

## Myocardium contractility: effects of subchronic lead intoxication in rats

A moderate subchronic lead intoxication was observed in outbred male rats after repeated intraperitoneal injections of lead acetate during 5 weeks. Half of so exposed and control rats were given a calcium preparation with fodder. The next day after the last injection the heart of each animal was excised, then the trabeculae, papillary muscles and tissue (for myosin extraction) from the right ventricle were used for *in vitro* investigations. Many of the indices describing the condition of the rat's organism toward the end of the subchronic exposure to lead were different from the corresponding control values. Some of them are regarded to be lead-specific effects.

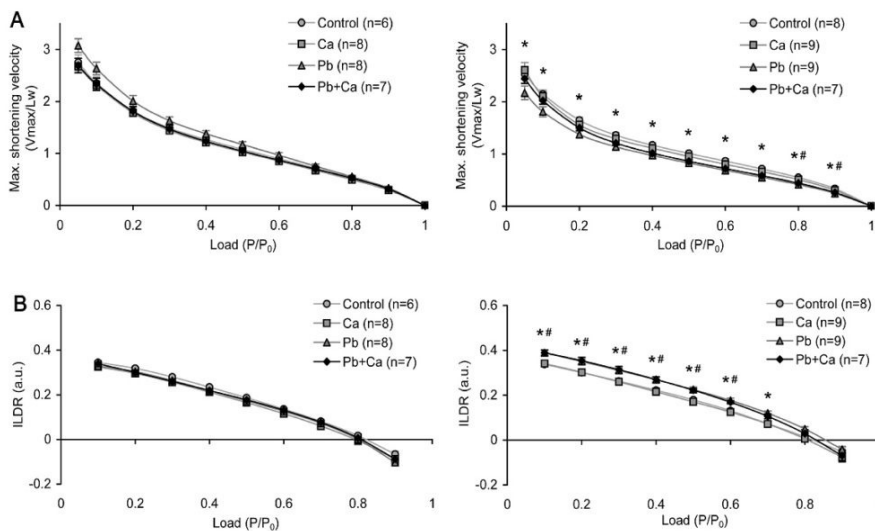


Fig. 1. (A) The relationships between the maximal velocity of isotonic shortening normalized to muscle length ( $V_{MAX}/L_W$ ,  $L_W$  – working muscle length) and the afterload ( $P/P_0$ ) obtained for right ventricular trabeculae (left) and papillary muscles (right) of rats in all experimental groups. (B) The relations of the index of load-dependent relaxation (ILDR) on afterload ( $P/P_0$ ) obtained for the ventricular trabeculae (left) and papillary muscles (right) of rats from all experimental groups. \* – differences between the control and Pb groups.

Using isolated preparations of trabeculae and papillary muscles we have shown that changes in lead-treated rats in most of the basic characteristics of isometric and afterload contraction-relaxation cycles are more pronounced for papillary muscles compared with trabeculae. Maximal rates of isotonic shortening for all afterloads in the papillary muscle are lower in the lead-exposed group (Fig.1A), and maximal velocity of papillary muscle shortening was  $2.69 \pm 0.19$  (units  $V_{max}/L_w$ ) comparing with  $3.05 \pm 0.15$  for control group and  $3.03 \pm 0.13$  for Pb+Ca group. This decrease is consistent with data obtained in an *in vitro* motility assay, where the maximum velocity of unloaded movement of regulated filaments along myosin was considerably lower for the lead-treated rats ( $1.5 \pm 0.2$   $\mu\text{m/s}$ ) comparing with the control ones ( $2.0 \pm 0.25$   $\mu\text{m/s}$ ).

Under subchronic lead intoxication, a reduction in the velocity of both the thin filament and the velocities of isotonic shortening correlates with a shift in the expression of isomyosins towards slower V3 isomyosin as revealed by gel electrophoresis. Thus, in this group  $\beta$ -chains constituted  $45 \pm 8\%$  and control value was  $15 \pm 4\%$ . This shift is an energy-saving mechanism contributing to the adaptation of the cardiac muscle to deterioration of its functioning. The persistence of the peak force of isometric contractions in the lead-exposed group compared with the control one can be explained by the fact that V1 and V3 rat isomyosins develop an equal isometric force. Therefore, no changes in the efficiency of the contractile apparatus estimated by the work produced by muscles over the entire range of afterloads were discovered in both kinds of cardiac muscle preparations. At the same time, an increase in the index of load dependence relaxation in the papillary muscle preparations of lead-treated rats in the wide range of afterloads (Fig. 1B), points to a reduced ability of these muscles to adapt to dynamic conditions of mechanical loading.

Noteworthy is that the myocardial trabecules and papillary muscles of lead-treated rats are characterized by lower rates of both isometric tension development and of relaxation compared with the preparations from the other groups of rats over the entire range of length as shown in Figure 2A drop in the passive (diastolic) mechanical tension in trabecules takes place, which can be explained by their possible hypertrophy since myocardial hypertrophy seems to enhance stiffness.

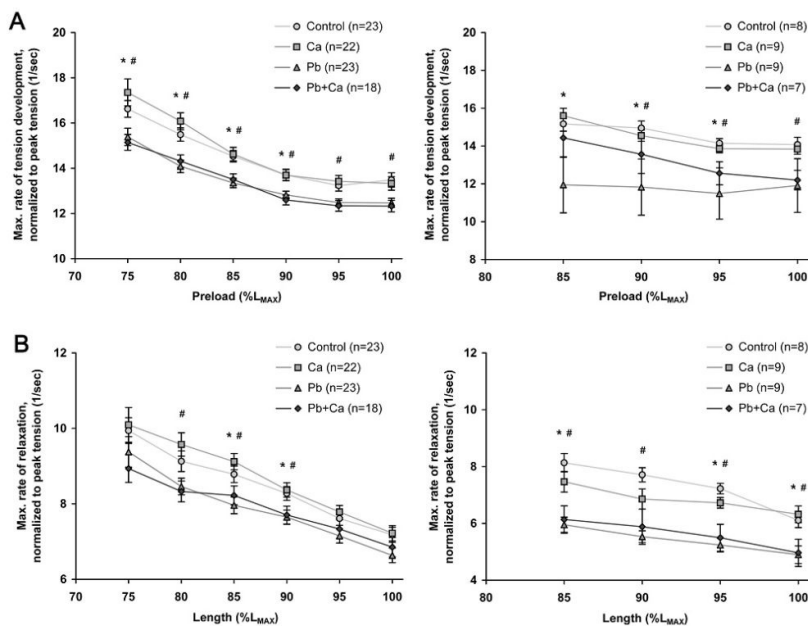


Fig. 2. (A) Averaged curves for the maximum rate of isometric tension development normalized to peak tension as a function of length, obtained for steady-state isometric contractions of right ventricular trabecules (left) and papillary muscles (right) from male rats of the control group and three exposed groups. (B) Averaged curves for the maximum rate of isometric relaxation normalized to peak tension as a function of length, obtained for steady-state isometric contractions of right ventricular trabecules (left) and papillary muscles (right). \* – differences between the control groups and Pb groups.

All these effects suggest impaired contractility of the cardiac muscle due to the subchronic lead intoxication. In the same time, a calcium-containing supplement has been shown to produce a moderate protective effect on both organism-level lead intoxication and related changes in rat myocardium.

*Yuri L. Protsenko, Larisa V. Nikitina, Svetlana V. Klinova, Oksana P. Gerzen, Boris A. Katsnelson  
Institute of Immunology and Physiology of the Ural Branch of the Russian Academy of Sciences,  
Ekaterinburg, Russia*

## **Publications**

### [Effects of subchronic lead intoxication of rats on the myocardium contractility.](#)

Protsenko YL, Katsnelson BA, Klinova SV, Lookin ON, Balakin AA, Nikitina LV, Gerzen OP, Minigalieva IA, Privalova LI, Gurchich VB, Sutunkova MP, Katsnelson LB  
*Food Chem Toxicol. 2018 Oct*

### [Further analysis of rat myocardium contractility changes associated with a subchronic lead intoxication.](#)

Protsenko YL, Katsnelson BA, Klinova SV, Lookin ON, Balakin AA, Nikitina LV, Gerzen OP, Nabiev SR, Minigalieva IA, Privalova LI, Gurchich VB, Sutunkova MP, Katsnelson LB  
*Food Chem Toxicol. 2019 Mar*