010/63/EU on the protection of animals used for scientific purposes and the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (ETS No. 123). The experimental protocol was approved by the Ethics and Bioethics Board of Kharkiv National Medical University.

Results

In all observations, microscopic examination of the thymus revealed lobules of varying size separated by interlobular connective tissue, which was more prominently developed in the thymuses of animals that did not receive tartrazine (Group C). This finding was confirmed by analysis of tissue sections stained using special histological techniques. With Van Gieson staining, the connective tissue component appeared red, whereas Mallory staining rendered it blue. In addition, connective tissue was more pronounced in the perivascular spaces of the thymic medulla in Group C animals.

Compared with controls, animals in Group T more frequently demonstrated incompletely formed lobules with scalloped borders and indistinct differentiation between cortical and medullary regions. In fully developed lobules, a hyperchromic cortex and a lighter medulla were clearly distinguishable. The hyperchromicity of the cortical region was associated with dense packing of thymocytes. Accordingly, the density of cortical thymocytes in Group T animals was significantly higher than in controls ($15,674.0 \pm 130.11$ vs. $13,123.0 \pm 134.23$ cells/mm², $p < 0.05$). Notably, the density of medullary thymocytes was also significantly increased in the thymuses of tartrazine-

treated animals compared with the control group ($13,267.0 \pm 114.67$ vs. $10,234.0 \pm 98.18$ cells/mm², $p < 0.05$).

Whereas in Group C the relative volume of the medulla slightly exceeded that of the cortex (cortex: $47.0 \pm 11.19\%$; medulla: $53.0 \pm 8.94\%$), animals in Group T demonstrated a marked predominance of the cortical region (cortex: $69.0 \pm 5.86\%$; medulla: $31.0 \pm 4.23\%$). In both groups, the subcapsular zone was clearly visualized; however, in Group T thymuses it was markedly expanded and consisted of 5–9 cell layers, whereas in Group C it was represented by only 2–3 cell layers.

Pronounced morphological alterations were identified in both the inner cortical zone and the medulla of thymuses from females in Group T. Specifically, signs of accidental thymic transformation were observed in the cortical region, including a characteristic “porous clearing” pattern corresponding to stage I accidental transformation of the thymus. Lymphocytes of various sizes, small, medium, and large, were detected within the inner cortical zone.

Follicular hyperplasia of mainly the internal parts of the cortical substance was characteristic of the thymuses of group T, germinative centers were detected in individual follicles (Fig. 1).

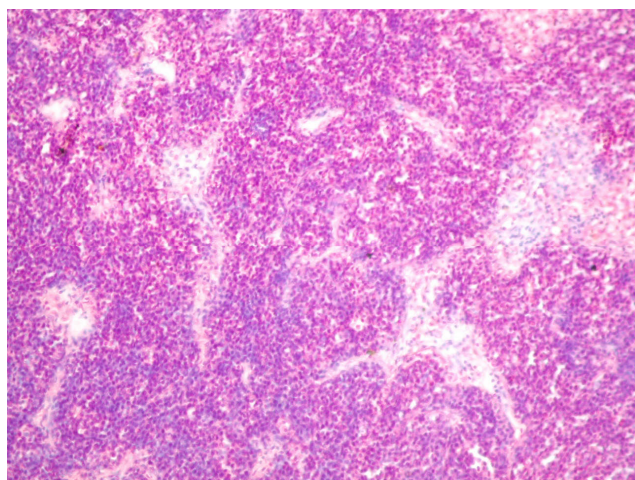


Fig. 1. Follicular hyperplasia of the thymus cortical substance in pregnant rats receiving tartrazine. Observation of group T. Hematoxylin and eosin, x 200

In the medullary regions of thymic lobules in all examined specimens, small lymphocytes predominated. These medullary lymphocytes were characterized by the presence of rounded, moderately basophilic nuclei surrounded by a narrow rim of cytoplasm.

Compared with the control group, thymic corpuscles located within the medulla were enlarged in tartrazine-treated animals; some demonstrated cystic degeneration accompanied by accumulation of eosinophilic detritus. In addition, the thymuses of animals exposed to tartrazine contained increased numbers of plasmablasts, plasma cells, and

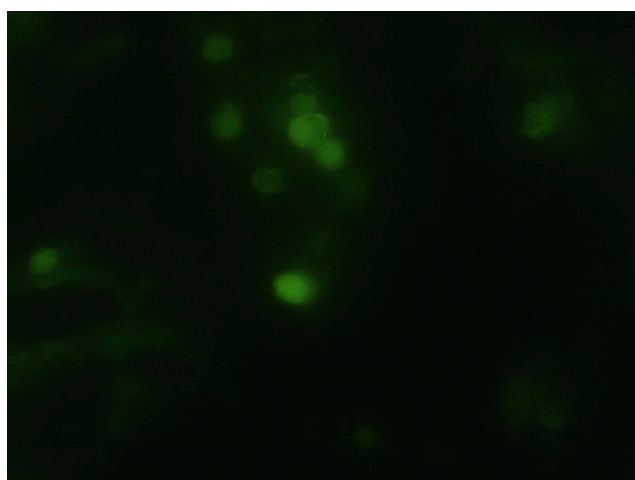


Fig. 2. Accumulation of CD45RA- lymphocytes in the thymus medulla of pregnant female rats receiving tartrazine. Observations of group T. Primary (direct) immunofluorescence (according to Coons) with MCA to CD45RA, x 400

macrophages within the perivascular spaces.

Immunohistochemical analysis using monoclonal antibodies against different immune cell populations revealed significant differences compared with controls. Among thymocytes, there was a significant increase in the proportion of immature pre-T lymphocytes expressing Thy-1 receptors ($7.85 \pm 0.404\%$ vs. $2.11 \pm 0.0306\%$), B lymphocytes expressing CD45RA ($6.85 \pm 0.594\%$ vs. $3.42 \pm 0.649\%$), and macrophages positive for ED1 ($15.28 \pm 0.565\%$ vs. $10.85 \pm 0.828\%$) ($p < 0.05$). These changes occurred against the background of a significant decrease in the population of mature

CD4⁺ lymphocytes ($54.57 \pm 0.947\%$ vs. $66.14 \pm 0.670\%$, $p < 0.05$) and a tendency toward an increased proportion of CD8⁺ suppressor T lymphocytes ($35.28 \pm 0.714\%$ vs. $33.71 \pm 1.084\%$).

Notably, the immunoregulatory index was significantly reduced in comparison with the control group (1.546 ± 0.0206 vs. 1.962 ± 0.0402 , $p < 0.05$). CD45RA⁺ and ED1-positive cells were localized predominantly within the medulla and perivascular spaces (Fig. 2).

Discussion

Analyzing the findings of the study, we paid attention to the fact that in rats of group C the relative volume of the medulla was slightly larger than that of the cortical substance of the lobules, although according to the literature, in the late stages of gestation the cortical substance prevails over the medulla [12]. This can be due to the minimal antigenic stimulation of the mother's body in the vivarium conditions, while in group T, on the contrary, the volume of the cortex significantly exceeds that of the medulla in the lobules of the thymus, and the ratio of these indicators was 2.22:1.0, which indicates a strong antigenic stimulation by tartrazine. This is due to hyperplasia of the lymphoid component of the cortex, which is confirmed by a significant ($P < 0.05$) increase in the density of thymocytes in the cortical substance. The scientific literature describes an increase in the average area of lobules, mainly through the cortical substance of the rat thymus against the background of hyperplastic changes under the influence of calcium at a concentration of 235 mg/l [13]. In the expanded, compared to the control, subcapsular zone of the thymus cortex in group T, the population of immature pre-T lymphocytes expressing receptors to Thy-1 was significantly increased ($P < 0.05$). It is known that this zone of the cortex is the site of intensive proliferation of the earliest forms of T cells, which provide replenishment of the cortex populations [14]. This may indicate thymopoiesis activation because of the enhanced migration of stem cells from the bone marrow to the thymus and active comitaton (fixation) of these cells to the T-cell development pathway [15]. In case of intoxication or genetic defects, the accumulation of immature forms may indicate preT-lymphocytes differentiation arrest, for example, into CD4⁺ and CD8⁺ thymocytes [16].

A significant feature of the thymus of rats of group T was follicular hyperplasia, which is not characteristic of the normal histological structure of this organ. In this case, individual lymphoid follicles had germinative (bright) centers. The presence of bright centers in a lymphoid follicle, regardless of the immune organ in which they are present, indicates a pronounced antigenic stimulation, or such a pathology as myasthenia [17]. The effect of tartrazine on the morphological state of the thymus lymphoid component is also manifested by stage 1 accidental transformation 1 in the form of the so-

called "starry sky" picture, or "2-hole enlightenment", which is a generally recognized sign of antigenic stimulation [18].

Among the thymocytes of group T, the number of mature CD4 lymphocytes significantly decreased ($P < 0.05$), while the number of CD8 had only a weak tendency to increase, as a result of which the immunoregulatory index significantly decreased ($P < 0.05$) compared to the controls, indicating a pronounced immunological imbalance and selective suppression of the helper link of T-cell immunity [19]. This may be considered as a consequence of blocking positive selection or a violation of transition from double positive CD4⁺CD8⁺ cells to single positive CD4⁺, CD8⁺ [20]. A decrease in the CD4/CD8 ratio is a classic marker of immunopathology and indicates a reduced ability of the body to recognize antigens and coordinate the immune response [21].

All of the above, detected under the influence of tartrazine in the lymphoid component of the thymus of pregnant rats, differs significantly from the literature data regarding the morphological state of the thymus during physiological pregnancy in rats. In pregnant rats, the thymus undergoes significant involution, characterized by a profound loss of early thymic precursors, as well as a decrease in thymocyte proliferation. These phenomena are associated with increased hormone levels, in particular estrogen, during normal pregnancy [22]. Progesterone also contributes to a significant decrease in the thymus size and thymocyte migration, which is involved in the mechanisms of maternal-fetal tolerance [23]. The growth of interlobular connective tissue and its presence in the perivascular spaces of the thymus medulla in group C, against the background of a low density of cortical and medulla thymocytes, are precisely the signs of involution processes.

The epithelial component in the thymuses of group T also differed from the controls. For example, a larger number of thymic corpuscles were present in the medulla, and they contained a larger number of epithelial cells, which indicates activation of the medulla epithelium and is interpreted as an increase in the processes of antigen presentation and maturation of T-lymphocytes in the medulla [24]. Moreover, among the thymic corpuscles in group T, cyst-like changed large corpuscles were found, which indicates the "aging" of the corpuscles as a result of their functional overload [25]. It is known that the functional activity of thymic epithelial cells directly affects the fact whether a precursor cell will turn into a functional T-lymphocyte or a cell of innate immunity [26]. Increase in the epithelial component is considered a factor of strengthening immunological tolerance [27].

In the thymuses of pregnant rats of group T, the population of B- lymphocytes (CD45RA), which are located both in the medulla among T- lymphocytes and in the perivascular spaces among plasmoblasts and plasma cells, significantly increased. B-cells of the thymus medulla have a number of unique char-

acteristics, they originate both from precursors that mature intrathymically and as a result of the arrival of recirculating mature B-cells that have signs of activated B-cells, undergo the process of switching immunoglobulin classes and express the transcription factor Aire. Such features are formed directly in the thymus and allow B-cells to function as specialized antigen-presenting cells in the medulla, contributing to the negative selection of self-reactive T-cells [28]. B-cells located in the perivascular spaces are memory B-cells and plasma cells, usually their appearance indicates increased immune activation, the formation of so-called "immune niches", when in the perivascular spaces plasmoblasts and plasma cells create local areas of antibody secretion, which affects the processes of T-cell selection [28].

Besides the lymphoid and epithelial components of the thymus of group T, signs of the macrophage link activation were found, namely a significant increase in the ED1⁺ population. It is known that the ED1 marker, which corresponds to the CD68 protein in rats, is a classic monoclonal antibody for identifying macrophages and monocytes in rats. Two types of macrophages are characteristic of the rat thymus - ED1⁺ and ED2⁺. ED1⁺ are monocytes that enter the thymus with blood and are characterized by active phagocytic properties, and ED2⁺ are resident macrophages [29]. The most important role of macrophages in the thymus is elimination of apoptotic thymocytes. In the process of negative and positive selection, about 95-98% of T-cell precursors undergo apoptosis [30]. Thymic macrophages produce cytokines (IL-1, IL-6, TNF- α), thus regulating both proliferation and differentiation of pre-T-thymocytes [29].

Thus, the findings of the study indicate that tartrazine intoxication leads to hyperplasia of the thymus cortex in pregnant rats (cortex to medulla ratio 2.22:1.0) due to proliferation of the lymphoid component and enhanced migration of T-precursors to the subcapsular zone, while thymocyte differentiation is disrupted, immature forms that express Thy-1 accumulate and the number of mature CD4⁺ cells is significantly reduced, which leads to a decrease in the immunoregulatory index and selective suppression of the helper component of immunity. Enlargement of the population of B-lymphocytes (CD45RA⁺) in the medulla and perivascular spaces indicates enhancement in the humoral immune response. Activation of the macrophage component, namely a significant increase in the ED1⁺ population, may be associated with an increase in apoptotic processes in the cortical zone of the thymus. The increase in the number and size of thymic corpuscles, as well as their cystic degeneration, indicates an active response of the epithelial component of the thymus to the toxic effect of tartrazine.

Conclusions

1. Exposure to tartrazine throughout gestation induces morphofunctional alterations in the thymus of pregnant rats that are opposite in direction to the

physiological thymic changes observed during uncomplicated pregnancy. Instead of hormonally mediated involution aimed at maintaining maternal-fetal tolerance, hyperplasia of both lymphoid and epithelial components, together with activation of the macrophage response, was observed.

2. Follicular hyperplasia and stage I accidental thymic transformation, accompanied by accumulation of immature T lymphocytes, indicate pronounced antigenic stimulation and toxic stress. These changes contribute to impaired thymocyte selection and the development of marked immunoregulatory imbalance, characterized by reduced helper T-cell activity accompanied by a tendency toward increased suppressor activity.

3. Tartrazine exposure in pregnant female rats was associated with activation of the humoral immune response in the thymus, as evidenced by an increased population of CD45RA⁺ B lymphocytes within the medulla and perivascular spaces. In addition, macrophage activity was enhanced, reflected by a significant increase in the ED1⁺ macrophage population, which actively participates in the clearance of apoptotic cells.

Prospects for Further Research

Further investigation into the impact of tartrazine on the morphofunctional state of the thymus in fetal and neonatal rats, integrated with the findings regarding maternal thymic status, will allow the data from this study to serve as a reference (comparison) group. This will facilitate the study of the thymus in fetuses and neonates from mothers with infectious pathologies, which constitutes the primary objective of our ongoing research.

Personal contribution of the authors

Sorokina I.V.: a) concept and design; c) analysis and interpretation of the results; d) writing the article.

Gubina-Vakulik G.I.: a) concept and design; b) data collection and analysis.

Markovskiy V.D.: b) data collection and analysis; e) editing the manuscript.

Kaluzhyna-Biletska O.V.: b) data collection and analysis.

Korneyko I.V.: d) writing the article; e) editing the manuscript.

Conflicts of interest

Author has no conflict of interest to declare.

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Реферат

ВПЛИВ СИНТЕТИЧНОГО БАРВНИКА ТАРТРАЗИНУ (Е102) НА МОРФОФУНКЦІОНАЛЬНИЙ СТАН ТИМУСУ ВАГІТНИХ САМИЦЬ ЩУРІВ

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Ключові слова: вагітні щури, тимус, морфофункціональні особливості, імуноморфологія, тартразин.

Вступ. Відомо, що навіть у межах допустимих добових доз, а саме не більш ніж 7,5 мг/кг маси тіла за добу регулярно вживання тартразину (Е102) здатне спричинити патологічні зміни в організмі людини. Тартразин долає плацентарний бар'єр, тому він може бути токсичним як для матері, так і для плоду. Аналіз сучасної наукової літератури свідчить про те, що інформація щодо особливостей імунного гомеостазу як вагітних, так і плодів під впливом тартразину вкрай обмежена.

Мета. Визначити морфофункціональні особливості тимусу вагітних самок щурів, що сформувалися під впливом дії синтетичного барвника тартразину (Е102).

Матеріал та методи. Експеримент проведено на самцях щурів популяції WAG. 1 група – контроль-

на (група К) ($n = 7$), 2 група – експериментальна (група Т) ($n = 7$). З віку у 2 місяці щури почали отримувати протягом одного місяця спочатку внутрішньошлунково через зонд, а потім як додаток до їжі 1 мл 0,1% розчину тартразину – синтетичного харчового фарбника Е 102. Тварини контрольної групи отримували 1 мл фізіологічного розчину. У віці 3 міс. усі тварини були підсажені до самців. Після запліднення та під час вигодовування нащадків самиці групи К продовжували отримувати 1 мл фізіологічного розчину, а тварини групи Т продовжували отримувати розчин тартразину. Тварини були виведені з експерименту у віці 8 місяців шляхом декапітації. Мікропрепарати тимусу забарвлювали гематоксилином-еозином, пікрофуксином за Ван Гізеном, методом Малорі. Імунні клітини диференціювали за допомогою моноклональних антитіл фірми Serotec, (Bio-Rad). Використовували МКА CD8, CD4, CD45RA, Thy-1, ED1. Середні значення показників у групах порівнювали за допомогою t-критерію Стьюдента та U-критерію Манна-Уїтні. Значимість відмінностей між показниками приймалася при рівні значимості $<0,05$. Статистичні розрахунки виконували з використанням програми Statistic Soft 6.0.

Результати. Тартразинова інтоксикація призводить до гіперплазії коркової речовини тимусу вагітних самиць щурів (співвідношення кори до мозкової речовини 2,22:1,0) за рахунок проліферації лімфоїдного компонента та посиленої міграції Т-попередників у субкапсулярну зону, при цьому порушується диференціювання тимоцитів, накопичуються незрілі форми, що експресують Thy-1 та достовірно знижується кількість зрілих CD4+ клітин, що веде до падіння імунорегуляторного індексу та вибіркового пригнічення хелперної ланки імунітету. Збільшуються популяції В-лімфоцитів (CD45RA+) у мозковій речовині та периваскулярних просторах та активується ED1⁺ макрофагальна ланка.

Висновок. Вплив тартразину протягом усієї вагітності на організм вагітних самиць щурів проявляється морфофункціональними змінами тимусу, що за своїм вектором протилежно відрізняються від фізіологічних змін тимусу при неускладненій вагітності. Фолікулярна гіперплазія та акцидентальна трансформація 1 стадії, накопичення незрілих Т-лімфоцитів, активація гуморальної та макрофагальної ланок вказують на інтенсивну антигенну стимуляцію та токсичне навантаження, що призводить до порушення процесів селекції тимоцитів та формування вираженого імунорегуляторного дисбалансу у вигляді зниження хелперної активності на тлі тенденції до підвищення супресорної активності.