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GRANT NO: OH-00349-02

TITLE: Vanadium Toxicity: A Study of Mechanisms

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PROGRESS REPORT

Objectives

The central hypothesis of the investigation is that toxic amounts of vanadium produce ill effects by interferring with the normal, biological utilization of chromium. The initial goal of the investigation was the production of marginal chromium deficiency in rats by dietary manipulation. Following this production, small amounts of vanadium compounds were to be added to the drinking water of the animals and the effects of this addition studied.

Experiments

As summarized on the report of last year, supplementation of rats fed a diet thought to be deficient in chromium with 5 μg Cr/ml of drinking water, produced no increase in the metabolism of glucose. These results were surprising as published reports have shown that amount of supplementation to be adequate.

Because the experimental conditions (1) were thought to be more severe than those used by other investigators, the experiment was repeated using a supplement of 10 μg Cr/ml drinking water. It was thought that 5 μg Cr/ml may have been an insufficient supplement when in addition to control of diet and water, the quality of the air in the animal room was also controlled.

The first measurement of cholesterol in plasma was done on the 134th day of the experiment. No difference was demonstrable between the group supplemented with chromium and the control group, the group

supplemented with vanadium (5 μg V/ml water) and the control group or the groups supplemented with chromium and vanadium.

The first measurement of glucose tolerance was done on the 155th day of the experiment. The group supplemented with chromium was significantly different from the other groups. Because it appeared as if only some of the animals in that group had responded to the supplement with an increased ability to metabolize glucose, it was decided to repeat the glucose tolerance tests in a few months. Measurement of plasma cholesterol showed no difference between the group supplemented with chromium and the control group on the 182nd day.

These latter measurements were done as I was leaving the Kettering Laboratory to join the staff of the USDA Human Nutrition Laboratory in Grand Forks, North Dakota. The experiment was discussed with Dr. Sandstead, the Director of the Human Nutrition Laboratory, Dr. Stevens of NIOSH and Dr. Foulkes of the Kettering Laboratory. Excellent cooperation of all parties made the shipment of the animals to Grand Forks possible so the experiment could be continued with the support of the Department of Agriculture.

The animals were shipped to Grand Forks on October 10, 1972, the 204th day of the experiment. Unfortunately they did not tolerate the trip as well as was hoped, but they are being maintained under experimental conditions identical to those at Kettering Laboratory except for the atmospheric control. This latter precaution is considered unnecessary in Grand Forks.

Personnel have been trained to make diets, care for the animals and to measure cholesterol and glucose tolerance with small blood samples.

These measurements will be repeated in the near future after the 300th day of the experiment.

Conclusions

Current data from these experiments are at variance with other published work, suggesting that only under certain circumstances do exposures to vanadium and chromium cause changes in the metabolism of cholesterol. If this conclusion withstands the trial of further experimentation, the experimental approach upon which this proposal was based is probably not appropriate for the study of vanadium intoxication in industrial settings. The utility of this approach in studies on the pathogenesis of athersclerotic heart disease has probably been enhanced by these results, however. Work on this problem will be continued at the USDA Human Nutrition Laboratory.

References

1. Klevay, L.M., H.G. Petering, and K.L. Stemmer. A Controlled Environment for Trace Metal Experiments on Animals, Environmental Science and Technology 5:1196-1199, 1971.

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15. Supplementary Notes

16. Abstract (Limit: 200 words) The purpose of the investigation was to produce marginal chromium (7440473) deficiencies in rats through manipulation of their diets. After this deficiency was produced, small amounts of vanadium (7440622) compounds were added to the drinking water of the animals and the effects of this addition were studied. One group of rats were fed a diet deficient in chromium with 5 micrograms of chromium/milliliter drinking water. No increase was noted in the glucose metabolism on this diet. A second group received 10 micrograms chromium/milliliter drinking water. No differences were noted between the group supplemented with chromium and the control group, or the group supplemented with vanadium at 5 micrograms vanadium/milliliter water and the control group or the groups supplemented with chromium and vanadium, concerning measurements of cholesterol in plasma. The findings were at variance with other published reports and indicated that only under certain circumstances did exposure to vanadium and chromium cause changes in the metabolism of cholesterol. The author suggests that this experimental approach is probably not appropriate for the study of vanadium intoxication in industrial settings. However, this approach may be useful in studies on the pathogenesis of atherosclerotic heart disease.

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