

O.I. Tiron, O.L. Appelhans, V.I. Gunas¹, I.L. Cheresniuk¹, D.A. Lysenko¹
 Odessa National Medical University, Odessa, Ukraine
¹National Pirogov Memorial Medical University, Vinnytsya, Ukraine

INDICES OF THE CELL CYCLE IN THE THYROID GLAND AFTER THERMAL BURNS OF THE SKIN WHEN USING SOLUTIONS OF LACTOPROTEIN WITH SORBITOL OR HAES-LX 5 %

e-mail: chekina.o@ukr.net

The DNA content in the nuclei of thyroid cells of 90 white male rats on the background of skin burns of 2-3 degrees (with a lesion area of 21-23 % of the body surface) and the introduction of solutions of lactoprotein with sorbitol or HAES-LX 5 % was determined by flow cytometry. At 1, 3, 7 and 14 days after thermal trauma to the skin and the use of lactoprotein with sorbitol or HAES-LX 5 %, only lower values of S-phase values were found compared to the groups without burns. 21 days after thermal damage to the skin in the group with infusion HAES-LX 5 %, the interval SUB-G0G1 is significantly higher than in the control group. After 30 days in the groups with prior administration of HAES-LX 5 % and lactoprotein with sorbitol solutions, the value of SUB-G0G1 is significantly higher than that in the groups without skin burns.

Key words: thyroid gland, thermal skin burn, DNA cytometry, HAES-LX 5 %, lactoprotein with sorbitol.

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Thermal damage to the skin and its systemic manifestation – burn disease (BD) remains the focus of modern medical research on both the study of the pathogenesis of this pathological condition and the development of new therapies [8]. It is noted that the insufficient effectiveness of existing methods of therapy is due to a complex cascade of factors of this pathology, leading to systemic damage to the body with thermal skin burns [11].

Although today the main stages of BD therapy for thermal damage to the skin, which consist in intensive replenishment of lost fluid, early necrectomy, effective antibiotic therapy, have a high mortality on the background of BD, even in the long term of this pathological condition [7]. That is why there is an active search for new methods of treatment of skin burns, mostly local, with the development of new synthetic materials that promote local synthesis of keratinocytes, but their use does not prevent the reduction of systemic manifestations of BD [5].

It is indicated [14] that the complex nature of burns necessitates the need for systemic treatment of thermal damage to the skin, which should affect all pathogenetic factors of this condition. It is well known [9] that the use of systemic, pathogenetically based therapy in the earliest terms improves treatment results, increases patient survival and reduces mortality even in the long term of BD. Therefore, the treatment of burns remains a topical issue in modern medicine and combustiology, which requires the development of new therapies that will affect the level of pathogenetic factors of the disease, as existing therapeutic agents do not provide sufficient effectiveness [10].

Our attention was drawn to the data on the positive results of the use of early active infusion therapy on the background of thermal skin burns of domestic drugs – solutions of lactoprotein with sorbitol (LPS) and HAES-LX 5 %, which showed a significant positive effect on various aspects of BD, including thymus, lungs, liver and other organs [3]. The application of the method of DNA cytometry allowed to establish the patterns of pathogenetic effects of burns on the body and on the cells in the studied organs. We did not find literature data on the study of thyroid cell division by DNA cytometry on the background of BD with the introduction of infusion solutions.

The purpose of the work was to study the dynamics of cell cycle parameters and DNA fragmentation in rat thyroid cells, against the background of skin burns and the introduction of lactoprotein with sorbitol or HAES-LX 5 %.

Material and methods. Experimental studies were performed on 90 white male rats weighing 160-180 g (obtained from the vivarium of the Institute of Pharmacology and Toxicology of the National Academy of Medical Sciences of Ukraine), conducted on the basis of research laboratory of functional morphology and genetics of development of National Pirogov Memorial Medical University, Vinnytsya. The keeping and manipulation of animals was carried out in accordance with the "General Ethical Principles of Animal Experiments" adopted by the First National Congress on Bioethics (Kyiv, 2001) and was guided by the recommendations of the "European Convention for the Protection of Vertebrate Animals for Experimental and Other Scientific Purposes" (Strasbourg, 1985), methodological recommendations of

the State Pharmacological Center of the Ministry of Health of Ukraine on "Preclinical studies of drugs" (2001), as well as rules of humane treatment of experimental animals and conditions approved by the Bioethics Committee of National Pirogov Memorial Medical University, Vinnytsya (Minutes № 1 of 14.01.2010).

Infusion of LPS or HAES-LX 5 % solutions was performed into the inferior vena cava after catheterization under aseptic conditions through the femoral vein. The catheter was sutured under the skin, its lumen along the entire length was filled with titrated heparin solution (0.1 ml of heparin per 10 ml of 0.9 % NaCl solution) after each administration of substances. Infusions were performed once a day for the first 7 days. Thermal burns of 2-3 degrees skin were performed by applying four copper plates (each with a surface area of 13.86 cm²) to the pre-depilated side surfaces of the rat body for 10 seconds, which were preheated for 6 minutes in water with a temperature of 100°C [7]. The total area of skin lesions was 21-23 %. Catheterization of the main vessels, thermal skin burns and decapitation of animals (after 1, 3, 7, 14, 21 and 30 days) were performed under propofol anesthesia (60 mg/kg i/v).

The DNA content in the nuclei of rat thyroid cells was determined by flow cytometry. Under conditions of propofol anesthesia (60 mg/kg i/v) in animals after removal of all its contents, prepared nuclear suspensions for flow cytometry using a solution for nuclear DNA CyStain DNA Step 1 company Partec (Germany), according to the manufacturer's protocol-instructions. This solution allows you to quickly perform the extraction of nuclei and label nuclear DNA with diamidinophenylindole, which is part of it. Disposable CellTrics 50 µm filters (Partec, Germany) were used in the process of manufacturing nuclear suspensions. Flow analysis was performed on a multifunctional flow cytometer "Partec PAS" company Partec, Germany, in the research center of National Pirogov Memorial Medical University, Vinnytsya.

UV radiation was used to excite diamidinophenylindole fluorescence. From each sample of the nuclear suspension 10,000 events were analyzed. Cell cycle analysis was performed using FloMax software (Partec, Germany) in full digital correspondence according to a mathematical model, which determined: G0G1 – the percentage of G0G1 phase cells to all cells of the cell cycle (DNA content = 2c); S is the percentage of the phase of DNA synthesis to all cells of the cell cycle (DNA content > 2c and < 4c); G2+M is the percentage of the G2+M phase to all cells of the cell cycle (DNA = 4c). Determination of DNA fragmentation (apoptosis) was performed by isolating the SUB-G0G1 region on RN2 DNA histograms before the G0G1 peak, which indicates cell nuclei with a DNA content < 2c.

Statistical processing of the obtained results was performed in the license package "STATISTICA 6.1" using non-parametric methods of evaluation of the obtained results. The mean values of each trait, standard deviation, and percentile range were evaluated. The significance of the difference in values between the independent quantitative values was determined using the Mann-Whitney U-test for independent samples.

Results of the study and their discussion. Indices of cell cycle and DNA fragmentation of thyroid cells in rats on the background of infusion for 7 days 0.9 % solution of NaCl, LPS or HAES-LX 5 %, as well as the use of infusion of 0.9 % NaCl solution on the background of thermal skin burns are reflected in our articles [12, 13].

A similar picture of cell cycle parameters in thyroid cells 1 day after thermal damage to the skin in rats infused with 0.9 % NaCl solution, LPS or HAES-LX 5 % (table 1). Thus, against the background of the use of LPS or HAES-LX 5 % also significantly lower values of the S-phase (p<0.01), and the difference between the indices G0G1, G2+M and SUB-G0G1 was not detected.

Table 1

Indices of the cell cycle in the cells of the thyroid gland of rats 1 day after skin burns when using infusion therapy according to flow DNA cytometry data (M±σ)

Group	Indices of the cell cycle (%)			
	S	SUB-G0G1	G0G1	G2+M
0.9 % NaCl	0.652±0.134	2.462±0.800	91.16±2.41	8.192±2.368
Burn + 0.9 % NaCl	0.234±0.094	2.732±1.141	91.90±2.65	7.868±2.678
LPS	0.548±0.118	2.814±0.707	90.87±1.69	8.576±1.759
Burn + LPS	0.272±0.061	2.868±0.901	90.64±1.72	9.090±1.731
p(LPS – burn+LPS)	<0.01	>0.05	>0.05	>0.05
HAES-LX 5 %	0.638±0.162	2.688±0.870	90.68±1.93	8.682±1.855
Burn + HAES-LX 5 %	0.326±0.063	2.626±0.870	90.93±1.45	8.748±1.431
p(HAES-LX5% – burn+HAES-LX 5%)	<0.01	>0.05	>0.05	>0.05
p(burn+0.9% NaCl – burn+ LPS)	>0.05	>0.05	>0.05	>0.05
p(burn+0.9% NaCl – burn+HAES-LX 5%)	>0.05	>0.05	>0.05	>0.05
p(burn + LPS – burn+HAES-LX 5%)	>0.05	>0.05	>0.05	>0.05

3 days after skin burn on the background of the use of HAES-LX 5 % or LPS solutions, only the maximum decrease in the percentage of thyroid cells that were in the S-phase ($p < 0.01$) compared to the corresponding groups without burns (table 2) was established. Between the data of groups 0.9 % NaCl solution and LPS or HAES-LX 5 % set significantly lower ($p < 0.01$ in both cases) the value of SUB-G0G1, as well as a trend ($p = 0.060$) for larger values of S-phase when using HAES-LX 5 % compared to 0.9 % NaCl solution (table 2).

Table 2

Indices of the cell cycle in the cells of the thyroid gland of rats 3 days after skin burns when using infusion therapy according to flow DNA cytometry ($M \pm \sigma$).

Group	Indices of the cell cycle (%)			
	S	SUB-G0G1	G0G1	G2 + M
0.9 % NaCl	0.622±0.110	2.594±0.628	90.99±2.48	8.392±2.375
Burn + 0,9 % NaCl	0.214±0.105	5.288±0.840	91.46±2.80	8.328±2.711
LPS	0.600±0.047	2.410±0.825	90.39±2.11	9.008±2.129
Burn + LPS	0.252±0.077	2.784±0.957	90.88±1.03	8.866±1.027
p(LPS – burn+LPS)	<0.01	>0.05	>0.05	>0.05
HAES-LX 5 %	0.616±0.134	2.480±0.812	90.21±1.78	9.174±1.811
Burn + HAES-LX 5 %	0.320±0.047	2.512±0.406	91.82±1.36	7.862±1.336
p(HAES-LX5% – burn+HAES-LX 5%)	<0.01	>0.05	>0.05	>0.05
p(burn+0.9% NaCl – burn+LPS)	>0.05	<0.01	>0.05	>0.05
p(burn+0.9% NaCl – burn+HAES-LX 5%)	=0.060	<0.01	>0.05	>0.05
p(burn+ LPS – burn+HAES-LX 5%)	>0.05	>0.05	>0.05	>0.05

7 days after thermal skin burn on the background of the use of solutions of LPS or HAES-LX 5 % significantly lower ($p < 0.01$ in both cases) values of the S-phase, compared with similar groups without burn damage, and significant or trends of differences between indicators G0G1, G2+M and SUB-G0G1 were not detected (table 3) No significant or trend differences were found when comparing the respective parameters of the thyroid cell cycle between groups with skin burns after 7 days using 0.9 % solution of NaCl, LPS and HAES-LX 5 % (table 3).

Table 3

Indices of the cell cycle in rat thyroid cells 7 days after skin burn when using infusion therapy according to flow DNA cytometry ($M \pm \sigma$).

Group	Indices of the cell cycle (%)			
	S	SUB-G0G1	G0G1	G2 + M
0,9 % NaCl	0.650±0.139	2.632±0.724	90.90±2.17	8.448±2.113
Burn + 0,9 % NaCl	0.350±0.088	3.994±1.204	88.70±3.13	10.95±3.14
LPS	0.672±0.133	2.510±1.006	91.06±1.68	8.276±1.647
Burn + LPS	0.342±0.036	2.888±0.523	91.51±1.81	8.146±1.814
p(LPS – burn+LPS)	<0.01	>0.05	>0.05	>0.05
HAES-LX 5 %	0.592±0.076	2.662±0.711	90.32±1.78	9.084±1.757
LPS + HAES-LX 5 %	0.384±0.072	2.900±1.043	91.17±1.47	8.446±1.474
p(HAES-LX5% – burn+HAES-LX 5%)	<0.01	>0.05	>0.05	>0.05
p(burn+0.9% NaCl – burn + LPS)	>0.05	>0.05	>0.05	>0.05
p(burn+0.9% NaCl – burn+HAES-LX 5%)	>0.05	>0.05	>0.05	>0.05
p(burn+ LPS – burn+HAES-LX 5%)	>0.05	>0.05	>0.05	>0.05

Against the background of the use of the first seven days of LPS or HAES-LX 5 % solutions 14 days after skin burn in rats, only significantly lower ($p < 0.01$ in both cases) S-phase values were found, compared with similar groups without burn damage, and significant or trends in discrepancies between G0G1, G2+M and SUB-G0G1 were not detected (table 4). When comparing the respective parameters of the cell cycle of thyroid cells 14 days after skin burns between groups of 0.9 % solution of NaCl and LPS or HAES-LX 5 % it was found: a slight trend ($p = 0.076$) of lower values of the interval SUB-G0G1 when using LPS compared to 0.9 % NaCl solution; significantly higher ($p < 0.01$) values of the number of cells in the S-phase, a slight trend ($p = 0.076$) of a larger value of the G0G1 phase and a smaller ($p = 0.076$) value of the G2+M phase when using HAES-LX 5 % compared to 0.9 % solution NaCl; the tendency ($p = 0.060$) of a larger number of cells in the S-phase when using HAES-LX 5 % compared with LPS (table 4).

Indices of the cell cycle in rat thyroid cells at 14, 21 and 30 days after skin burns when using infusion therapy according to flow DNA cytometry (M±σ).

Group	Indices of the cell cycle (%)			
	S	SUB-G0G1	G0G1	G2 + M
14 day				
0,9 % NaCl	0.562±0.153	2.304±0.835	91.29±1.49	8.146±1.520
Burn + 0,9 % NaCl	0.322±0.043	3.664±0.239	89.15±3.56	10.53±3.54
LPS	0.658±0.168	2.812±0.772	90.54±1.69	8.798±1.736
Burn + LPS	0.354±0.042	2.864±0.603	91.31±1.17	8.334±1.164
p(LPS – burn+LPS)	<0.01	>0.05	>0.05	>0.05
HAES-LX 5 %	0.586±0.146	2.326±1.096	91.24±1.85	8.176±1.881
Burn + HAES-LX 5 %	0.394±0.021	3.104±0.893	92.00±1.22	7.602±1.226
p(HAES-LX5% – burn+HAES-LX 5%)	<0.01	>0.05	>0.05	>0.05
p(burn+0.9% NaCl – burn + LPS)	>0.05	=0.076	>0.05	>0.05
p(burn+0.9% NaCl – burn+HAES-LX 5%)	<0.05	>0.05	=0.076	=0.076
p(burn + LPS – burn+HAES-LX 5%)	=0.060	>0.05	>0.05	>0.05
21 day				
0,9 % NaCl	0.522±0.075	2.622±0.677	90.60±2.48	8.986±2.370
Burn + 0,9 % NaCl	0.364±0.092	3.250±0.755	87.98±3.30	11.66±3.27
LPS	0.556±0.166	2.742±0.513	91.88±1.74	7.558±1.595
Burn + LPS	0.392±0.067	2.616±0.984	89.13±3.29	10.48±3.28
p(LPS – burn+LPS)	=0.076	>0.05	>0.05	>0.05
HAES-LX 5 %	0.594±0.157	2.266±0.623	90.60±2.11	8.804±2.187
Burn + HAES-LX 5 %	0.444±0.063	3.844±0.372	91.01±1.11	8.544±1.119
p(HAES-LX5% – burn+HAES-LX 5%)	=0.076	<0.01	>0.05	>0.05
p(burn+0.9% NaCl – burn + LPS)	>0.05	>0.05	>0.05	>0.05
p(burn+0.9% NaCl – burn+HAES-LX 5%)	>0.05	>0.05	>0.05	>0.05
p(burn + LPS – burn+HAES-LX 5%)	>0.05	=0.060	>0.05	>0.05
30 day				
0,9 % NaCl	0.592±0.193	2.630±0.717	91.16±1.82	8.252±1.851
Burn + 0,9 % NaCl	0.408±0.063	2.900±1.078	83.11±2.14	16.50±2.18
LPS	0.590±0.216	2.600±1.013	90.84±1.94	8.570±1.767
Burn + LPS	0.444±0.052	3.624±0.487	90.84±4.33	8.716±4.319
p(LPS – burn+ LPS)	>0.05	<0.05	>0.05	>0.05
HAES-LX 5 %	0.582±0.133	2.232±0.417	91.31±2.49	8.110±2.409
Burn + HAES-LX 5 %	0.478±0.041	3.244±0.710	88.85±3.70	10.67±3.72
p(HAES-LX5% – burn+HAES-LX 5%)	>0.05	<0.05	>0.05	>0.05
p(burn+0.9% NaCl – burn+LPS)	>0.05	>0.05	<0.05	<0.05
p(burn+0.9% NaCl – burn+HAES-LX 5%)	>0.05	>0.05	<0.05	<0.05
p(burn + LPS – burn+HAES-LX 5%)	>0.05	>0.05	>0.05	>0.05

21 days after thermal burn of the skin on the background of the first seven days of LPS solution, only a slight tendency ($p=0.076$) to lower values of the number of cells in the S-phase compared with the same group without burns (table 4). At this time after the burn on the background of the first seven days of HAES-LX 5 % solution also found a slight tendency ($p=0.076$) to lower values of the number of cells in the S-phase and significantly ($p<0.01$) higher values of DNA fragmentation in the range SUB-G0G1 compared with a similar group of animals without burns (table. 4).

After 30 days in animals after skin burns on the background of the first seven days of LPS or HAES-LX 5 % solutions were found significantly ($p<0.05$ in both cases) higher values of DNA fragmentation in the range of SUB-G0G1 compared to similar groups without burns (table 4). When comparing the corresponding parameters of the cell cycle of thyroid cells 30 days after skin burns between groups of 0.9 % NaCl solution and LPS or HAES-LX 5 % found significantly higher ($p<0.05$ in both cases) values of the G0G1 phase, as well as smaller ($p<0.05$ in both cases) value of the phase G2+M when using LPS or HAES-LX 5 % compared with 0.9 % NaCl solution (table 4).

Summing up the results, it should be noted that the most pronounced disorders of the cell cycle were observed 3 days after thermal damage to the skin, although the first signs of these disorders in the form of a significant decrease in DNA synthesis ($p<0.01$) were observed after 1 day. In our opinion, this indicates a powerful damage to the thyroid gland caused by exogenous factors and activation of the endocrine system of the whole organism, which was mainly realized at the level of inhibition of DNA synthesis [4]. However, we cannot deny the possible protective nature of this phenomenon, because inhibition of cell division reduces

further cell destruction [2]. Our data support the assumption of the occurrence of 3 days after the burn of complex thyroid damage with the development of a deficit of energy and repair processes, which was also found by other researchers at similar times [2, 4, 14]. It is likely that in this period occurs peak deepening of cell damage that occurred at the time of thermal injury and their mass death in the form of apoptosis, which was established in similar clinical and laboratory studies [9-11] and begins to actively implement the protective effect of the studied hyperosmolar solutions. Note that the use of HAES-LX 5 % or LPS solutions, compared with 0.9 % NaCl solution has a more significant protective effect on the activation of apoptosis (interval SUB-G0G1) in thyroid damage on the background of thermal skin burns.

In favor of this hypothesis indicate the changes detected in the future, 7 days after the burn – when we found a violation of the cell cycle in the form of a decrease in S-phase, stored in the groups of burns + 0.9 % NaCl solution, burn + LPS and burn + HAES-LX 5 %, although other indices of the cell cycle of thyroid cells did not differ significantly from similar indices of the control groups. In our opinion, this indicates the need for longer infusion therapy with hyperosmolar solutions, which corresponds to the general trend of prolongation of infusion therapy against the background of thermal damage [5].

In the subsequent terms of research, the long-term negative effect of thermal damage of skin on indices of a cellular cycle of cells of a thyroid gland by a DNA cytometry was established. In our opinion, this indicates the existence of a long-term negative impact of the effects of thermal skin burns on the cell cycle of thyroid cells, which may cause long-term manifestations of BD, which are found in other organs and systems [3]. The obtained results are consistent with the results of studies of long-term effects of various toxic factors on the thyroid gland [1, 2]. This assumption is supported by the absence of changes in G0G1 phase and, accordingly, G2+M phase in groups using HAES-LX 5 % or LPS after 30 days, while maintaining larger ($p < 0.05$) values of the interval SUB-G0G1 compared to the same indices of groups without burn.

Thus, compared with 0.9 % NaCl solution, the use of LPS and HAES-LX 5 % more effectively corrected the violation of cell division, starting 3 days after the burn skin injury, which, in our opinion, indicates a more significant renewal of thyroid cells gland, which occurs in this organ by apoptosis [1].

A further perspective of the study is to study the different modes of administration of hyperosmolar solutions on the indices of the cell cycle of thyroid cells.

Conclusion

After 1, 3, 7 and 14 days after thermal trauma of the skin and the use of hyperosmolar solutions of LPS or HAES-LX 5 %, only lower ($p < 0.05-0.01$) values of S-phase values were found in comparison with the indices of groups without burns. 21 days after thermal damage to the skin in the group with infusion HAES-LX 5 %, the interval SUB-G0G1 is significantly higher ($p < 0.01$) compared with the same control group. After 30 days of thermal skin injury in the groups with prior administration of HAES-LX 5 % and LPS solutions, the value of SUB-G0G1 is significantly higher ($p < 0.05$) than in groups without skin burns.

References

1. Pavlov AV, Bezdenezhnykh AV. Proliferativnaya i sekretornaya aktivnost follikulyarnykh tirocitzov pri razlichnykh rezhimakh myshechnoy deyatelnosti. Vestnik novykh meditsinskikh tekhnologiy. 2018;25(3):202-8. [in Russian]
2. Batista G, Hensch TK. Critical period regulation by thyroid hormones: potential mechanisms and sex-specific aspects. Frontiers in molecular neuroscience. 2019; 12:77. <https://doi.org/10.3389/fnmol.2019.00077>
3. Cherkasov VG, Dzevulska IV, Cherkasov EV, Kaminsky RF, Pastukhova VA, Kovalchuk OI, Trofimenko YuYu. Influence of HAES-LX-5% infusion solution on the DNA content of endocrine glands cells against the background of thermal burn of skin in rats. World of Medicine and Biology. 2017;4(62):168-73. DOI: 10.26724/2079-8334-2017-4-62-168-173
4. D'Asta F, Cianferotti L, Bhandari S, Sprini D, Rini GB, Brandi ML. The endocrine response to severe burn trauma. Expert review of endocrinology & metabolism. 2014;9(1):45-59. <https://doi.org/10.1586/17446651.2014.868773>
5. Gillenwater J, Garner W. Acute Fluid Management of Large Burns: Pathophysiology, Monitoring, and Resuscitation. Clinics in plastic surgery. 2017;44(3):495-503. <https://doi.org/10.1016/j.cps.2017.02.008>
6. Gunas I, Doygan I, Masur O. Method of thermal burn trauma correction by means of cryoinfluence. Jena-München: Der Urban & Fischer Verlag; 1997. 105.
7. Mason SA, Nathens AB, Byrne JP. Increased rate of long-term mortality among burn survivors: A population-based matched cohort study. Annals of surgery. 2019;269(6):1192-9. doi: 10.1097/SLA.0000000000002722
8. Oryan A, Alemzadeh E, Moshiri A. Burn wound healing: present concepts, treatment strategies and future directions. Journal of wound care. 2017;26(1);5-19. <https://doi.org/10.12968/jowc.2017.26.1.5>
9. Porter C, Tompkins RG, Finnerty CC, Sidossis LS, Suman OE, Herndon DN. The metabolic stress response to burn trauma: current understanding and therapies. The Lancet. 2016;388(10052):1417-26. [https://doi.org/10.1016/S0140-6736\(16\)31469-6](https://doi.org/10.1016/S0140-6736(16)31469-6)
10. Rae L, Fidler P, Gibran N. The physiologic basis of burn shock and the need for aggressive fluid resuscitation. Critical care clinics. 2016;32(4):491-505. <https://doi.org/10.1016/j.ccc.2016.06.001>
11. Stanojic M, Abdullahi A, Rehou S, Parousis A, Jeschke MG. Pathophysiological response to burn injury in adults. Annals of surgery. 2018;267(3):576-84. doi: 10.1097/SLA.0000000000002097
12. Tiron OI, Appelhans OL, Gunas IV, Chereshniuk IL. Indicators of the cell cycle in the thyroid gland in rats when applying infusion of 0.9 % solution of NaCl, lactoprotein with sorbitol or HAES-LX 5 %. Reports of Morphology. 2019;25(1):62-7. [https://doi.org/10.31393/morphology-journal-2019-25\(1\)-09](https://doi.org/10.31393/morphology-journal-2019-25(1)-09)
13. Tiron OI. Indicators of the cell cycle in the thyroid gland in rats when using infusion of 0.9 % NaCl solution on the background of thermal skin burns. Reports of Morphology. 2019;25(3):52-7. [https://doi.org/10.31393/morphology-journal-2019-25\(3\)-09](https://doi.org/10.31393/morphology-journal-2019-25(3)-09)
14. Williams FN, Herndon DN. Metabolic and endocrine considerations after burn injury. Clinics in plastic surgery. 2017;44(3):541-53. <https://doi.org/10.1016/j.cps.2017.02.013>

Реферати

**ПОКАЗНИКИ КЛІТИННОГО ЦИКЛУ
В ЩИТОПОДІБНІЙ ЗАЛОЗІ ПІСЛЯ
ТЕРМІЧНОГО ОПІКУ ШКІРИ ПРИ
ЗАСТОСУВАННІ РОЗЧИНІВ ЛАКТОПРОТЕІНУ
З СОРБИТОЛОМ АБО HAES-LX 5 %**

**Тирон О.І., Аппельханс О.Л., Гунас В.І.,
Черешнюк І.Л., Лисенко Д.А.**

Вміст ДНК в ядрах клітин щитоподібної залози 90 білих шурів-самців на фоні опіку шкіри 2-3 ступеня (із площею ураження 21-23 % поверхні тіла) і введення розчинів лактопротеїну з сорбітолом або HAES-LX 5 % визначали методом проточної цитометрії. Через 1, 3, 7 та 14 діб після термічної травми шкіри і застосування лактопротеїну з сорбітолом або HAES-LX 5 % встановлено лише менші значення показників S-фази у порівнянні із показниками груп без опіку. Через 21 добу після термічного uszkodження шкіри в групі з інфузією HAES-LX 5 % показник інтервалу SUB-G0G1 суттєво більший порівняно з аналогічним показником контрольної групи. Через 30 діб в групах з попереднім введенням розчинів HAES-LX 5 % та лактопротеїну з сорбітолом величина показнику SUB-G0G1 значно більша від аналогічного в групах без опіку шкіри.

Ключові слова: щитоподібна залоза, термічний опік шкіри, ДНК-цитометрія, HAES-LX 5 %, лактопротеїн із сорбітолом.

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**ПОКАЗАТЕЛИ КЛЕТОЧНОГО ЦИКЛА
В ЩИТОВИДНІЙ ЖЕЛЕЗЕ ПОСЛЕ
ТЕРМИЧЕСКОГО ОЖОГА КОЖИ ПРИ
ПРИМЕНЕНИИ РАСТВОРОВ ЛАКТОПРОТЕИНА
С СОРБИТОЛОМ ИЛИ HAES-LX 5 %**

**Тирон О.И., Аппельханс Е.Л., Гунас В.И.,
Черешнюк И.Л., Лысенко Д.А.**

Содержание ДНК в ядрах клеток щитовидной железы 90 белых крыс-самцов на фоне ожога кожи 2-3 степени (с площадью поражения 21-23 % поверхности тела) и введение растворов лактопротеина с сорбитолом или HAES-LX 5 % определяли методом проточной цитометрии. Через 1, 3, 7 и 14 суток после термической травмы кожи и применения лактопротеина с сорбитолом или HAES-LX 5 % установлено только меньшие значения показателей S-фазы по сравнению с показателями групп без ожога. Через 21 день после термического повреждения кожи в группе с инфузией HAES-LX 5 % показатель интервала SUB-G0G1 существенно больше по сравнению с аналогичным показателем контрольной группы. Через 30 суток в группах с предварительным введением растворов HAES-LX 5 % и лактопротеина с сорбитолом величина показателя SUB-G0G1 значительно больше аналогичного в группах без ожога кожи.

Ключевые слова: щитовидная железа, термический ожог кожи, ДНК-цитометрия, HAES-LX 5 %, лактопротеин с сорбитолом.

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O.V. Fedosieieva

Zaporizhzhia State Medical University, Zaporizhzhia

**MORPHOGENESIS OF RAT'S THYROID GLAND IN PREWEANING PERIOD AFTER
PRENATAL INFLUENCE OF STAPHYLOCOCCAL TOXOID**

e-mail: fedoseeva.ov.1@gmail.com

The results were obtained about morphogenesis of rat's thyroid after intrauterine antigenic action of staphylococcal toxoid. Prenatal influence of staphylococcal toxoid led to the formation of a more pronounced structure of the parenchyma and stroma, but they showed signs of functional immaturity, which led to the presence of a morphological picture of hypothyroidism after birth (rats 1-7 days of postnatal ontogeny). With the beginning of the middle sucking period (7-21 days of life) there is a lymphoid infiltration in separate sites of a thyroid gland, processes of reorganization of the synthetic device and resorption of colloid, so functional "maturation" of already morphologically formed structures begins. Such abrupt changes in the thyroid gland of experimental animals are due to systemic prenatal antigenic influence on the body as a whole and is adaptive-compensatory in nature.

Keywords: thyroid gland, antigen, staphylococcal toxoid, morphogenesis, experiment.

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The current stage of the morphology development is characterized by increasing interest to the morphological and functional components of tissues, organs and their systems, that's why the issue of dynamic morphology is gaining more and more recognition. The thyroid gland (thyroid), is a heterogeneous tissue complex system [2, 6]. Structural and functional alteration of thyrocytes in various pathological conditions is a topical problem of biology and medicine, because thyroid hormones influence to the numerous processes of the vital activity in the body. Many authors note lability in morphology and functional activity of the thyroid gland in response to various aggressive factors of both exogenous and endogenous nature [2, 4, 6]. Antigenic influence at critical terms of ontogenesis can cause significant changes in the child's immune system. It is known that the entry of antigens into the fetus causes premature release of T-lymphocytes from the thymus and their migration to various organs. In these organs the tempo and terms change in formation of the basic structural components [1, 3, 5]. The appearance of more "aggressive" bacterial and viral pathogens led to a significant increase in the number of thyroid pathology [7, 8]. The thyroid gland, like every other organ, is characterized by a specific algorithm of functioning, which has the appropriate morphological design in the form of a hierarchy of cellular, tissue and organ units [2, 4, 6, 8].