

1937

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Recommended Citation

Sutton, W. R. and Nelson, Victor E. (1937) "Growth, Reproduction, and Blood Changes Produced in Rats by Means of Zinc Carbonate," *Proceedings of the Iowa Academy of Science*, 44(1), 117-121.

Available at: <https://scholarworks.uni.edu/pias/vol44/iss1/25>

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GROWTH, REPRODUCTION, AND BLOOD CHANGES
PRODUCED IN RATS BY MEANS OF ZINC
CARBONATE

W. R. SUTTON AND VICTOR E. NELSON

The literature bearing on the toxicity of zinc to the animal body is very confused. D'Amore, Falcone, and Marmaldi (1) fed zinc oxide to dogs; they called attention to the loss of appetite and the weak condition of their animals with the further observation that the blood color and the number of red cells were greatly diminished. During the last days of the poisoning, the white cells markedly increased. Urine of the dogs was diminished in volume and contained casts and albumin. Lehmann (2) fed zinc carbonate to dogs for eleven months with no evidence of poisoning. Batchelor, Fehnel, Thompson, and Drinker (3) observed no anemia from administration of zinc. More recent studies have been made by Heller and Burke (4) and Myers, Beard and Broda (5). The latter investigators (5) fed adult rats zinc chloride to the extent of one per cent of zinc and observed that, while the body weight remained constant, the hemoglobin was reduced from 14.3 to 11.1 grams per cent; but the red cells did not change in number. Myers and Beard (6) also found, when zinc chloride was used to supplement iron chloride in blood regeneration, that more than one-tenth of a milligram of zinc daily prolonged the time necessary for the blood to be restored to normal. Keil and Nelson (7) fed two-tenths of a milligram of zinc as zinc chloride daily to rats, without any effect upon the rate of development of anemia.

EXPERIMENTAL

For this investigation young rats weighing between 40 and 50 grams were placed in groups of five, three females and two males, in screen bottom cages. Food and water were supplied ad libitum. Zinc carbonate was incorporated in the growing ration at three levels corresponding to 0.10, 0.50, and one per cent of zinc. The growing ration is composed of a mixture of naturally occurring foods and has served this laboratory well, during many years, for the growth and reproduction of rats. C. P. zinc carbonate was used, which contained as a maximum the following impurities:—

arsenic 0.000 per cent, chloride 0.002 per cent, iron 0.01 per cent, lead 0.002 per cent, nitrate 0.000 per cent, and sulphate 0.01 per cent. Hemoglobin was determined by the Newcomer method.

Growth of the animals was normal on the rations containing 0.10 and 0.50 per cent of zinc. The animals were vigorous when the experiment terminated, and there was practically no difference in the weight of the rats receiving zinc and those receiving the stock diet. The limit of tolerance of the animals to zinc carbonate lies between 0.50 and one per cent of zinc in the diet. The animals on the one per cent zinc diet failed to grow normally in all cases, although some individuals weighed 140 to 160 grams after ten to twelve weeks on this level. Some of the animals began dying within four weeks after being placed on this diet. If not removed at once from the cage, they were usually partly eaten.

Reproduction on the lowest level of zinc intake was normal. The young were healthy and grew normally. Several generations of these rats continued on the same zinc diet have shown no abnormalities. Reproduction was markedly affected when the animals received 0.50 per cent of zinc in the diet. The females on this diet became pregnant between the fourteenth and seventeenth weeks. One female which had given birth to three young lost thirty grams at parturition. Another female had three young (one born dead) and lost forty grams in weight at parturition. Another female when observed had five dead young in the cage. The young were fully matured but appeared white and bloodless. The total weight of the five stillborn young was twenty-four grams. The females with the live young mothered them satisfactorily. The young weighed almost thirty grams at twenty-one days of age. The original females again mated when returned to their cages. The young that were born were dead in every case. No live young were born after the first pregnancy to any of these females. A total of twenty-three stillborn rats were counted and others were undoubtedly missed, having been consumed by the mothers. The females on 0.50 per cent zinc ceased to become visibly pregnant after five months on the ration, although their weights and outward appearances were normal. No reproduction occurred on the one per cent zinc level.

Table I gives hemoglobin and red blood cell counts on the various levels of zinc intake.

Normal hemoglobin values were found in the group of rats receiving 0.10 per cent of zinc after thirty-nine weeks on this diet.

Table I—The Effect of Zinc Carbonate on Hemoglobin and Red Cells of Rat Blood

Lot No.	Zinc Intake percentage	Initial HHb Gms. Per 100 cc.	Final HHb Gms. Per 100 cc.	Initial R. B. C. Millions Per Cu. mm.	Final R. B. C. Millions Per Cu. mm.	Weeks on Ration
1	0.10	14.5	14.7	8.4	9.1	39
2	0.50	13.9	10.2	8.6	8.5	39
3	1.00	14.2	6.1	8.5	6.6	12-16
4	1.00	13.6	6.5	7.8	6.5	10-16
5	1.00	13.7	6.8	8.0	6.8	12-16
6	1.00	13.5	7.8	8.1	5.8	10
7	0.00	14.1	14.1	7.8	8.9	34
8	0.00	14.6	15.1	30

That there was something organically wrong with the animals on the 0.50 per cent zinc level was first made evident from observations on their reproductive behavior. At the age of initial reproduction of these females the hemoglobin values were only slightly lower than those of the control group. They were still within the limits given by some investigators as normal. As the observation of hemoglobin was continued, it became evident that the rats, as they were kept longer on the ration, became anemic. An average value of 10.2 grams per cent was found after thirty weeks. No change in the number of R. B. C. was observed. Both hemoglobin and red blood corpuscles were diminished on the one per cent zinc diet. Hemoglobin values in this lot usually started to decrease after three to five weeks on the ration. Low values of four grams per cent were sometimes observed. A striking thing in this study was the fact that no correlation between the hemoglobin value and the apparent state of well being of the rat could be found. Rats often lived for five weeks with hemoglobin values below six grams per cent, while others succumbed with the hemoglobin only slightly below normal. The blood cell picture of the animals on one per cent of zinc was interesting. Although the red cells became irregular in size and shape within five weeks after being placed on this diet, the number was not appreciably diminished until after eight to ten weeks on this regime. There was apparently an excess of white and immature red blood corpuscles in every case.

Table II illustrates the change in hemoglobin that occurs in normal animals during pregnancy.

The hemoglobin values are for females receiving the basal diet used in all of the experiments. These observations were made in the study on normal hemoglobin values and are inserted in order to show the anemia that develops in pregnancy. It is possible that

Table II—Hemoglobin of Normal Adult Female Rats

Rat No.	One Week Before Birth of Young	Day Before Birth of Young	At Birth of Young	Week After Birth of Young
1	14.0	12.6	12.0	14.4
2	14.7	13.0	13.0	14.5
3	14.6	11.0	10.0	12.0
4	14.4	12.0	12.5	13.2
5	15.4	12.0	11.4	13.5
6	14.0	13.5	13.6	17.0
7	14.2	12.5	12.5	13.9
8	15.4	14.4	12.8	15.0
Ave.	14.6	12.6	12.2	14.2

this normal anemic condition is so increased by zinc, when ingested at a 0.50 per cent level, that normal reproduction is impossible, although growth is not impaired.

The symptoms of zinc carbonate poisoning disappear when the salt is removed from the diet. Hemoglobin and reproduction became normal in the animals on 0.50 per cent zinc, when the salt was removed from the ration. The same is true of the hemoglobin of rats on one per cent zinc; whether reproduction is permanently impaired on the highest level of zinc is not known.

SUMMARY

Data are given to show that zinc in the form of carbonate is poisonous to rats at levels of 0.50 to one per cent of metal in the diet.

Zinc in a concentration of 0.10 per cent in the diet does not seem to materially influence growth, reproduction, or the normal blood picture of rats.

Reproduction in rats is markedly affected when 0.50 per cent zinc as carbonate is present in the diet. No reproduction occurred in the rats receiving one per cent of zinc.

Anemia developed in the rats receiving 0.50 per cent of zinc, although no change in number of red blood corpuscles occurred.

Both hemoglobin and red blood corpuscles were diminished on the one per cent zinc diet.

Hemoglobin and reproduction became normal in the animals on the 0.50 per cent zinc level, when the zinc carbonate was removed from the ration.

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