UDC 575: 612: 613: 616
DOI: 10.21668/health.risk/2025.1.10.eng

Read online

Research article

COMPARATIVE ASSESSMENT OF ISOLATED INFLUENCE EXERTED BY PHYSICAL AND CHEMICAL FACTORS ON RELATIVE TELOMERE LENGTH OF LABORATORY ANIMALS IN A MODEL EXPERIMENT

O.A. Savchenko[1], I.I. Novikova[1], O.A. Savchenko[2]

[1]Novosibirsk Scientific Research Institute for Hygiene, 7 Parkhomenko St., Novosibirsk, 630108, Russian Federation
[2]Omsk State Medical University, 12 Lenina St., Omsk, 640099, Russian Federation

Assessment of effects produced by physical and chemical occupational factors on changes in the relative telomere length (RTL) in workers is a promising trend in contemporary research. It can be used as a marker of not only ageing but also intensity of oxidative stress and chronic inflammation. Simulation of such effects in experiments on laboratory ICR mice and Wistar rats enriches our knowledge on the subject.

In this study, we were interested in performing comparative assessment of isolated effects produced by physical and chemical factors on the relative telomere length of laboratory animals in a model experiment. The study involved using laboratory animals (mice, n = 65; rats, n = 65) divided into the experiment (total vibration, noise and a mixture of aromatic hydrocarbons) and the control groups. Animals in the control group were intact. Exposure to chemical and physical factors was simulated in a model animal experiment. The relative telomere length was established using the quantitative real-time polymerase chain reaction. The experimental data were analyzed by non-parametric analysis techniques in Statistica 10 software package. Intergroup differences were estimated using the Mann – Whitney test. Critical significance in testing of statistical hypotheses was taken below 0.05.

Physical and chemical factors had the greatest influence on RLT shortening in the experimental animals relative to the control (intact animals). This indicates activation of the accelerated ageing pathways and growing risks of diseases associated with these exposures. The fastest RLT shortening rates were established upon exposure to total vibration and the chemical factor in mice after 30 days in the experiment; rats, after 60 days. The maximum growth in RLT shortening upon exposure to noise was established in mice after 60 days in the experiment; rats, after 180 days. Differences in RLT in comparison with its initial value were lost in mice on the 90^{th} day in the experiment and in rats on the 180^{th} day of the modeled chemical and physical exposure, which may be interpreted as overall ageing of the experiment animals.

RLT shortening in biological objects upon long-term exposure to adverse chemical and physical factors gives evidence of accelerated ageing of the biological systems in the body and can create elevated risks of cardiovascular and aging-associated diseases.

Keywords: *occupational factors, periodic effects, physical exposure, chemical exposure, mice, rats, relative telomere length, comparative assessment, comparability of the results, accelerated ageing, risks.*

Assessment of effects produced by physical and chemical occupational factors on changes in the relative telomere length (RTL) in workers is a promising trend in contemporary research. It can be used as a marker of not only ageing but also intensity of oxidative stress and chronic inflammation. Simulation of such effects in experiments on laboratory ICR mice and Wistar rats enriches our knowledge on the subject [1].

Chronic effects produced by physical [2] and chemical [3] occupational factors (stressors) [4] on employable population can lead to health impairments, increase risks of

Oleg A. Savchenko – Candidate of Biological Sciences, Leading Researcher (e-mail: Savchenkooa1969@mail.ru; tel.: +7 (383) 343-44-43; ORCID: https://orcid.org/0000-0002-7110-7871).

Irina I. Novikova – Doctor of Medical Sciences, Professor, director (e-mail: novikova_ii@niig.su; tel.: +7 (383) 343-34-01; ORCID: https://orcid.org/0000-0003-1105-471X).

Olga A. Savchenko – Candidate of Medical Sciences, Associate Professor of the Department of Pediatrics with a PhD course (e-mail: Olgasav1978@mail.ru; tel.: +7 (381) 236-28-35; ORCID: https://orcid.org/0000-0003-2035-5653).

various diseases [5] and trigger accelerated ageing [6, 7].

Long-term exposure to various stressors can induce accelerated biological ageing (reduced leucocyte telomere length) and chronic hyperactivation of the body's physiological stress systems [8]. Combined exposure to physical and chemical stressors, both at workplace and at home, also promotes prevalence of occupational diseases and accelerated ageing [9].

A study by L.Y. Hao et al., 2005, established that the progressive worsening of disease was directly associated with decreasing telomere length, which was manifested by stem cell failure [10]. This is also confirmed by findings reported in some other studies; thus, M. Shoeb et al., 2021, found that accelerated ageing and incidence were closely related to telomere length [11]. Several foreign studies accomplished by leading experts (H. Li et al., 2021; B. Celtikci et al., 2021) reported that reduced RTL was a biomarker of human ageing and was associated with developing age-related renal diseases [12]; it also increased the risk of diseases associated with weaker cell proliferation and tissue degeneration [13]. However, at present biomedical studies with their focus on investigating isolated periodical impacts exerted by physical and chemical factors on changes in RTL commonly rely on using model experimental animals, such as ICR mice and Wistar rats [14, 15]. This helps investigate processes and pathways of accelerated ageing.

The aim of this study was to perform comparative assessment of isolated effects produced by physical and chemical factors on the relative telomere length of laboratory animals in a model experiment.

Materials and methods. The study involved using laboratory animals**,** ICR mice (n = 65) and Wistar rats (n = 65) for 90 and 180 days accordingly considering the recommendations stipulated in European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes[1] and Guide for the Care and Use of Laboratory Animals (Washington, 2011)[2].

According to the experiment design, the animals were divided into four groups; each group included the equal number of animals. The first group (n = 15 + 15) was the control one (animals not exposed to any physical or chemical occupational factors).

The second animal group (n = 15 + 15) was exposed to vibration similar to technological one typical for stationary workplaces[3]: vibration acceleration levels in octave bands with center frequencies were 1–63 Hz, OX – 57.3–100.2; OY – 51.4–101.5; OZ – 62.5–103.6 dB; equivalent adjusted vibration acceleration level was as follows, dB: OX – 98.6; OY – 99.9; OZ – 102.1; the exposure lasted for 0.5 hour every day.

The third animal group (n = 15 + 15) was exposed to noise at the level of 81.5–85.3 dBA in a noise chamber for 0.5 hours every day. The fourth animal group (n = 15 + 15) was exposed to a chemical mixture of hydrocarbons, 200 liter volume, in an inhalation exposure chamber: dimethyl benzene (a mixture of 2-, 3-, 4-isomers), 225 mg/m^3; benzine fuel sol-

[1] European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes ETS N 123 (Strasburg, March 18, 1986). *GARANT: information and legal support*. Available at: https://base.garant.ru/4090914/?ysclid=lx32x1xmrq588324754 (December 12, 2024).

[2] National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Guide for the Care and Use of Laboratory Animals, 8th ed. Washington (DC), National Academies Press Publ., 2011. DOI: 10.17226/12910

[3] SanPiN 1.2.3685-21. Gigienicheskie normativy i trebovaniya k obespecheniyu bezopasnosti i (ili) bezvrednosti dlya cheloveka faktorov sredy obitaniya (s izmeneniyami na 30 dekabrya 2022 goda), utv. postanovleniem Glavnogo gosudarstvennogo sanitarnogo vracha Rossiiskoi Federatsii ot 28 yanvarya 2021 goda № 2 [Hygienic standards and requirements to providing safety and (or) harmlessness of environmental factors for people (last amended as of December 30, 2022), approved by the Order of the RF Chief Sanitary Inspector on January 28, 2021 No. 2]. *KODEKS: electronic fund for legal and reference documentation.* Table 5.4. Available at: https://docs.cntd.ru/document/573500115 (December 12, 2024) (in Russian).

vent, 225 mg/m^3; methyl benzene, 450 mg/m^3; propane-2-on, 1200 mg/m^3 in a concentration equal to 1.5 MPL for 0.5 hour daily.

To perform a background analysis, control groups were made of five animals each (n = 5 + 5), which were kept separately from the rest.

RTL was established on the Day 0, 30 (60), 60 (120) and 90 (180) in the experiment. DNA was extracted from biological samples of transversal striated muscle fiber of the animal thigh by phenol-chloroform extraction[4] using quantitative real-time PCR based on the methodology developed by R.S. Lee et al. [16] and modified by V.N. Maksimov [17]. DNA concentration was measured with an Epoch microplate spectrophotometer (BioTek Instruments, USA).

The albumin gene was taken as a single-copy reference gene. Separate quantitative reactions for telomeres and the albumin gene were set in pair 96 well plates in identical positions. Each plate included a series of DNA dilutions (0.5; 1.0; 2.0; 5.0; 10; 20 and 30 ng), which were used to create a calibration curve and quantitative estimation of each sample.

A reaction mixture for the telomere analysis contained the following reagents: 270 nM tel1b primer (5′ ACACTAAGGT-TTGGGTTTGG-GTTTGGGTTT-GGGTTAGTGT 3′); 900 nM tel2b primer (5′ TGTTAGGTAT-CCCTAT CCCT-ATCCCTATCC-CTATCCCTAACA-3′); 0,2X SYBR Green I; 5 mM DTT (dithiothreitol); 1 % DMSO (dimethyl sulfoxide); 0.2 mM of each dNTP; 1.5 mM MgCl2; 1.25 units of DNA polymerase in the total volume of 15 μl of the PCR buffer. The PCR cycles were as follows: 10 minutes at 95 °C, then 25 cycles as 15 seconds at 95 °C, 30 seconds at 54 °C, and 90 seconds at 72 °C. A reaction mixture for the albumin gene analysis contained the following reagents: 300 nM Albd primer (5′ GCTGACT GCT-GTACAAAACA-AGAG-3′), Albr primer (5′ TGACTATCAG-CATAAGTGTT-ACTA-3′), 0.2X SYBR Green I; 5 mM DTT (dithiothreitol); 1 % DMSO (dimethyl sulfoxide); 0.2 mM of each dNTP; 1.5 mM MgCl2; 1.25 units of DNA polymerase in the total volume of 15 μl of the PCR buffer. The PCR cycles were as follows: 3 minutes at 95 °C, then 35 cycles as 15 seconds at 95 °C, 20 seconds at 58 °C, and 20 seconds at 72 °C. Both reactions were set on a QuantStudio 5 amplifier (Thermo Fisher Scientific, USA). The quality control was performed and the T / S (telomeres to the single copy gene) ratio was calculated. If sample amplification curves had standard deviation > 0.5 in three replicas, than this sample was excluded from further analysis [18].

Experimental data were statistically analyzed using non-parametric analysis methods in the Statistica 10 software. Intergroup differences were estimated using the Mann – Whitney test. Critical significance in statistical hypothesis testing was taken at the level below 0.05.

Results and discussion. The experiment on Wistar rats continued our previous experiments on ICR mice [18], which made it possible to compare repeatedly obtained experimental data basing on biomechanical simulation. Analysis of RTL in muscle thigh tissue samples in the experimental groups revealed a significant association between RTL and age during the 90 days of observation for ICR mice and 180 days of observation for Wistar rats. RTL differences were also established between the experimental group and the control. For example, RTL turned out to be reduced in control ICR mice on Day 90 in the experiment (0.33 [0.32; 0.35] relative units) against Day 0 (0.84 [0.81; 0.93] relative units). In control Wistar rats, a similar result was obtained as regards RTL reduction (Table) on Day 180 (1.52 [1.48; 1.61] relative units) against Day 0 (2.38 [1.92; 2.41] relative units).

[4] Smith K., Kalko S., Cantor Ch. Pul's-elektroforez i metody raboty s bol'shimi molekulami DNK [Pulsed-field gel electrophoresis of large DNA molecules]. In book: *Analiz genoma [Genome analysis]*. Moscow, Mir Publ., 1990, pp. 58–94 (in Russian).

Table

Comparative results obtained for isolated effects produced by occupational factors on RTL of ICR mice [18] and Wistar rats in model experiment, *Me* [*LQ*; *HQ*]

Group	*n*	Day 30	*n*	Day 60	*n*	Day 90	*n*	Day 60	*n*	Day 120	*n*	Day 180
	RTL of ICR mice [18]						*RTL of Wistar rats*					
Group 1 (control)	5	0.79 [0.73; 0.81]	5	0.62 [0.55; 0.76]	5	0.33 [0.32; 0.35]*	5	1.84 [1.82; 2.38]	5	1.79 [1.66; 2.22]	5	1.52 [1.48; 1.61]*
Group 2 (vibration)	5	0.61 [0.61; 0.66]	5	0.47 [0.38; 0.55]*,#	5	0.29 [0.28; 0.32]*,#	5	1.79 [1.72; 2.31]	5	1.11 [0.98; 1.27]*,#	5	0.69 [0.62; 0.82]*,#
Group 3 (noise)	5	0.61 [0.61; 0.66]	5	0.47 [0.38; 0.55]*,#	5	0.29 [0.28; 0.32]*,#	5	1.72 [1.51; 1.79]	5	1.47 [0.96; 1.49]*,#	5	0.83 [0.77; 0.93]*,#
Group 4 (chemicals)	5	0.56 [0.56; 0.69]*	5	0.37 [0.28; 0.41]*	5	0.25 [0.25; 0.35]*	5	1.51 [1.39; 1.57]*	5	1.03 [1.01; 1.13]*	5	0.67 [0.67; 0.82]*

Note: Table provides significant ($p < 0.05$) differences from the respective indicators: * – on Day 0, # – against the control; table also contains the results obtained in our previous study focused on RTL of ICR mice [18].

Comparative assessment of isolated impacts exerted by physical factors on mice RTL (Group 2 and 3) revealed a significant RTL reduction on Day 60 (Group 2 and Group 3 (0.47 [0.38; 0.33] relative units) and Day 90 (Group 2 and Group 3 (0.29 [0.28; 0.32] relative units) against the control on Day 60 (0.62 [0.55; 0.76]) and Day 90 (0.33 [0.32; 0.35]). A similar picture involving RTL reduction was observed for the experimental Wistar rats exposed to the selected physical factors on Day 120 in Group 2 (exposed to vibration (1.11 [0.98; 1.27] relative units) and Group 3 (exposed to noise (1.47 [0.96; 1.49] relative units)) and on Day 180 (Group 2 (0.69 [0.62; 0.82] relative units) and Group 3 (0.83 [0.77; 0.93] relative units)) against the control on Day 120 (1.79 [1.66; 2.22]) and Day 180 (1.52 [1.48; 1.61]). The analyzed physical factors affected the central nervous system (CNS) and cerebellum functioning, which led to RTL reduction and accelerated ageing of the biological systems in the experimental animals (on Day 60 and 90 in mice; on Day 120 and 180 in rats) against the control.

Exposure to a mixture of toxicants resulted in a considerable RTL reduction in the mice and rats from the chemically exposed groups against the control and those groups exposed to isolated impacts of the analyzed physical factors (see Table). In the experimental mice, RTL reduction occurred on Day 30 (0.56 [0.56; 0.69]) and only grew later on Day 60 (0.37 [0.28; 0.41]) and 90 (0.25 [0.25; 0.35]) against the control on Day 30 (0.79 [0.73; 0.81]), Day 60 (0.62 [0.55; 0.76]) and Day 90 (0.33 [0.32; 0.35]) [18]. Similarly, reduced RTL was established in the experimental rats (see Table) starting from Day 60, 1.51 [1.39; 1.57], against the control (1.84 [1.82; 2.38]); Day 120, 1.03 [1.01; 1.13], against the control (1.79 [1.66; 2.22]); and Day 180, 0.67 [0.67; 0.82], against the control (1.52 [1.48; 1.61]). Exposure to the 4-component mixture of hydrocarbons affected the alveolar-capillary lung membrane and the olfactory bulb and had negative effects on the CNS together with RTL reduction and accelerated ageing in the experimental mice and rats from the exposed groups against the control.

The results obtained by the previous experiments performed on ICR mice (Figure) [18] turned out to be quite comparable with experimental data repeatedly obtained in the experiment on Wistar rats (% of the RTL value on Day 0).

The greatest RTL reduction rates upon chemical exposure were established in the experimental mice after Day 30 in the experiment; the rats, day 60 in the experiment. RTL reduced most considerably upon exposure to vibration and noise on Day 60 in the experimental mice and Day 120 in the experimental rats. Differences in RTL against its initial level (% of the RTL value on Day 0) were lost in the experimental mice on Day 90 in the experiment and in the rats on Day 180 upon exposure to the analyzed physical and chemical

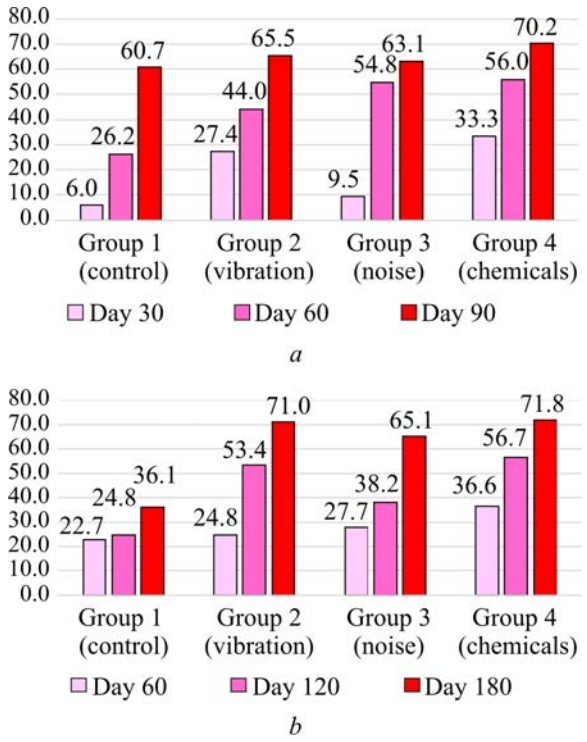

Figure. Changes in RTL (*a*) in ICR mice [18] and (*b*) Wistar rats upon periodic isolated exposure to physical and chemical factors

factors. This may be interpreted as overall ageing of the animals and elevated risks of chronic non-communicable diseases (as a percentage of their initial level on Day 0).

Available literature does not contain any publications, which allow us to fully estimate isolated effects produced by physical and chemical factors on RTL of Wistar rats in dynamics. The only exclusion was our own experimental study performed on ICR mice [18] and few works by various researchers (J. Lin et al., 2012; D. Stefler et al., 2018; D.D. Karimov et al., 2021), which reported a negative role played by exposure to stress [19] on RTL reduction [20] and developing cellular ageing in industrial workers [21]; this had a direct negative effect on life quality and life expectancy. Given that, we conducted several subchronic and chronic experiments to obtain comparable data about effects produced by periodical physical and chemical exposures (at the level of 1.5 MPL) on different animal species (mice and rats). This made it possible to get more profound knowledge of how to establish health risks and processes of accelerated ageing in biological systems of warm-blooded organisms.

Conclusion. The following conclusions can be drawn basing on the accomplished experimental studies. Telomeres protect the ends of chromosomes and play the key role in maintaining the genome stability and regulating cellular ageing. Our findings can be considered as a confirmation of the hypothesis that RTL reduction in biological objects upon long-term occupational physical and chemical exposure gives evidence of premature cellular ageing. This conclusion is consistent with findings reported in previous studies about the telomere length being a marker of risks of age-related diseases and occupational diseases, including cardiovascular ones (infarctions and strokes) [22]. In addition, isolated periodical exposure to physical and chemical factors (at the level of 1.5 MPL) in a chronic experiment on animal models induced RTL reduction [19], weakened motion, emotional and exploratory activity [1] as well as provoked morphological changes in two and more internal organs (biomarker of accelerated ageing) in animal models. Vascular changes were the most pronounced on Day 180 in the experiment but some initial manifestations occurred on Day 60 and 120 [23], which may indicate that ageing of biological systems was triggered and life expectancy of such animals can be affected.

The greatest effect that promoted RTL reduction in the experimental animals was produced by long-term chemical and vibration exposure in comparison with the control group (the intact animals).

At the initial stage, the smallest effect on RTL in the experimental mice and rats was produced by exposure to noise; later on, noise exposure continued to have the minimal effect on RTL in both species. These manifestations may imply that initially noise does not affect DNA considerably and does not induce the same levels of oxidative stress as total vibration and exposure to a mixture of hydrocarbons. However, despite its less considerable influence, long-term noise exposure can also trigger pathology of many organs and systems

[23] and have negative consequences for health of the whole body [24].

Changes in RTL were the most pronounced in the ICR mice on Day 90 in the experiment and in the Wistar rats on Day 180 upon periodical isolated exposure to the analyzed chemical and physical factors. This term can be recalculated for humans (1.3 weeks of a mouse's life are equal to one human year; 1 week of a rat's life is equal to one human year) and the result may indicate that negative outcomes of occupational exposures appear starting from 10–15 years of work. It should be noted that initial RTL reduction [18] and changes in animals' internal organs start developing when work records reach 5–9 years [23].

RTL reduction in biological objects upon long-term physical and chemical exposures indicates accelerated ageing of the biological systems in the body and may increase risks of cardiovascular and age-related diseases. Some experimental results give evidence of accelerated cellular ageing in the test groups against the control, which is also confirmed by appearing angiopathies in internal organs [23], weaker orientation and exploratory behavior and overall signs of accelerate ageing in experimental animals [1].

Our study emphasizes how important it is to reduce risks of accelerated (cellular) ageing, cardiovascular diseases (infarctions and strokes) in biological objects upon long-term adverse exposure to physical and chemical factors (at the level of 1.5 MPL). Our findings give evidence of the necessity to conduct hygienic control and qualitative hygienic assessment of working conditions at workplaces; to minimize physical and chemical exposures for workers by implementing additional preventive measures, breaks, use of necessary personal protective equipment (protection for eyes, skin and respiratory organs including ear-plugs, gas masks, respirators, goggles, and gloves) and protective clothing and footwear; to conduct ultrasound examinations during mass health examinations aimed at early diagnostics of diseases in workers exposed to occupational adverse factors in order to achieve career longevity.

In future, we plan to have a more profound investigation of pathways through which the above mentioned factors influence telomere length and processes of accelerated ageing of the biological systems in the body.

Funding. The study was accomplished with the Research Subject 'Investigation of Cellular Ageing Processes and Biological Ageing of Workers Exposed to Various Adverse Occupational Factors in Management of Career Longevity' (Registration No. AAAA-A19-119070190016-3. The State Task No. 141-00094-23-00 for 2023 and the plan of 2025).

Competing interests. The authors declare no competing interests.

References

1. Savchenko O.A., Novikova I.I., Chuenko N.F., Savchenko O.A. Assessment of the influence of production factors on physiological parameters, behavioral reactions and accelerated aging of laboratory animals in a chronic experiment. *Sanitarnyi vrach*, 2024, no. 11, pp. 780–793. DOI: 10.33920/med-08-2411-03 (in Russian).

2. Baudin C., Lefevre M., Champelovier P., Lambert J., Laumon B., Evrard A.-S. Self-rated health status in relation to aircraft noise exposure, noise annoyance or noise sensitivity: the results of a crosssectional study in France. *BMC Public Health*, 2021, vol. 21, no.1, pp. 116. DOI: 10.1186/s12889-020-10138-0

3. Zhang H., Li H., Peng Z., Cao J., Bao J., Li L., Wang X., Ji Y., Chen Z. Meta-analysis of the effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts in China. *J. Environ. Sci. (China)*, 2022, vol. 114, pp. 204–210. DOI: 10.1016/j.jes.2021.08.035

4. Sheppard A., Ralli M., Gilardi A., Salvi R. Occupational Noise: Auditory and Non-Auditory Consequences. *Int. J. Environ. Res. Public Health*, 2020, vol. 17, no. 23, pp. 8963. DOI: 10.3390/ijerph17238963

5. Zainullina A.Z., Nesterova O.V., Biryukova N.V. Faktory riska i profilaktika shumovogo vozdeistviya na organizm cheloveka [Risk factors and prevention of noise exposure for the human

body]. *Tendentsii razvitiya nauki i obrazovaniya*, 2021, no. 74–1, pp. 69–74. DOI: 10.18411/lj-06-2021-14 (in Russian).

6. Wang Y., Chen H., Liu B., Yang M., Long Q. A systematic review on the research progress and evolving trends of occupational health and safety management: A bibliometric analysis of mapping knowledge domains. *Front. Public Health*, 2020, vol. 8, pp. 81. DOI: 10.3389/fpubh.2020.00081

7. Karimov D.D., Erdman V.V., Kudoyarov E.R., Valova Ya.V., Smolyankin D.A., Repina E.F., Karimov D.O. Influence of occupational risk factors on human aging (literature review). *Gigiena i sanitariya*, 2022, vol. 101, no. 4, pp. 375–381. DOI: 10.47470/0016-9900-2022-101-4-375-381 (in Russian).

8. Révész D., Verhoeven J.E., Milaneschi Y., de Geus E.J.C.N., Wolkowitz O.M., Penninx B.W.J.H. Dysregulated physiological stress systems and accelerated cellular aging. *Neurobiol. Aging*, 2014, vol. 35, no. 6, pp. 1422–1430. DOI: 10.1016/j.neurobiolaging.2013.12.027

9. Descatha A. Retirement, arduousness, premature aging: the role of occupational health practitioners and physicians. *Arch. Maladies Prof. Environ.*, 2023, vol. 84, no. 2, pp. 101807. DOI: 10.1016/j.admp.2023.101807

10. Hao L.Y., Armanios M., Strong M.A., Karim B., Feldser D.M., Huso D., Greider C.W. Short telomeres, even in the presence of telomerase, limit tissue renewal capacity. *Cell*, 2005, vol. 123, no. 6, pp. 1121–1131. DOI: 10.1016/j.cell.2005.11.020

11. Shoeb M., Meier H.C.S., Antonini J.M. Telomeres in toxicology: Occupational health. *Pharmacol. Ther.*, 2021, vol. 220, pp. 107742. DOI: 10.1016/j.pharmthera.2020.107742

12. Li H., Wang B., Li D., Li J., Luo Y., Dan J. Roles of telomeres and telomerase in age-related renal diseases (Review). *Mol. Med. Rep.*, 2021, vol. 23, no. 2, pp. 96. DOI: 10.3892/mmr.2020.11735

13. Celtikci B., Erkmen G.K., Dikmen Z.G. Regulation and Effect of Telomerase and Telomeric Length in Stem Cells. *Curr. Stem Cell Res. Ther.*, 2021, vol. 16, no. 7, pp. 809–823. DOI: 10.2174/1574888x15666200422104423

14. Mukherjee P., Roy S., Ghosh D., Nandi S.K. The role of animal models in biomedical research: a review. *Lab. Anim. Res.*, 2022, vol. 38, no. 1, pp. 18. DOI: 10.1186/s42826-022-00128-1

15. Koterov A.N., Ushenkova L.N., Zubenkova E.S., Wainson A.A., Biryukov A.P. The relationship between the age of the based laboratory animals (mice, rats, hamsters and dogs) and the age of human: actuality for the age-ralated radiosensitivity problem and the analysis of published data. *Meditsinskaya radiologiya i radiatsionnaya bezopasnost'*, 2018, vol. 63, no. 1, pp. 5–27. DOI: 10.12737/article_5a82e4a3908213.56647014 (in Russian).

16. Lee R.S., Zandi P.P., Santos A., Aulinas A., Carey J.L., Webb S.M., McCaul M.E., Resmini E., Wand G.S. Cross-species Association Between Telomere Length and Glucocorticoid Exposure. *J. Clin. Endocrinol. Metab.*, 2021, vol. 106, no. 12, pp. e5124–e5135. DOI: 10.1210/clinem/dgab519

17. Maximov V.N., Malyutina S.K., Orlov P.S., Ivanoschuk D.E., Voropaeva E.N., Bobak M., Voevoda M.I. Length telomere leukocytes as aging markers and risk factors for age-related diseases in humans. *Uspekhi gerontologii*, 2016, vol. 29, no. 5, pp. 702–708 (in Russian).

18. Savchenko O.A., Svechkar P.E., Novikova I.I. Effect of Production Factors on the Relative Telomere Length of ICR Mice. *Cell Tiss. Biol.*, 2025, vol. 19, no. 2, pp. 161–165. DOI: 10.1134/S1990519X25020087

19. Lin J., Epel E., Blackburn E. Telomeres and lifestyle factors: roles in cellular aging. *Mutat. Res.*, 2012, vol. 730, no. 1–2, pp. 85–89. DOI: 10.1016/j.mrfmmm.2011.08.003

20. Stefler D., Malyutina S., Maximov V., Orlov P., Ivanoschuk D., Nikitin Y., Gafarov V., Ryabikov A. [et al.]. Leukocyte telomere length and risk of coronary heart disease and stroke mortality: prospective evidence from a Russian cohort. *Sci. Rep.*, 2018, vol. 8, no. 1. pp. 16627. DOI: 10.1038/s41598-018-35122-y

21. Karimov D.D., Kudoyarov E.R., Mukhammadiyeva G.F., Ziatdinova M.M., Baigildin S.S., Yakupova T.G. Biomarkers of ageing in the study of occupational harm impacts (literature review). *Gigiena i sanitariya*, 2021, vol. 100, no. 11, pp. 1328–1332. DOI: 10.47470/0016-9900-2021-100-11-1328-1332 (in Russian).

22. Tian Y., Wang S., Jiao F., Kong Q., Liu C., Wu Y. Telomere length: a potential biomarker for the risk and prognosis of stroke. *Front. Neurol.*, 2019, vol. 10, pp. 624. DOI: 10.3389/fneur.2019.00624

23. Savchenko O.A., Novikova I.I. Assessment of the influence of production factors on the condition of the internal organs of model animals in a 180-day experiment. *Sibirskii nauchnyi meditsinskii zhurnal*, 2025, vol. 45, no. 1, pp. 109–121. DOI: 10.18699/SSMJ20250112 (in Russian).

24. Bazarova Ye.L., Fedoruk A.A., Roslaya N.A., Osherov I.S., Babenko A.G. Assessment of occupational risk caused by noise exposure in workers at metallurgical plant subunits under modernization. *Meditsina truda i promyshlennaya ekologiya*, 2019, vol. 59, no. 3, pp. 142–148. DOI: 10.31089/1026-9428-2019-59-3-142-148 (in Russian).

Savchenko O.A., Novikova I.I., Savchenko O.A. Comparative assessment of isolated influence exerted by physical and chemical factors on relative telomere length of laboratory animals in a model experiment. Health Risk Analysis, 2025, no. 1, pp. 106–113. DOI: 10.21668/health.risk/2025.1.10.eng

Received: 14.01.2025
Approved: 12.03.2025
Accepted for publication: 24.03.2025