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# CONTENTS

# RATES WEIGHT CHANGE AND STEEL AFFECTIONS BY LEAD ACETATE INTOXICATION

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***Annotation.*** *The study of the effect of lead acetate on embryo morphogenesis was initiated from the analysis of changes in embryo and rat mass. The main method of measurement was the weighing of animals, embryos and the heart. Animals of the control and experimental groups were characterized by habitual social behavior, changes in nutrition, and bowel movements. Changes in the weight of rats that were toxic by lead acetate were analyzed, and a comparative analysis of the incidence of congenital heart defects and morphometric parameters of the embryonic hearts of animals in the control and experimental group of rats was performed. Detection of structural alterations of the embryonic heart exposed to lead acetate during the prenatal ontogeny period. The difference in changes in embryo weight and offspring of rats due to lead acetate was determined, the negative effect of the intoxicant on prenatal and postnatal development of rats was proved.*

*The cardioprotective effect of lycopene and inulin, as well as their restorative function, affecting the weight gain of embryos and rats at all times of the experiment have been investigated and proven.*

***Key words:*** *heart, morphogenesis, lead acetate, toxic effect, inulin, lycopene.*

**Formulation of the problem.** Establishing peculiarities of morphogenesis of organs of different systems in the comparative-embryological aspect in the norm, as well as changes in their structural and functional organization due to the negative impact of the environment is a priority task of modern morphology. Research into the patterns of development of tissues, organs and systems of the human and animal organisms at various stages of ontological and phylogeny, respectively, should play an important role in the development of general questions of biology and medicine. Scientific interest in the effects of anthropogenic factors on the body is caused by significant environmental pollution by heavy metals, with lead and its compounds being the priority toxicant. In the last decades, the industry's demand for lead has increased significantly, leading to irrational use of natural resources and an increase in the level of natural gas.environmental pollution [1]. An unfavorable environmental situation increases the risk of lead entering the human and animal body, and there is a risk of contamination of this heavy metal with food, especially in man-made areas. Lead is a metal with high accumulative toxicity [2].

Experimental studies have identified therapeutic and toxic doses of some substances, but to date there is no information on doses that are teratogenic [3, 4]. One of the urgent tasks of modern embryology and toxicology is to establish the influence of

lead acetate on prenatal development of organs of different systems and morphological preconditions for possible formation of developmental defects [5, 6, 7, 3]. However, the effect of lead acetate on cardiogenesis under experimental conditions has not yet been sufficiently studied. The sources of literature contain reports on the accumulation of lead in the heart [8] and the features of pathobiochemical changes due to acute and chronic lead intoxication, which causes the accumulation of reactive oxygen species and cyclooxygenase-dependent vasoconstrictors, as well as exerts an inhibitory effect on itself, to expressed endothelial dysfunction [9, 10]. Long-term oral administration of lead acetate causes focal ischemia and myocardial damage [11, 8].

**Main results of the study.** The experimental study was performed on laboratory rats, the morphological material of the study were the hearts of embryos at 14, 16 and 18 gestational days and the hearts of rats at 1, 5 and 7 days postnatal development with the action of 2.5% lead acetate solution and with correction of lycopene and inulin.

Observations on pregnant females of the Wistar rats during pregnancy showed the preservation of social and research behavior, grooming, consumption of water and food, reaction to stress factor (urination and deficiency during examination and work of the researcher with animals), bending and grasping reflexes of extremities. Behavioral disorders that would indicate acute toxicity of lead acetate were not detected in the experimental groups of rats. There were also no behavioral changes in the rats treated with lead acetate with lycopene and inulin. At the same time, the weight of the experimental rats (according to the weight monitoring diary) varied over the observation deadline, which did not reach the values of the control group of rats. The main method of measurement was the weighing of animals, embryo and the heart. Animals of the control and experimental groups were characterized by habitual social behavior, changes in diet, defecation, and reflex reactions to the researcher were not recorded. No manifestations of acute intoxication in laboratory rats were detected.

A statistically significant decrease in the weight of the experimental group of rats with lead acetate (1st series of experiment - animals from which received embryos at stages E14, E16 and E18 prenatal development) was found in almost the entire observation period, except 10-12 days, from 7.4% up to 9.2% in the first 9 days of the experiment and from 7.2% to 15.7% on the 13 and 18 days of the experiment ($P \leq 0.05$).

An analysis of the changes in the weight of the study groups of rats treated with lead acetate and the investigational agents - inulin and lycopene - showed the following results. Until the 13th day of the experiment, no statistically significant difference was found between the comparison groups. At 14-18 days of observation, the weight gain of rats in the inulin group was greater than in the lead acetate group. However, this weight of the experiment showed a lower weight gain in the lycopene group compared to the inulin group ($P \leq 0.05$).

The changes in the weight of pregnant rats in the second series of experiments, that is, groups with offspring at the early stage of postnatal development (P1, P5, P7), were statistically significantly smaller than controls.

Long-term use of lead acetate resulted in a decrease in weight gain over the whole

experiment - an average of 13.2% (with a maximum difference of 20.8% at 14 days of experiments, P <0.05). Indicators of the 1st and 2nd series of experiments had no significant difference. No statistically significant difference in the lead acetate group was found in the study drug groups.

Thus, the average weight gain of intact rats was 34.1% (P <0.05), in rats with lead acetate - 19.6% (P <0.05), and lead acetate with the introduction of inulin - 18.7% ( P <0.05), lead acetate with the introduction of lycopene - 14.5% (P <0.05). That is, the mean difference in the weight gain of pregnant females was 17.1% (P <0.05). The rat mass in the comparison groups with lycopene and inulin did not differ from the main group, which showed a negative effect of lead acetate on the metabolism and morphogenesis of pregnant rats.

The next stage of the study was to evaluate changes in the weight of embryos and rats at the prenatal and postnatal stages of development. The mean weight gain of embryos at day 18 compared to day 14 in the control group was 151.7% (P <0.05), in rats with lead acetate - 145.5% (P <0.05), and lead acetate with inulin administration - 168.7% (P <0.05), lead acetate with the introduction of lycopene - 154.8% (P <0.05).

The weight of the embryos in the lead acetate group was statistically significantly lower at all times in the experiment. The indicator in the drug groups approached the values of the control group at 16 and 18 days (P <0.05). These data indicate the delayed prenatal development of rats under the action of lead acetate and the prevention of toxic effect on embryonic morphogenesis with the introduction of inulin and lycopene.

The results of the analysis of the weight of newborn rats and the assessment of the dynamics of growth in the next 7 days postnatal development showed the following results. The toxic effect of lead acetate led to a delay in the weight gain of rats by an average of 17.4% (P <0.05). No significant weight loss was detected in the pharmacocorrectional groups (data were within the statistical error of the intact rat group), which is evidence of a reversible morphogenesis process in early postnatal development.

Before sampling the material for histological examination, the weight of the heart and the ratio of the weight of the heart to the weight of the embryos / rats were further evaluated. The results of the studies are shown in Table 1.

A decrease in the average heart mass was found on the background of a lack of weight gain in rats. The ratio (index) of organ weight to offspring mass was less than the control values only at day 7 postnatal development in the lead acetate group, at days 1 and 7 in the lead and inulin acetate group. The action of inulin and lycopene is indicated by an increase in heart weight.

*Table 1*

**Changes in heart mass in the prenatal and postnatal stages of development**

| Development period | Indicator | Control group | Lead acetate | Lead acetate + inulin | Lead acetate + lycopene |
|---|---|---|---|---|---|
| E18 | Body weight, g | 1,93±0,04 | 1,67±0,05* | 1,90±0,04^ | 1,85±0,03 |
| | Weight of heart, mg | 8,66±0,08 | 7,45±0,16* | 7,96±0,11^ | 7,75±0,10*^ |
| | Weight of heart / body, mg / g | 4,48±0,10 | 4,43±0,21 | 4,45±0,06 | 4,47±0,03 |
| P1 | Body weight, g | 5,73±0,15 | 4,83±0,20* | 5,55±0,24 | 5,51±0,19 |
| | Weight of heart, mg | 23,1±0,45 | 17,15±0,30* | 20,73±0,62*^ | 20,88±0,78*^ |
| | Weight of heart / body, mg / g | 4,05±0,15 | 3,58±0,18 | 3,76±0,14* | 3,81±0,20 |
| P5 | Body weight, g | 7,25±0,14 | 6,20±0,16* | 7,26±0,17^ | 6,98±0,22 |
| | Weight of heart, mg | 43,33±1,02 | 35,83±1,49* | 42,5±1,02^ | 39,66±0,88* |
| | Weight of heart / body, mg / g | 5,98±0,18 | 5,77±0,09 | 5,85±0,12 | 5,70±0,13 |
| P7 | Body weight, g | 9,45±0,19 | 7,96±0,31* | 8,81±0,37* | 9,00±0,36 |
| | Weight of heart, mg | 59,10±0,53 | 45,43±1,21* | 51,73±1,03*^ | 53,38±1,18*^ |
| | Weight of heart / body, mg / g | 6,27±0,18 | 5,73±0,15* | 5,92±0,26* | 5,96±0,16 |

*Note: * - likely to control (P <0.05); ^ - likely in the lead acetate group (P <0.05)*

**Conclusions.** The elucidation of changes in the structural and functional organization of the heart in the process of histo- and organogenesis under the action of lead acetate under the conditions of experiment and the expediency of the development of cardioprotective agents for the treatment of diseases, the etiological factor of which was the influence of technogenic compounds of lead, determined the relevance of this study.

Thus, during 2 series of experiments we found a natural delay in the weight gain of pregnant female rats receiving lead acetate and delayed prenatal and early postnatal development of rats. The inhibition of morphogenesis can be explained by the toxic effect of lead acetate on metabolic processes in the body of pregnant rats, which negatively affected the morphogenesis of embryos. The use of lycopene and inulin as pharmacological agents with detoxifying effect affected the recovery of weight gain at 16 and 18 days prenatal development and postnatal period. It should be noted that the effect of lycopene and inulin did not differ in terms of the weight of embryos and rats, indicating the non-selective effect of the investigated agents. Indices in pregnant females

did not change or increased compared with the main experimental group, and in embryos increased from 16 days and reached control values in postnatal development, which was interpreted as a positive effect of agents on morphogenesis.

The dynamics of changes in the structural organization of the heart of rats under the influence of lead acetate at the stages of prenatal and postnatal development were first established. A regular delay in the recruitment of pregnant female rats, embryos and newborn rats under chronic intoxication with lead acetate was detected.

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