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DISTRIBUTON OF TRACE ELEMENTS IN ORGANS OF MICE OF DIFFERENT INBRED STRAINS

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In eight organ systems of five different inbred strains of mice the concentrations of rubidium, zinc and iron were investigated. In the case of rubidium two of the inbred strains showed relatively low concentrations in all organ systems, whereas zinc and iron exhibited a rather irregular distribution within the eight organ systems. The differences in concentrations found in the various organs of the five inbred strains – especially the distribution pattern of rubidium – may allow further genetic experiments and thus help to elucidate the physiology and pathology of trace elements.

Introduction

Essential trace elements in different organ systems often show a wide spectrum of function within the narrow limits of their concentration. Deviations from the normal concentrations often signal disease.[1,2] Some hereditary diseases are known to be accompanied by changes of trace element concentrations.[3,4] For instance the hepatolenticular degeneration in Wilson's disease, a rare recessive ailments, shows high concentrations of copper in the extrapyramidal system of the brain, liver and cornea, due to a deficiency of the copper transporting protein, coeruloplasmin.[4]

On the other hand, exposure to unphysiological high doses of trace elements may cause toxic reactions, also depending on the individual hereditary state. Thus, TAYLOR et al. found that the resistance to cadmium-induced testicular damage in mice was genetically controlled.[5]

In order to obtain more information about the genetic control of trace element concentrations, we measured the concentrations of Zn, Fe and Rb in different organs of 5 different inbred strain of mice.

Material and methods

Five inbred strains ($F \approx 130$ generations) of mice from the Jackson Laboratory, Bar Harbor, Maine (USA), were used: C57L/J (strain I), BALB/cJ (strain II), DBA/2J (strain III), AKR/J (strain IV) and C57BL/6J (strain V).

The mice were 6 to 8 weeks old and kept under identical conditions. Five male mice were investigated from each of the 5 strains.

The mice were decapitated in ether anesthesia and the blood was collected as far as possible.

The brain, heart, spleen, liver, kidneys, testes and mesenteric lymph nodes were excised, washed with bidestilled water and sealed in quartz tubes.

The concentration of Zn, Fe and Rb per gram dry weight was determined in each organ per mouse by the aid of instrumental neutron activation analysis.[6] The significances of the results were calculated according to the Student test and differences accepted to be significant with p-values lower than 0.01.

Results

Zinc

The concentration of Zn in the different organ systems of the 5 inbred streams is presented in Fig. 1; concentrations range from about 20 μg Zn/g dry weight in the blood to about 125 μg/g dry weight in the testes. In the brain, heart, spleen, liver and kidneys concentrations of about 75 μg Zn/g dry weight are found. With the exception of the liver and the mesenterical lymph nodes, the differences in Zn concentration between the 5 inbred strain are not significant.

The liver of strain III has a significantly higher Zn concentration than the livers of the other strain ($p = 0.0005$); however mesenteric lymph nodes of this strain have a significantly lower Zn concentration than those of the other strain with the exception of strain IV, from which only the mesenterical lymph nodes of 2 mice could be measured.

Iron

Of the three trace elements measured, iron shows the greatest range of concentrations between the different organ systems (Fig. 2). For this reason the graph is drawn semilogarithmically. As expected, the highest concentration of about 3.300 μg Fe/g dry weight is found in the blood; the brain, lymph nodes and testes have the lowest concentrations of about 100 μg Fe/g dry weight. Whereas there are only small differences in the Fe concentration of the blood and brains between the dif-

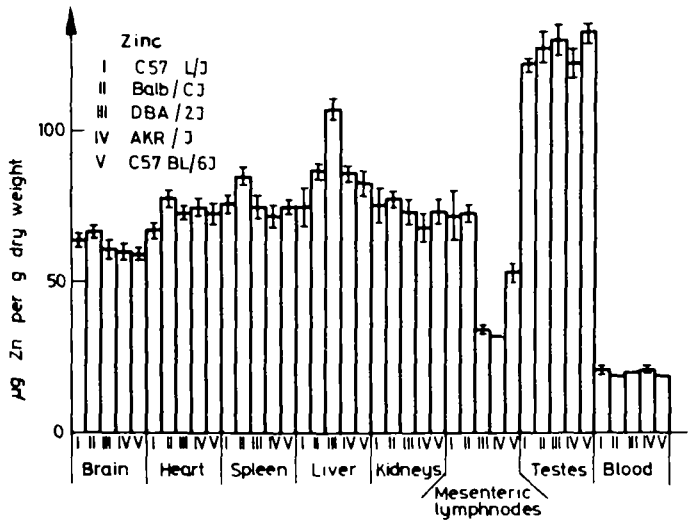

Fig. 1. Zinc concentration of 8 organ systems of 5 inbred strains. The height of the columns represents mean values. Standard error is listed when the number of aliquots exceeds 3

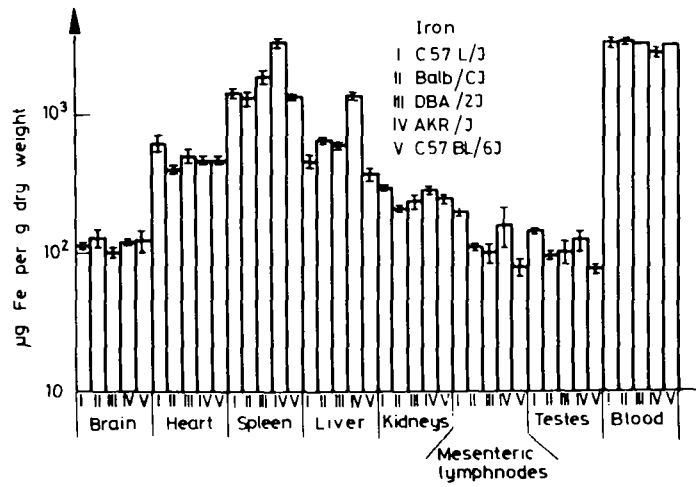

Fig. 2. Iron concentration of 8 organ systems of 5 inbred strains. The height of the columns represents mean values. Standard error is listed when the number of aliquots exceeds 3

ferent strains, in the other organ systems, significant differences for the 5 inbred strains are apparent.

For instance the iron concentration of strain IV in the liver is 2–3 fold higher than in the livers of the other strains. Also the other measured organ systems of the so called reticulo-endothelial system (RES), namely the spleen and the mesenteric lymph nodes, of strain IV show higher iron concentration than the other strains, except for the mesenteric lymph nodes of strain I.

Rubidium

Rb is the only trace element investigated which shows a strain dependent distribution pattern for all systems (Fig. 3). The Rb concentration is all organ systems in stream I, II and V is from about 30 to 60% higher than in strain III and IV. The p-factor for these differences is usually 0.0005.

Discussion

Zinc

Zn is a component of a large number of enzymes.[7] Great changes in Zn concentrations, if they are genetically determined, would be linked to alterations of enzyme distribution and should only be detectable if several of the Zn containing enzymes are diminished or increased at the same time. This, however, should lead to drastic disturbances of the normal physiological state of the animals; such manifestations were not observed. Therefore it is not surprising that the Zn concentrations found in most organ systems are rather uniform for the five strains. We have no explanation for the in strains III isolated significantly higher concentration of Zn in the liver and the lower concentration of Zn in the mesenterical lymph nodes.

Iron

Infections or neoplastic diseases may activate the RES and lead to an iron accumulation in organs of this system.

It is rather improbable that the higher iron concentration found in the liver, spleen and mesenteric lymph nodes of strain IV is caused by an infection because an infection would likely have affected the animals of all strains since they were kept under identical conditions.

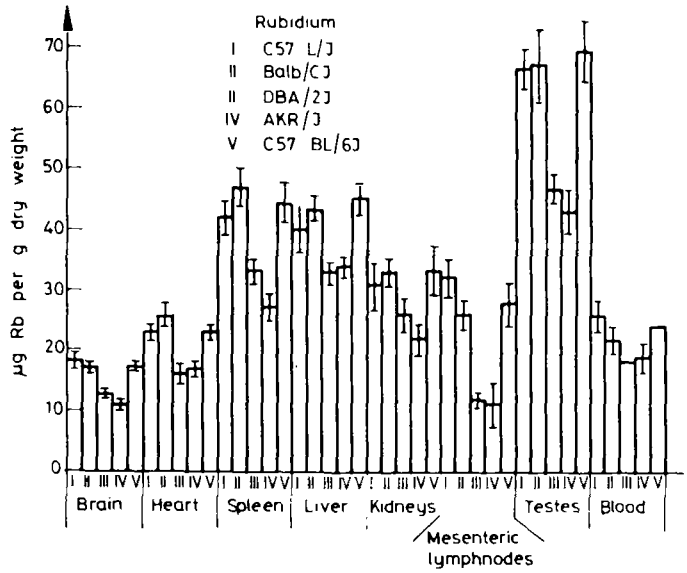

Fig. 3. Rubidium concentration of 8 organ systems of 5 inbred strains. The height of the columns represents mean values. Standard error is listed when the number of aliquots exceeds 3

There might be a connection between the high Fe concentration in the organs containing the RES and the very high spontaneous rate of leukemia for strain IV. This leukemia occurs at rather young age and decreases the life span of the mice of this strain to less than 1/2 of the others.[8]

Rubidium

Until now it was not possible to unequivocally demonstrate the essentiality of Rb; however, recent results show that Rb may be counted among the essential elements.[9,10]

The strain dependent concentration differences of Rb suggest that the Rb concentration is genetically controlled and cannot be explained by different nutritional or other environmental conditions. Further hybridization experiments should help in deciding if Rb concentrations are under genetic control and may help to elucidate the physiological and pathological role of Rb and certify the essentiality of Rb. Additional experiments should also show that the differences in Rb concentrations are not caused by differences of other elements like potassium, which seems to compete with Rb.

Until now mostly immunological or biochemical parameters such as enzyme deficiencies are used for genetic mapping. It might be possible to broaden the tools of genetic analysis

by trace element studies and at the same time make it possible to learn more about the function and trace elements pathology. Genetically caused pathological differences are known between the mice strains investigated in this study. For example, unlike the other strains, strain III and IV which show low Rb concentrations, both have a higher rate of spontaneous leukemia than the other strains. Moreover, high iron concentrations are observed in liver, mesenteric lymph nodes and spleen of strain IV, which may be due to the early appearance of spontaneous leukemia that occurs in this strain at a higher rate than in strain III.[8]

Conclusions

During the last decade there is an increasing evidence for trace element changes be ing associated with disease. Nevertheless, the complexity of manifestations caused by deficiences or toxic concentrations of trace elements is little understood.

Genetic studies may help to get more insight into the normal role and pathology of trace elements.

It is evident from our experiments that there is a genetically controlled distribution of trace elements in various organs. The distribution pattern found for Rb will be especially helpful for further research of the physiology and pathology of trace elements

References

1. W. KEIDERLING, H. R. SCHARPF, Münch. Med. Wschr., 95 (1953) 437.
2. R. J. SHAMBERGER, E. RUKENOVA, A. K. LONGFIELD, S. A. TYTKO, S. DEODHAR, C. E. WILLIS, J. Natl. Cancer Inst., 50 (1973) 863.
3. I. LOMBECK, H. G. SCHNIPPERING, K. KASPEREK, F. RITZL, H. KÄSTNER, L. E. FEINENDEGEN, H. J. BREMER, Z. Kinderheilk., 120 (1975) 181.
4. G. HENKE, H. MÖLLMANN, W. ALTHOFF, Klin. Wschr., 49 (1971) 284.
5. B. A. TAYLOR, H. J. HEINIGER, H. MEIER, Proc. Soc. Exp. Biol. Med., 143 (1973) 629.
6. K. KASPEREK, Proc. 2nd Intern. Conf. on Nuclear Methods in Environ. Res. Univ. Missouri, Columbia, July, 1974.
7. A. S. PRASAD, in Zinc Metabolism, Charles C Thomas Publisher, Springfield, Illinois, USA, 1966.
8. E. L. GREEN, Handbook on Genetically Standardized Jax Mice, 2nd ed., The Jackson Laboratory, Bar Barbor, Maine, USA, 1975.
9. A. HÖCK, U. DEMMEL, H. SCHICHA, K. KASPEREK, L. E. FEINENDEGEN, Brain, 98 (1975) 49.
10. H. SCHICHA, W. MÜLLER, K. KASPEREK, R. SCHRÖDER, Beitr. Path., 151 (1974) 281.