клітини були виявлені на кріостатних зрізах тканини глотки за допомогою методу Вахштейна-Мейзеля. Встановлено, що у новонароджених експериментальних тварин абсолютна кількість дендритних клітин більша, ніж в контролі, та не змінюється протягом першого тижня, на відміну від контролю, де цей показник значно не змінюється протягом двох тижнів життя. У всіх груп тварин абсолютна кількість дендритних клітин збільшується протягом третього тижня життя, одночасно зі збільшенням антигенного навантаження на організм. В експерименті, незалежно від способу введення антигену, активація дендритних клітин відбувається раніше, ніж у контролі, тобто на 7 добу життя. У експериментальних тварин, порівняно з контролем, збільшується кількість відростків дендритних клітин, а також самі дендритні клітини забарвлені темніше, ніж у контролі, що свідчить про більш активне накопичення АТФ.

Ключові слова: АТФ, внутрішньоутробне введення антигену, дендритні клітини, глотка,

Стаття надійшла 25.08.2019 р.

срезах ткани глотки с помощью метода Вахштейна-Мейзеля. Установлено, что у новорожденных экспериментальных животных абсолютное количество дендритных клеток больше, по сравнению с контролем, на протяжении первой недели жизни и не изменяется, в отличие от контроля, где этот показатель значительно не изменяется в течение двух недель. У животных всех исследуемых групп абсолютное количество дендритных клеток увеличивается на протяжении третьей недели жизни, одновременно с увеличением антигенной нагрузки на организм. В эксперименте, активация дендритных клеток происходит раньше, чем в контроле, то есть на 7 сутки жизни. У экспериментальных животных, по сравнению с контролем, увеличивается количество отростков дендритных клеток. У экспериментальных животных увеличивается количество дендритов по сравнению с контролем, а также установлено, что сами дендритные клетки окрашены темнее, чем в контроле, что свидетельствует о более активном накоплении АТФ.

Ключевые слова: АТФ, внутриутробное введение антигена, дендритные клетки, глотка, местный иммунитет.

Рецензент Єрошенко Г.А.

DOI 10.26724/2079-8334-2020-3-73-168-175
UDC 616.12/.14–091.8:546.815/.819–022.513.2:57.084.1

I.V. Gubar[1,2], O.L. Apykhtina[1], R.F. Kaminsky, Yu.B. Chaikovsky, O.P. Yavorovsky, L.M. Sokurenko[2]
Bogomolets National Medical University, Kyiv, [1]SI "Kundiiev Institute of Occupational Health", NAMS of Ukraine, Kyiv, [2]Educational and Scientific Center "Institute of Biology and Medicine" of Taras Shevchenko National University, Kyiv

ORGANOTOXIC EFFECT OF SINGLE INTRATRACHEAL ADMINISTRATION OF LEAD NANOPARTICLES OF DIFFERENT SIZES

e-mail: ginna5@ukr.net

Cardiovasotoxic effect of a single intratracheal administration of lead nanoparticles of different sizes was studied in the experiment. Colloidal solutions of lead sulfide (PbS in sodium polyphosphate) with an average size of 26–34 nm and 50–80 nm, and lead nitrate $Pb(NO_3)_2$ in ionic form which is well soluble in water were used. Toxic effects were assessed 12 days after exposure. Morphological changes were found in the myocardium and to a greater extent in the atria. Mild disorders, such as enlarged interstitial space and dystrophic changes of individual cardiomyocytes were found after administration of $PbS_{26–34nm}$ and $Pb_{50–80nm}$ nanoparticles. Thus, with intratracheal administration of lead, the toxic effect of nanoparticles $PbS_{26–34nm}$ and $PbS_{50–80nm}$ was manifested more compared with an effect caused by the action of the ionic form of lead $Pb(NO_3)_2$. The toxic effect of lead nanoparticles was mainly evident in the atrial myocardium cardiomyocytes, while the aortic wall remained almost unaffected. The most pronounced structural changes were observed in the lungs and bronchi, which may be due to the route of the toxicant administration.

Key words: lead, nanoparticles, intratracheal intoxication, morphological changes, myocardium, aorta, lungs.

The work is a fragment of the research projects "Investigation of cardiovasotoxic action mechanisms of heavy metal nanoparticles (on the problem of biosafety of nanomaterials)", state registration No. 0119U100182; "Changes in internal organs and regulatory systems under the conditions of experimental damage and historical aspects of histology, cytology and embryology development in Ukraine", state registration No. 0116U000121 and "Study the of tissue reaction features and their modulation in lesions of various origins", state registration No. 0120U102691.

New physicochemical properties of the engineered nanoparticles make them very attractive for industrial and biomedical use. Nowadays, the manufacturing and application of nanotechnological products has reached industrial scale worldwide and has the potential for further growth and expansion. This raises concerns about the unforeseen adverse health effects on both nanoindustry workers and nanoproduct consumers [13, 8].

Zhao L [15] noted that nanoparticles (NPs) released to the work area air might contribute to the cardiopulmonary effects observed in workers. Biomarkers of lung damage, cardiovascular diseases, as well as biomarkers of oxidative stress and inflammation which were associated with the occupational exposure to the studied NPs were found in the workers of the NP factory.

It was experimentally established that the cardiotoxic effect of NPs of titanium oxide, zinc oxide, silver, carbon, silicon dioxide and iron oxide depended on both the toxicity of these compounds and the

size of their nanoparticles [3]. Therefore, the morbidity rate of workers can be due to both the toxicity of the studied substances and the ability of their ultrafine particles to deeply penetrate into the body tissues.

Studies conducted by [12] allowed to obtain results on nanoparticle emissions in real working conditions during various technological processes of manufacturing and use of nanotechnological products. During one of the repeated processes an unexpected and extremely high emission of nanoparticles was registered, which in the long run might endanger the workers' health. Measurements of the actual level of nanoobjects impact have shown the necessity to monitor the work area air and the importance of collective protective measures.

Lebedova J et al. [10] focused their experiment on the acute and subchronic inhalation effects of lead oxide nanoparticles, as in the production environment it is the inhalation exposure that is most likely. The authors found that accumulation of lead oxide NPs in all tissues depended on the duration of exposure and the concentration of PbO NPs, with lungs and kidneys being the most vulnerable among the studied organs. Histological analysis documented numerous morphological changes and tissue damage, mainly in the lungs.

Dumková J [4] had studied the subchronic inhalation effect of lead oxide nanoparticles on mice. Microscopic and ultramicroscopic changes caused by PbO NPs in the primary and secondary target organs (lungs, brain, liver, kidneys, spleen and blood) were specifically determined. Lead content was also found to be the highest in the lungs and kidneys, slightly lower in the liver and spleen; the lowest lead content was found in the brain. Nanoparticles were found in all the studied tissues, with their amount being the highest in lungs and liver. Moreover, in the lungs of animals exposed to PbO NPs the authors found hyperemia, small areas of atelectasis, alveolar emphysema, focal acute catarrhal bronchiolitis, as well as hemostasis with siderophages in some animals. Nanoparticles were located in phagosomes or formed clusters inside cytoplasmic vesicles. Thus, subchronic inhalation exposure of mice to PbO NP causes severe adverse effects at both cellular and tissue levels [4].

The results of Lucie Bláhová's experiment [2] also showed that subchronic inhalation of PbO nanoparticles had caused histopathological changes in mice, mainly found in the lungs and liver and indicating inflammation and a general toxicity reaction.

Thus, both *in vivo* and *in vitro* studies have shown that specific features of NPs surfaces allow them to cross cellular barriers, damage structures and disrupt functions of body cells [1, 9]. However, the mechanisms underlying nanotoxicity have not been fully studied.

Therefore, the social and commercial benefits of nanomaterials should not outweigh the potential adverse effects on human health and the environment associated with occupational and consumer exposure to them, which necessitates comprehensive toxicological studies of nanosized compounds [14].

The current scarcity of data on the toxic effects of nanoscale lead particles on the cardiovascular system makes the study of their cardiovasotoxic effects features relevant.

The purpose of the study was to examine features of morphological changes in the lung, myocardium and aorta under the action of lead sulfide nanoparticles of different sizes in the experimental model of single acute intratracheal administration.

Materials and methods. The experiments were conducted on rats (mean weight of 160–180 g). Animals were kept in the vivarium on a standardized diet with free access to drinking tap water. In simulating intoxication colloidal solutions of lead sulfide (PbS in sodium polyphosphate) with an average size of 26–34 nm ($PbS_{26–34nm}$) and 50–80 nm (PbS50–80nm), and lead nitrate $Pb(NO_3)_2$ in ionic form which is well soluble in water were used [7]. The control group was injected with normal saline.

NPs dimensions were determined by electron microscopy. The studied substances were administered intratracheally once at a dose calculated by lead content 5 × 10–3 Mol / L. Toxic effects were assessed 12 days after exposure.

The animals were sacrificed by decapitation under mild ether anesthesia and their internal organs were harvested. All manipulations with animals were performed in accordance with the provisions of the "European Convention for the Protection of Vertebrate Animals, Used for Experimental and Other Scientific Purposes" (Strasbourg, 1985) and approved by the Bioethics Committee of the NAS of Ukraine. The experiment plan is approved by the Bioethics Commission of State Institution "Kundiiev Institute of Occupational Health of the National Academy of Medical Sciences of Ukraine" (Minutes № 5, session of bioethics commission from 23.11.2017).

The heart with aorta and lungs were fixed in 10% neutral formalin, dehydrated in isopropanol and embedded in paraffin (Leica Surgipath Paraplast Regular). Paraffin sections were made on a Thermo Microm HM 360 microtome. The sections were deparaffinized and stained with H&E and azure–eosin.

The slides were studied using Olympus BX51 microscope. Morphometric analysis was performed using software Carl Zeiss (AxioVision SE64 Rel.4.9.1), magnification ×200, ×400.

Aorta wall thickness (mkm), adventitia of aorta thickness (mkm), comparative amount of collagen fibers in tunica adventitia (%), number of elastic membranes in tunica media (conventional units) were examined. The statistical study was performed in Origin Lab version 8.0 using the One–way ANOVA test. Data are presented as medians with smaller and larger quartiles (M[Q1-Q3]), becourse normality wasn`t proven.. The difference was considered statistically significant at $P < 0.05$.

Results of the study and their discussion. After the administration of $PbS_{26–34nm}$ and $PbS_{50–80nm}$ pronounced structural changes in the rats' lungs were found. Dystrophic changes of the epithelial plate, desquamation of dead cells into the bronchial lumen, and accumulation of cellular detritus were found in the bronchial wall. The wall integrity was disrupted at different levels of the small bronchi (Fig. 1). Increased lymphocyte density, emergence of neutrophils and eosinophils were observed around the small and terminal bronchi in the $PbS_{26–34nm}$ and $PbS_{50–80nm}$ group, which is the evidence of inflammatory infiltration. The acinar structure of the respiratory part of the lungs is severly distorted. The relative density of the alveoli at the optical examination was reduced, due to the increased content of the structurally altered stromal elements (paratrachial and paravasal connective tissue) and infiltrated leukocytes. Clusters of macrophages were found in the alveolar lumen, with almost no structurally preserved alveoli present in the $PbS_{50–80nm}$ group, the reorganization of the acinar structure of the lungs has been severe until the complete loss of the respiratory part of the lungs morphology. Most large and medium caliber blood vessels were structurally preserved, dilated, with the stasis of blood cells observed. Administration of $Pb(NO_3)_2$ to rats also caused a pronounced inflammatory process in the lungs with the development of degenerative changes in the bronchial wall and in the respiratory part of the lungs. Changes in the respiratory part of the lungs were similar to the disorders in the $PbS_{26–34nm}$ and $PbS_{50–80nm}$ groups, but relatively preserved areas of the lungs were still found (individual alveoli, blood capillaries). Results of histological examinations allowed to state the development of an inflammatory reaction in the respiratory part of the lungs with impaired morphology of the pulmonary acinuses and dystrophic changes of the bronchial mucosa after administration of $PbS_{26–34nm}$, $PbS_{50–80nm}$ and $Pb(NO_3)_2$.

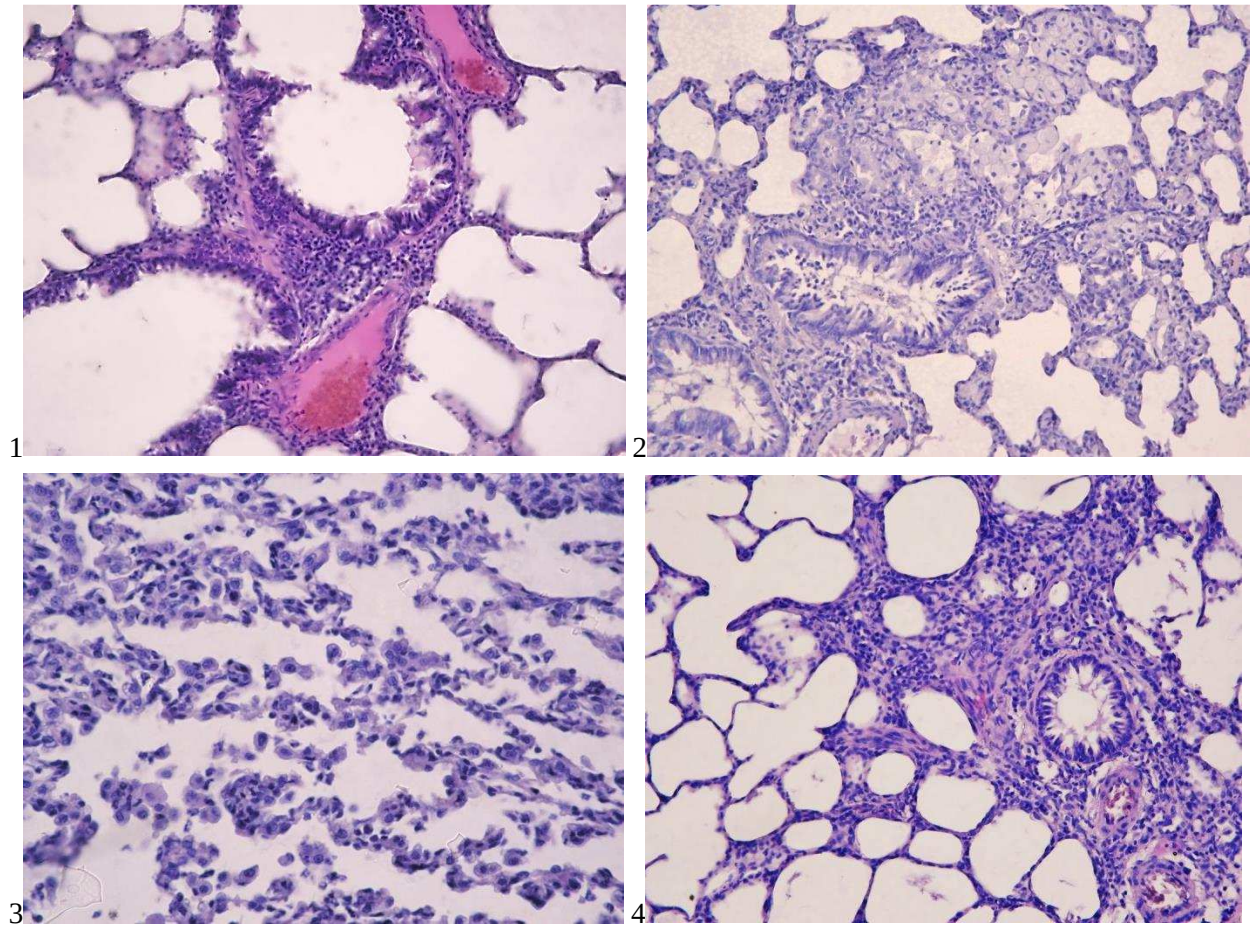


Fig. 1. Rats' lungs after intratracheal administration of lead. Accumulation of macrophages and damaged epitheliocytes in the lumen of the alveoli and bronchi in the $PbS_{26–34nm}$ and $PbS_{50–80nm}$ groups. Note: 1 – control; 2 – $PbS_{26–34nm}$; 3 – $PbS_{50–80nm}$; 4 – $Pb(NO_3)_2$ H&E, ob. 20, e.p. 10.

In all samples the general morphology of the rats' heart was preserved, endo–, myo– and epicardium were detected as in the control group. But in the myocardium structural changes were observed. A nonspecific disorder found in all experimental groups was the increased interstitial space, which in the $PbS_{26–34nm}$ and $PbS_{50–80nm}$ groups was more pronounced in the atria.

In the $PbS_{26–34nm}$ group nuclear diameters of atrial cardiomyocytes were increased with hypochromic staining of cytoplasm and optically transparent areas around the nuclei, which is the evidence of their dystrophic changes. In the $PbS_{50–80nm}$ group, on the contrary, the diameters of cardiomyocytes and nuclei were reduced, and the transverse striation of cardiomyocytes distorted. In the group with $Pb(NO_3)_2$ administration structural changes in the myocardium were weakly expressed (slightly increased interstitial space), with the transverse striation partially preserved (fig. 2).

No significant disorders at the level of the endocardium and epicardium in the comparison groups ($PbS_{26–34nm}$, $PbS_{50–80nm}$, $Pb(NO_3)_2$) were detected. Figure 3 shows the results of morphometric evaluation of the cardiomyocytes diameter of the comparison groups. Morphometric changes allow us to state the damage to the ventricular myocardium in the $PbS_{26–34nm}$ and $PbS_{50–80nm}$ groups represented by the reduced diameter of cardiomyocytes; in the atrium, on the other hand, edema and dystrophic changes were observed in the $PbS_{26–34nm}$ group, and in the $PbS_{50–80nm}$ group – a decreased diameter (similar to changes in the ventricle). No changes of the kind were detected in the $Pb(NO_3)_2$ group.

The analysis of the results of histological and morphometric studies of the aortic wall did not reveal any significant morphofunctional or dystrophic changes. The aortic wall in the experimental groups was structurally unchanged, the layers of the vessel were clearly differentiated (fig. 4). The main wall thickness was represented by the *t.media*, comprising 8 to 12 elastic membranes. The number and density of elastic membranes did not differ between the comparison groups (Fig. 3). *T.adventicia* made up almost one third of the aortic wall. There is a dense network of collagen fibers and single blood vessels in the connective tissue of the outer tunica.

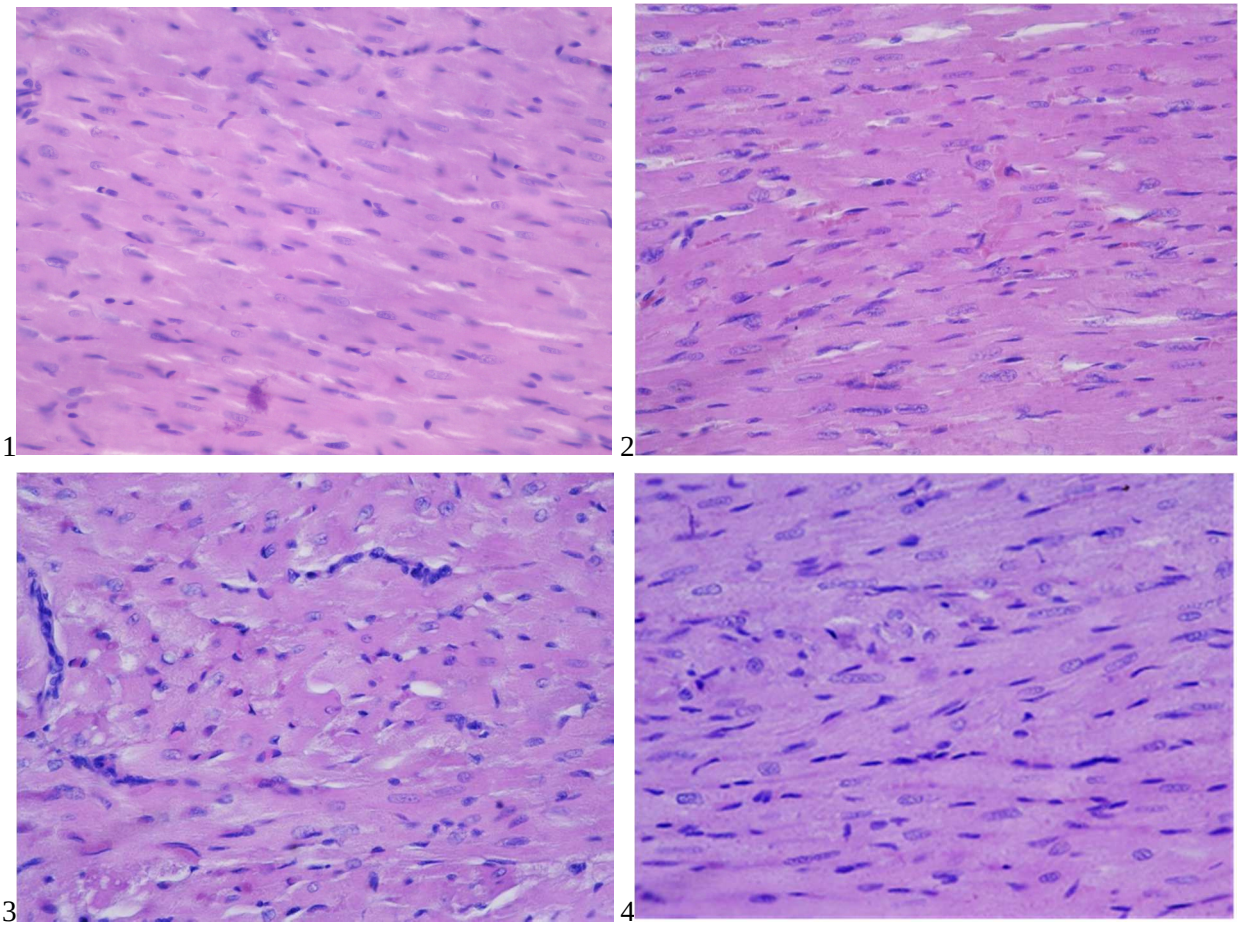
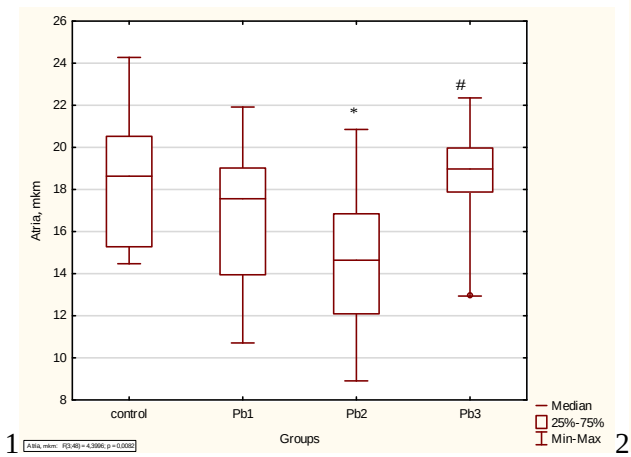
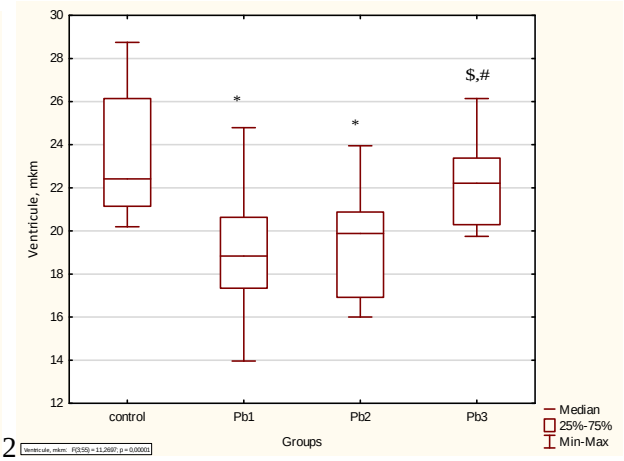


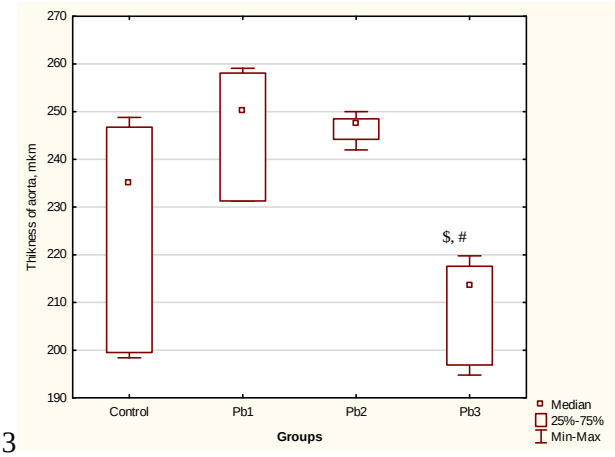
Fig. 2. Ventricular myocardium of rats after intratracheal administration of lead. Note: 1 – control; 2 – $PbS_{26–34nm}$; 3 – $PbS_{50–80nm}$; 4 – $Pb(NO_3)_2$. H&E, ob. 40, e.p. 10.



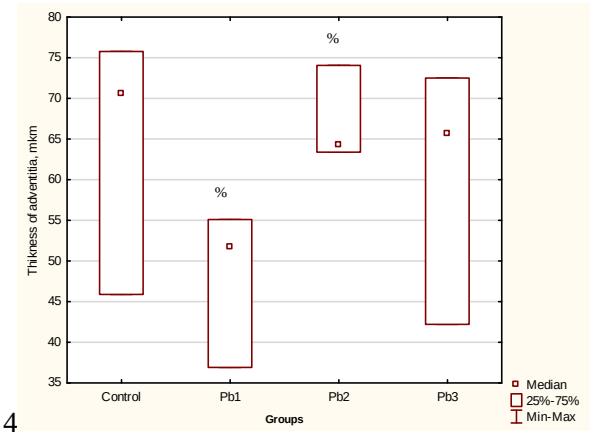
1



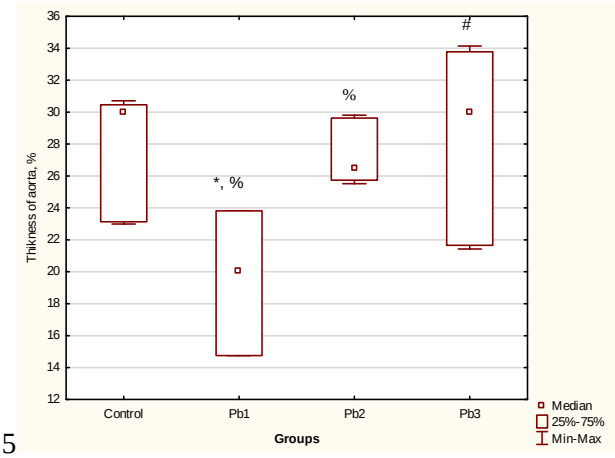
2



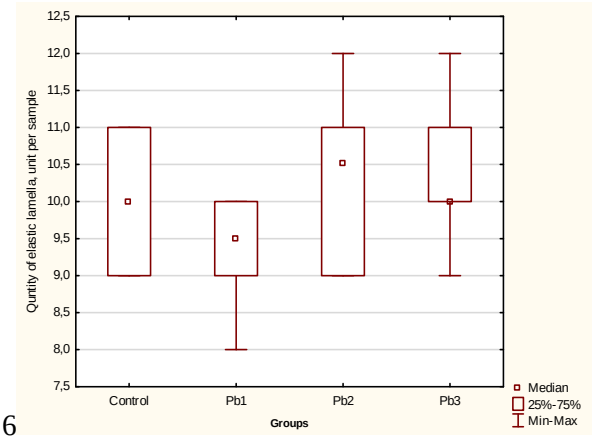
3



4



5



6

Fig. 3. The diameter of the rats' heart cardiomyocytes and aorta after intratracheal administration of lead. Note: 1 – atrium; 2 – a ventricle; 3 – aortic thickness, µm; 4 – thickness of the adventitia, µm; 5 – relative thickness of the adventitia,%; 6 – the number of elastic membranes in the aortic wall, units per sample. * – statistically significant difference from control (P <0,05); $ – statistically significant difference from $PbS_{26–34nm}$ (P <0,05), # – statistically significant difference from $PbS_{50–80nm}$ (P <0,05), % – statistically significant difference between Pb (P <0,05) NP.

In our previous work [6] we studied the cardiovasotoxic effect of PbS NP 26–34 nm and 50–80 nm under subchronic intraperitoneal uptake. The results of the conducted experiments indicated damage to the rats' heart myocardium, which consisted in the increased interstitial space between the cardiomyocytes fibers, cardiomyocyte dystrophy, and blood stasis in the ventricular microvessels. Greater sensitivity of the atrial myocardium to the toxic effects of Pb NP was found. Structural changes in the aorta included dissection of the elastic membranes of the aortal *m. tunica*, decreased density of the adventitial membrane connective tissue and showed a tendency to progressive changes.

In this experiment we aimed at studying the effect of NP PbS 26–34 nm and 50–80 nm on the heart and aorta in acute intratracheal uptake, as it is the inhalation exposure that is most likely in the production environment.

It turned out that the heart myocardium had also experienced the toxic effects of PbS NP of different sizes, which affected the morphological changes of cardiomyocytes. These changes were mild

and to a greater extent emerged in the atrium. The general morphological organization of the heart chambers remained intact and the heart tunicas were clearly seen. We concluded that there was a mild toxic effect of PbS NP on the myocardium under a single intratracheal administration, and morphological changes, such as increased interstitial space between cardiomyocytes, dystrophic changes in their cytoplasm did not have any obvious differences between PbS NP of different sizes. At the light–optical level there were no changes in the aortic wall.

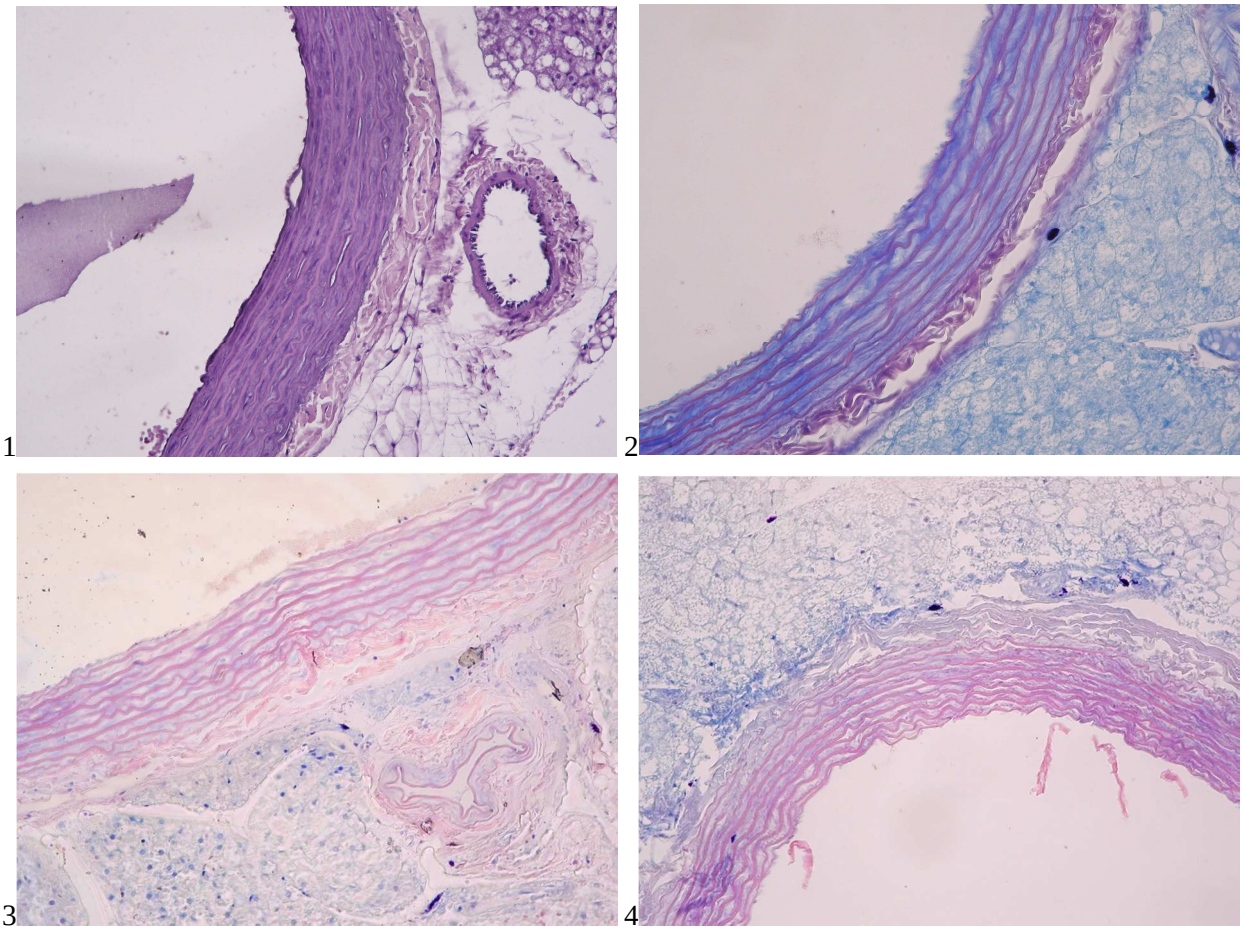


Fig. 4. The rats' aorta after intratracheal administration of lead. Note: 1 – control; 2 – $PbS_{26–34nm}$; 3 – $PbS_{50–80nm}$; 4 – $Pb(NO_3)_2$. H&E (1), azure–eosin (2,3,4). Ob. 20, e.p. 10.

Li Q. has experimentally established that the inhalation effect of PbS NP caused inhibition of the activity of SOD, T–AOC and an increase in the content of MDA in blood serum; both effects were also observed in the lung tissue of rats and were accompanied by a pronounced inflammatory reaction. Therefore, the main mechanism of pulmonary toxicity of PbS NP may be oxidative stress and inflammatory response in lung tissue [11].

According to other authors [4], pathological changes at both cellular and tissue levels during inhalation exposure of mice to PbO NP do not correspond to the concentration of lead in this organ, but to the number of nanoparticles detected in the cells.

In the study of molecular and cellular mechanisms promoting the elimination of nanoparticles variability between target organs was recorded. In particular, it was found that the elimination of ionic lead and PbO NP from the lungs and liver was effective, with lead almost completely eliminated from the lungs, which helped to restore the physiological state of lung tissue [5].

In our experiment we have recorded morphological changes of different intensity of organs resulting from acute intratracheal exposure to PbS NPs of different sizes and $Pb(NO_3)_2$: toxicants had a more pronounced damaging effect on the lungs and myocardium; the most resistant to their influence were the aortic wall tissues. We have not found any morphometrically significant relationship between the size of the studied lead nanoparticles and the severity of their cardiovasotoxic effects, although the histological picture of toxic manifestations is more expressed in the group of NP $PbS_{50–80nm}$.

Conclusion

With a single intratracheal administration of lead cardiovasotoxic effect of $PbS_{26–34\ nm}$ and $PbS_{50–80nm}$ NP was manifested more compared with a significantly milder effect caused by the action of the ionic form of lead – $Pb(NO_3)_2$.

The cardiotoxic effect of lead nanoparticles mainly affected the atrial myocardial cardiomyocytes, and the aortic wall remained almost unaffected. The most pronounced structural changes were observed in the lungs, which may be due to the route of a toxicant administration.

References

1. Aleksijchuk VD, Sokurenko LM, Omelchuk ST. Peculiarities of lead sulfide and nitrate nanoparticles influence on organisms of experimental animals in different research periods and methods of its negative impact correction. World of medicine and biology. 2015; 4 (54): 97–101.
2. Bláhová L, Nováková Z, Večeřa Z, Vrlíková L, Dočekal B, Dumková J et.al. The effects of nano–sized PbO on biomarkers of membrane disruption and DNA damage in a sub–chronic inhalation study on mice. Nanotoxicology 2020; 14(2): 214–231. DOI: 10.1080/17435390.2019.1685696
3. Bostan NB, Rezaee R, Valokala MG, Tsarouhas K, Golokhvast K, Tsatsakis AM et.al. Cardiotoxicity of nanoparticles. Life Sciences. 2016; 165: 91–99. DOI: 10.1016/j.lfs.2016.09.017
4. Dumková J, Smutná T, Vrlíková L, Le Coustumer P, Večeřa Z, Dočekal B et.al. Sub–chronic inhalation of lead oxide nanoparticles revealed their broad distribution and tissue–specific subcellular localization in target organs. Part Fibre Toxicol. 2017; 14(1): 55. DOI: 10.1186/s12989–017–0236–y
5. Dumková J, Smutná T, Vrlíková L, Kotasová H, Dočekal B, Čapka L et.al. Variability in the Clearance of Lead Oxide Nanoparticles Is Associated with Alteration of Specific Membrane Transporters. ACS Nano 2020; 14(3): 3096–3120. https://doi.org/10.1021/acsnano.9b08143
6. Gubar IV, Lavrynenko VE, Chuchrai SM, Savosko SI, Sokurenko LM, Apykhtina OL et.al. Cardiovasotoxic effect of different sizes lead nanoparticles introduction. World of Medicine and Biology. 2020; 2 (72): 146–151. DOI 10.26724/2079–8334–2020–2–72–146–151.
7. Gubar IV, Sokurenko LM, Savosko SI, Apykhtina OL, Yavorosky OP, Chaikovsky YuB Evaluation of protective effect of Thiocetam drug by morphological changes in the heart and vessels after administration of lead nanoparticles of various sizes (experimental study). Reports of Morphology. 2019; 25 (4): 5-19. DOI: 10.31393/morphology-journal-2019-25(4)-01
8. Khan I, Saeed K, Khan I. Nanoparticles: Properties, applications and toxicities. Arabian Journal of Chemistry, 2019; 12(7): 908–931. https://doi.org/10.1016/j.arabjc.2017.05.011
9. Khanna P, Ong C, Bay BH, Baeg GH. Nanotoxicity: an interplay of oxidative stress, inflammation and cell death. Nanomaterials (Basel, Switzerland) 2015; 5: 1163–1180. https://doi.org/10.3390/nano5031163
10. Lebedová J, Nováková Z, Večeřa Z, Buchtová M, Dumková J, Dočekal B et.al. Impact of acute and subchronic inhalation exposure to PbO nanoparticles on mice. Nanotoxicology. 2018; 12(4): 290–304. doi: 10.1080/17435390.2018.1438679.
11. Li Q, Hu X, Bai Y, Alattar M, Ma D, Cao Y et.al. The oxidative damage and inflammatory response induced by lead sulfide nanoparticles in rat lung. Food Chem Toxicol. 2013; 60: 213–217. doi: 10.1016/j.fct.2013.07.046.
12. Oberbek P, Kozikowski P, Czarnecka K, Sobiech P, Jakubiak S, Jankowski T. Inhalation exposure to various nanoparticles in work environment – contextual information and results of measurements. J Nanopart Res. 2019; 21: 222. https://doi.org/10.1007/s11051–019–4651–x
13. Porcari A, Borsella E, Benighaus C, Grieger Kh, Isigonis P, Chakravarty S et.al. From risk perception to risk governance in nanotechnology: a multi–stakeholder study. J Nanopart Res 2019; 21: 245. https://doi.org/10.1007/s11051–019–4689–9
14. Warheit DB. Hazard and risk assessment strategies for nanoparticle exposures: how far have we come in the past 10 years? F1000Res. 2018; 7:376. https:// doi.org/10.12688/f1000research.12691.1.
15. Zhao L, Zhu Y, Chen Z, Xu H, Zhou J, Tang S et.al. Cardiopulmonary effects induced by occupational exposure to titanium dioxide nanoparticles. Nanotoxicology. 2018; 12(2):169–184

Реферати

ОРГАНОТОКСИЧНИЙ ЕФЕКТ ОДНОКРАТНОГО ІНТРАТРАХЕАЛЬНОГО ВВЕДЕННЯ НАНОЧАСТИНОК СВИНЦЮ РІЗНОГО РОЗМІРУ

Губар І.В., Апихтіна О.Л., Камінський Р.Ф., Чайковський Ю.Б., Яворовський О.П., Сокуренко Л.М.

В експерименті вивчався кардіовазотоксичний ефект одноразового інтратрахеального введення наночастинок свинцю різного розміру. Використовували колоїдні розчини сульфіду свинцю (PbS у поліфосфаті натрію) з середнім розміром 26–34 нм та 50–80 нм, а також нітрат свинцю $Pb(NO_3)_2$ в іонній формі, який добре розчинний у воді. Токсичні ефекти оцінювали через 12 днів після впливу. Морфологічні зміни були виявлені в міокарді (більшою мірою в передсердях). Після введення наночастинок $PbS_{26–34nm}$ та $Pb_{50–80nm}$ визначались незначні порушення, такі як збільшений інтерстиційний простір та дистрофічні зміни окремих кардіоміоцитів. Таким чином, при інтратрахеальному введенні свинцю токсичний ефект наночастинок $PbS_{26–34nm}$ та $PbS_{50–80nm}$ виявлявся більшою мірою порівняно з ефектом, спричиненим дією іонної

ОРГАНОТОКСИЧЕСКИЙ ЭФФЕКТ ОДНОКРАТНОГО ИНТРАТРАХЕАЛЬНОГО ВВЕДЕНИЯ НАНОЧАСТИЦ СВИНЦА РАЗНОГО РАЗМЕРА

Губарь И.В., Апыхтина Е.Л., Каминский Р.Ф., Чайковский Ю.Б., Яворовский А.П., Сокуренко Л.М.

В эксперименте изучался кардиовазотоксический эффект однократного интратрахеального введения наночастиц свинца разного размера. Использовали коллоидные растворы сульфида свинца (PbS в полифосфате натрия) со средним размером 26–34 нм и 50–80 нм, а также нитрат свинца $Pb(NO_3)_2$ в ионной форме, хорошо растворимый в воде. Токсические эффекты оценивали через 12 дней после воздействия. Морфологические изменения были обнаружены в миокарде (в большей степени в предсердиях). После введения наночастиц $PbS_{26–34nm}$ и $Pb_{50–80nm}$ определялись незначительные нарушения, такие как увеличенное интерстициальное пространство и дистрофические изменения отдельных кардиомиоцитов. Таким образом, при интратрахеальном введении свинца токсический эффект наночастиц $PbS_{26–34nm}$ и $Pb_{50–80nm}$ был выявлен в большей степени по сравнению с эффектом, вызванным действием

форми свинцю $Pb(NO_3)_2$. Токсичний ефект наночастинок свинцю спостерігався в основному в кардіоміоцитах міокарда передсердь, в той час як стінка аорти залишалася майже інтактною. Найбільш виражені структурні зміни спостерігалися в легенях та бронхах, що може бути обумовлено способом введення токсикантів.

Ключові слова: свинець, наночастинки, інтратрахеальна інтоксикація, морфологічні зміни, міокард, аорта, легені.

Стаття надійшла 25.08.2019 р.

ионной формы свинца $Pb(NO_3)_2$. Токсический эффект наночастиц свинца наблюдался в основном в кардиомиоцитах миокарда предсердий, в то время как стенка аорты оставалась почти интактной. Наиболее выраженные структурные изменения наблюдались в легких и бронхах, что может быть обусловлено способом введения токсикантов.

Ключевые слова: свинец, наночастицы, интратрахеальная интоксикация, морфологические изменения, миокард, аорта, легкие.

Рецензент Єрошенко Г.А.

DOI 10.26724/2079-8334-2020-3-73-175-178
UDC 616.316:615.9:599.323.4

G.A. Yeroshenko, K.V. Shevchenko, O.D. Lisachenko, O.V. Vilhova, O.S. Yakushko, T.A. Skotarenko, V.P. Bilash
Ukrainian Medical Stomatological Academy, Poltava

ULTRASTRUCTURAL REMODELING OF RAT SUBMANDIBULAR GLANDS IN CHRONIC ETHANOL INTOXICATION

e-mail: kvshevchenko2017@gmail.com

The study presents a detailed analysis of the ultramicroscopic structure of the rat submandibular glands in chronic ethanol intoxication at the later stages of the experiment. It has been established that prolonged exposure to ethanol at the later stages of the experiment was characterized by the appearance of signs of adaptive-compensatory responses of the parenchymal elements nd v ss ls f th bl d m r v s ul r s st m w th th m rg n f d str h h ng s nd t s s f du t l th l um; however, no complete regeneration of the structure was detected.

Keywords: ethanol, salivary glands, acini, ducts, rats.

The work is a fragment of the research project "Experimental morphological study of the effect of cryopreserved cord blood products and embriofetoplacental complex (EFPC), diphereline, ethanol and 1 % methacrylate on the morphofunctional condition of several internal organs", state registration No. 0119U102925.

Chronic ethanol intoxication causes multiple alterations in the structure and functions of the oral cavity organs; however, the study was focused on the prevalence and intensity of diseases of the oral mucosa and periodontal diseases. The findings have shown that alcohol consumption is accompanied by salivary dysfunction, as well as the destructive changes in the salivary glands; however, these data are often fragmentary and sometimes ambiguous [6]. Ethyl alcohol, due to its physicochemical properties, is able to easily penetrate through the cell membranes and have both direct and indirect toxic effects, which leads to the matrix and transport dysfunction of membranes and the formation of adaptive changes in long-term effect of ethanol, manifested by elevated cholesterol, thickening of the phospholipid layer and higher membrane density, which in turn is accompanied by alterations in the mode of functioning of enzyme, receptor and immune complexes [2].

Electron microscopic method, used to investigate ultrastructural changes in tissues, has established that at the early stages of the experiment, chronic ethanol intoxication causes significant changes in both parenchymal elements and vessels of the blood microvascular system, which is expressed by intensification of secretion in the acini and increased functional activity of the ductal system; therefore, the study on the effect of ethanol at the late stages enables disclosure of a full picture of restructuring of the submandibular glands during the experiment.

The purpose of the work was to study structural changes in the elements of the rat submandibular glands' lobules in chronic ethanol intoxication at late stages of the experiment.

Materials and methods. 20 outbred albino rats were involved into electron microscopic study. The rodents were administered with 12 mg/kg 40° ethanol 4 times a day directly into the stomach [4]. The animals were killed under 25 mg/kg thiopental anesthesia overdose on day 12 and 30 of the experiment. The fragments of submandibular glands were embedded into epon-812 according to standard procedure [1].

Ultrathin sections were made on the LKB-3 (Sweden) ultramicrotome. Contrast staining of the sections were performed first with 1% uranyl acetate solution in methanol, and then with lead citrate according to Reynolds [1].

The sections were studied in the PEM-125K electron microscope (serial number 38-76, TU 25-07-871-70) at accelerating voltage (50 - 75) kW.