CHANGES OF MOUSE BONE-MARROW CELLS AFTER SINGLE MANGANESE INTRODUCTION

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The uncommonly high and the insufficient manganese content in the organism is related to abnormalities of the activity of various systems. Manganese compounds, similarly to those of other metals, damage the biological defence against exogenic toxins (6). It is established that some metals and their compounds amid which is also MnCl₂ strengthen the effect of different mutagenic factors (7). Our previous investigations of the action of another heavy metal, namely mercury, showed HgCl₂ inhibitory influence on blast cell and mitotic activity of rat bone-marrow cells in conditions of an acute (2) and subchronic (1) intoxication.

Manganese compounds are used in numerous industrial processes; therefore, manganese appears to be a leading noxa in the corresponding branches. The increase of the number of workers in occupational contact with manganese necessitates the clarifying of all the aspects of manganese effect on organism.

The purpose of our work was to study MnCl₂ influence upon mouse bone-marrow cells in conditions of an acute poisoning with this compound. That is why we studied blast cell and mitotic activity and blast cell nucleolus count.

Material and Methods

Our study covered 31 experimental and 15 control mature male mice of Swiss breed with average weight of 17.6 g. Its deviation in both directions did not exceed 5 per cent of this value. This fact enabled us to apply one and the same dosage of the product introduced. All the experimental animals were administered 3.3 mg MnCl₂ diluted in 0.1 ml saline each by single s.c. injection. The dosis applied was LD₅₀ for mice of this compound amounting to 187 mg/kg b.w. (3). The control animals were injected by the same way the same quantity of saline. On the day of manganese chloride introduction designated as zero-day as well as on the 1st, 3rd, 8th and 11th day after injection three animals of the experimental and control series each were killed by decapitation under ether narcosis and processed for investigation. These days for killing the animals were selected on the basis of the observation that with most heavy metals most active adaptation changes were established during the first 15 days after intoxication (4).

Preparations were routinely elaborated from materials taken from femoral and tibial bone marrow (5). However, hypotonic processing was carried out by using of 0.56 M solution of potassium chloride instead of sodium citrate. Both blast cell index (BI) and mitotic index (MI) were read on these preparations according to generally accepted methods — as percentage frequency of blast and dividing cells, respectively. Separately, blast cells were read according to their nucleolus count.

Results and Discussion

Control animals' BI demonstrates a slightly expressed temporal tendency towards increase without any modulations (fig. 1). As the difference between its minimal (on the zero-day) and maximal (on the 11th day) rate does not exceed 2 per cent its level in control animals can be
considered practically constant. However, the finding with experimental animals is rather different: the values are many times higher than those of the controls when every single day of the trial is concerned. Besides BI curve in experimental animals is strongly modulated during the period of investigation showing well-expressed peaks on the 3rd and 11th day after toxic product introduction.

![Graph](image-url)

**Fig. 1.** Dynamics of the changes in the percentages of mitotic (MI) and blastic (BI) cells in experimental and control animals.

1 - BI experimental; 2 - BI control; 3 - MI experimental; 4 - MI control; * - dyed animals

Immediately after product introduction, on the zero-day and on the 1st day, MI is higher in control than in experimental animals. Between the 1st and the 3rd day both levels cross over but on the 3rd, 8th and 11th day experimental animals demonstrate a higher mitotic activity as compared with controls.

Comparisons between two indexes reveal not only a definite parallelism but also essential differences between them. Both mitotic and blastic activity are higher in experimental animals reaching maximal levels on the 3rd and 11th day. This fact can be interpreted as manifestation of mobilization of bone marrow immune and haemopoietic functions thus reacting against intoxication. However, while blastic activity increase is very great and sets in immediately after agent's introduction mitotic activity one is less expressed and sets in after overcoming of a considerable reduction during the first two days. This different dynamics of the two indexes can be considered manifestation of greater vulnerability of mitotic apparatus to exogenic and toxic influences inclusive.

In our previous investigation of the acute HgCl₂ poisoning in rats (2) we found out a certain discrepancy between the higher BI and the low MI. We assumed that there was a certain inadequacy of blast cells or inhibition of transition to mitosis.
There are two observations from the present trial which seem unexplainable at present, namely: the considerably higher BI level in experimental animals still on the day of product introduction as well as the significant MI modulations in control animals and especially the reduction on the 3rd day. Various factors can be taken into consideration being the reasons for these two observations, the artificial character of the differences related to the small number of animals studied inclusive. We hope that investigation enlargement will provide data capable to reduce the size of these modulations or even help to explain them adequately.

The results from the study of blast cell nucleolus count are presented on table 1. Experimental animals show a higher frequency of blast cells without nucleolus, with 1 and 2 nucleoli but a lower one of those cells with 3 and even more nucleoli as compared with that of the controls. Both differences are strongly statistically significant and argue for undoubted nucleolus formation inhibition. Even if with some reservation, this observation enables us to presume a similar effect on protein synthesis, too. On the other hand, even if lower than these of the corresponding controls, frequencies of cells with more than 3 nucleoli tend to increase during the experiment. This indicates that definite compensatory mechanisms are involved here, too. Naturally, we always pay attention to the fact that the study is carried out on 50 per cent of the experimental animals survived the intoxication, i.e. exactly on these individuals which demonstrate the most effective compensatory mechanisms.

Our former results show that single manganese introduction induces changes of both mitotic and blastic activity and of nucleolus formation. Therefore, enlargement and profounding of investigation will aim the specifying of their extent and the clarifying of some of their mechanisms.

**References**

ИЗМЕНЕНИЯ В КОСТНОМОЗГОВЫХ КЛЕТКАХ МЫШЕЙ ПОСЛЕ ОДНОКРАТНОГО ВВЕДЕНИЯ МАРГАНЦА

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РЕЗЮМЕ

Увеличение числа рабочих, находившихся в профессиональном контакте с марганцем, а также его превращение в ведущий вредный фактор в ряде отраслей, делают необходимым исследование действия этого металла на организм. После однократного введения MnCl₂ в количестве LD₅₀ лабораторным животным установлено подавление образования ядрышек и повышение бластной и митотической активности. Повышение бластной активности происходит раньше и более значительно, а повышение митотической активности — позже и более умеренно. Очевидно повышение этих двух показателей является выражением иммунных и гемопоэтических функций костного мозга, а разницу между ними можно объяснить большей способностью митотического аппарата попадать под влияние токсических воздействий.