Proc. Nutr. Soc. Aust. (1978) 3:25

TRACE ELEMENTS IN HUMAN NUTRITION - WITH SPECIAL REFERENCE TO ZINC

I. E. DREOSTI*

Summary

Of the 14 trace elements known to be essential for health in animals only 2 or 3 probably present a problem of frank deficiency in man. For the remainder it is rather the conditioned insufficiencies that are important. Such deficiencies arise as a consequence of environmental or dietary factors which modify the requirement for trace elements, or their availability from food sources.

Zinc deficiency in man is principally of the latter type, and is of particular interest since a regular supply of the element is necessary for normal cell division and growth in animals.

Experiments in this laboratory with rats showed that alcohol, which represents a typical "conditioning" factor, induced an immediate redistribution of zinc in the animals' bodies. Plasma zinc levels rose during the experimental period and appeared to be able to compensate in part for a concurrent nutritional zinc deficiency. Thus, foetal brain DNA synthesis which was depressed during maternal zinc deprivation was restored to control levels following the administration of 10%, but not 20% alcohol to the dams.

I. TRACE ELEMENTS IN GENERAL

In common with a number of other dietary components, the essentiality of trace elements in nutrition is rather better defined for animals than it is for humans. With animals, of the some 100 elements appearing in the Periodic System of Classification only 14 are considered at present to be essential (Table 1) although a number of others (B, Al, Ti, As and Pb) are currently under consideration.

TABLE 1. Trace elements essential in animal nutrition (Schwartz 1975)

Element	Atomic No.	Recognition date
F	9	1972
Si	14	1972
V*	23	1971
Cr*	24	1959
Mn*	25	1931
Fe*	26	17th century
Co*	27	1935
Ni*	28	1973
Cu*	29	1928
Zn*	30	1934
Se*	34	1957
Mo**	42	1953
Sn	50	1970
I	53	1850

* Set 1 transition elements
** Set 2 transition elements

* CSIRO Division of Human Nutrition, Adelaide, South Australia 5000.

With humans, although most of the 14 microelements are recognized to be of importance, only 3 (I, Fe and Zn) have actually been allocated Recommended Daily Allowances (RDA's) by the U.S. National Research Council, and zinc, the most recent addition to the triad, only gained this status in the mid 1970's.

The existence of trace element problems in human nutrition have not been well defined. Certainly, some specific deficiencies are known to occur but in general insufficiencies due to inadequate dietary intake would appear to be less likely in humans, who consume a variety of foods from differing sources, than in animals whose intake derives entirely from locally-grown plant material. Thus, with the exception of iodine and fluorine which often require regional supplementation, and iron which is of greater significance to the nutrition of women, the remainder of the trace elements seem unlikely to present serious problems of frank dietary deficiency. On the other hand modifying influences, many of particular relevance to man, may lead to the production of a conditioned trace element deficiency even in the presence of an apparent abundant supply of all essential minerals.

The factors responsible for conditioned trace element deficiencies in man and animals are widely varied (Table 2) and, in all likelihood, are not yet fully documented. Food processing and the interaction of dietary constituents are of considerable importance but so too may be genetic disorders, defects in digestion absorption or excretion, disease, trauma or the functional condition of the animal.

TABLE 2. Causes of conditioned trace-element deficiencies in humans and animals.

Conditioning factor	Mechanism of action
Food processing	Removal of elements by partition or in the cooking process.
Dietary constituents	Antagonism with other elements or complex formation with other compounds (e.g. phytate, fibre or protein).
Genetic disorders	1. Increased requirement 2. Impaired digestion and absorption 3. Increased urinary or faecal excretion.
Disease	1. Redistribution of element in body 2. Impaired digestion and absorption 3. Increased urinary or faecal excretion 4. Blood loss and exudation.
Trauma	1. Redistribution of element in body 2. Blood loss and exudation 3. Catabolic wastage.
Medications	1. Decreased absorption 2. Increased excretion 3. Altered anabolism or catabolism.
Total parenteral nutrition	Deficiency of element in infusion fluid.
Pregnancy and lactation	1. Hormonal effects 2. Anabolic demand.

The clinical symptoms of a microelement deficiency in animals usually reflect an impairment of the major biochemical functions of the element in the body. Lately it has become evident that the defects are often more patently manifest in growing and foetal tissues, and the microelement status of the mother should therefore be adequately maintained at all stages throughout pregnancy. Fortunately, in most cases, body reserves of trace elements are mobilized sufficiently rapidly to meet the demand of a temporary dietary insufficiency. With zinc, however, this does not appear to be the case, as rats require a regular intake of the element to ensure satisfactory foetal development. The rapidity of onset and the seriousness of a zinc deficiency in animals have made it one of the most widely studied of the trace elements in recent years. Accordingly attention will now be focussed on this element and on certain aspects of its metabolism of relevance to man. No doubt many of the observations made concerning zinc could apply equally to certain other essential microelements and the comments should therefore be viewed at all times against the broader background of the trace elements in general.

II. ZINC

Although zinc is distributed ubiquitously in nature, it occurs in appreciable amounts only in meats, shell-fish, legumes and nuts. In addition, the refining of many foods results in loss of zinc from the original material (Table 3).

TABLE 3. Zinc content of some natural and processed foods (Sandstead 1973; Mertz 1975)

Foodstuff	Zinc content (µg/g fresh wt.)
Oysters, herrings	700 - 1600
Other seafoods	20 - 30
Meats	30 - 50
Whole grains, Lima beans, peas, nuts	20 - 30
Whole wheat bread	5 - 6
White bread	1 - 2
Unpolished rice	6 - 7
Polished rice	1 - 2
Potatoes	8 - 9
Whole milk	0.1 - 0.5
Banana	0.2

Recent evidence in fact suggests that the average western diet barely supplies the RDA of 15 mg of zinc (Sandstead 1973). Furthermore, it seems that the sequestering effects of phytate (Davies et al. 1977), fibre (Ismail-Beigi et al. 1977) and certain plant proteins (Nielsen et al. 1966; Harvey-Anderson et al. 1976) probably compound the problem. Thus, while the question of zinc deficiency in humans was hitherto considered to be of importance only in certain regions of the Middle East (Prasad et al. 1961) the view is now emerging that changing patterns in the western diet may have placed these populations too at risk from suboptimal zinc nutriture. Data from four research groups in the U.S.A.

point to the existence of a marginal zinc deficiency among school children (Hambridge et al. 1972), college age women (White 1969), and two groups of hospital patients (Henkin 1971; Pories et al. 1971) in America. Because of the teratogenic consequences of zinc depletion in rats (Hurley and Swenerton 1966) and the deleterious effect of the condition on parturition (Apgar 1968), the question has lately been raised whether the deficiency may exist in women from both middle-eastern (Sever and Emanuel 1973) and western countries (Sandstead 1973; Warkany and Petering 1973; Jameson 1976).

These considerations, together with an interest in the effect of alcohol on zinc metabolism, led to a study being undertaken in this laboratory concerning the influence of alcohol on zinc balance in rats and on foetal brain development in rats receiving different levels of zinc during pregnancy.

III. ZINC AND ALCOHOL

Alcohol represents an important "conditioning" factor in zinc nutrition and chronic alcoholism in man has been reported to be accompanied by lowered plasma zinc levels and hyperzincuria (Vallee et al. 1956). Generally, the condition is associated with cirrhosis of the liver and kidney damage but the precise mechanism of excretion is not known (Underwood 1976). Little work has been performed concerning the initial response to alcohol consumption in man or animals although Wang and Pierson (1975) have reported a 60% decline in liver zinc levels in rats 2 weeks after receiving 20% alcohol in their drinking water. Plasma zinc levels fell consistently at about 3% per week from the second week of study. Investigations performed in these laboratories on young adult female rats pointed to an immediate rise in plasma zinc levels following ingestion of 20% alcohol as the sole drinking fluid, accompanied by a decline in liver and bone zinc levels (Table 4).

TABLE 4. Tissue zinc levels in rats following administration of 20% alcohol (Dreosti et al. 1978).

Period on 20% alcohol (weeks)	Tissue zinc concentration (µg/g fresh wt.)*				
	Plasma	Liver	Bone	Brain	Hair
0	1.06 ± 0.2	30.2 ± 0.49	224 ± 13	12.5 ± 0.5	189 ± 1
1	1.36 ± 0.1	25.2 ± 1.1	-	13.5 ± 2.0	-
2	1.83 ± 0.5	26.9 ± 1.0	216 ± 5	13.4 ± 0.5	195 ± 1
4	1.25 ± 0.1	25.8 ± 1.7	-	12.2 ± 0.6	-
6	1.43 ± 0.1	26.2 ± 0.7	202 ± 6	12.1 ± 0.1	190 ± 3
10	1.29 ± 0.1	27.3 ± 0.9	202 ± 9	12.4 ± 0.1	204 ±13

* Mean ± SEM of 3 animals in each group.

The data indicate that a short period of exposure to alcohol in rats seriously disturbs the distribution of zinc within the body of otherwise well-nourished animals. It seems reasonable to suppose that the loss of zinc from the liver and bones of the alcohol-treated rats might precipitate a serious zinc deficiency if prolonged or if superimposed on a suboptimal zinc intake. In the initial stages, however, the flux of

zinc into the plasma may temporarily compensate for a dietary insufficiency by mobilizing zinc deposits at a rate faster than would occur in the absence of alcohol.

Thus, studies performed on 20-day old rat foetuses in which the incorporation of ^{3}H-thymidine into brain DNA was measured as an index of cell division (Table 5), showed that while DNA synthesis was reduced in foetuses from zinc-deficient dams, consumption of 10% alcohol by the dams restored foetal incorporation rates to control levels. Foetuses from rats receiving 20% alcohol reacted differently and DNA synthesis was diminished, possibly due to the inhibitory effect of alcohol on brain growth (Bauer-Moffett and Altman 1977).

TABLE 5. Effect of maternal zinc deficiency and alcohol consumption of the incorporation of ^{3}H-thymidine into brain DNA of foetal (20 day) rats (Dreosti et al. 1978).

Treatment of dam	Incorporation of ^{3}H-thymidine* cpm/mg DNA
Zinc-supplemented (100 ppm) ad lib.	3705 ± 292
Zinc-supplemented (100 ppm) pair-fed	3631 ± 380
Zinc-deficient (< 0.5 ppm)	2588 ± 559**
Zinc-deficient (< 0.5 ppm) + 10% alcohol	3574 ± 466
Zinc-deficient (< 0.5 ppm) + 20% alcohol	2323 ± 523**

* Mean ± SEM of 3-5 animals in each group
** $P < 0.05$ vs ad lib. controls

Histological examination of the ependymal and subependymal layers of foetal brains from the same dams (Table 6) confirmed the biochemical evidence concerning the interaction of zinc and alcohol on neural cell division.

TABLE 6. Effect of maternal zinc deficiency and alcohol consumption on the mitotic index in foetal (20 d) rat brains (Dreosti et al. 1978).

Treatment of dam	Mitotic index (%)*	
	Subependymal	Ependymal
Zinc-supplemented (100 ppm) ad lib.	0.59 ± 0.02	12.3 ± 0.46
Zinc-supplemented (100 ppm) pair-fed	0.58 ± 0.04	13.7 ± 2.5
Zinc-deficient (< 0.5 ppm)	0.52 ± 0.04**	8.7 ± 1.2+
Zinc-deficient (< 0.5 ppm) + 10% alcohol	0.66 ± 0.09++	10.1 ± 1.8
Zinc-deficient (< 0.5 ppm) + 20% alcohol	0.51 ± 0.04**	10.5 ± 1.7

* Mean ± SEM of 4 animals in each group
** $0.05 > P < 0.1$ vs ad lib. controls
\+ $P < 0.01$ vs ad lib. controls
++ $0.05 > P < 0.1$ vs zinc-deficient group

Decreased cell division was again evident in the ependymal and subependymal layers of the zinc-deficient foetal brains. Consumption of 10% alcohol by the dam again appeared to reverse the effect while 20% alcohol reduced the mitotic index in the subependymal layer even further than did maternal zinc deficiency alone.

The studies on rats reported in this paper demonstrate that the consumption of alcohol immediately brings about a redistribution of zinc in the animal body. Whether this occurs with humans is not known although it has been established that chronic alcoholism is often accompanied by hyperzincuria (Vallee et al. 1956). It may be that the intake of alcohol interferes with zinc metabolism throughout the ingestion period by a series of changing mechanisms. The limited temporary benefit obtained by the initial consumption of alcohol must be seen against this overall debilitating trend.

The findings presented in the latter half of this paper serve to highlight the effect of a single "conditioning" factor on the metabolism of one trace element in the body, and to demonstrate the profound effect of this interaction on other biochemical pathways. Very few studies have been made concerning the multitude of "conditioning" factors to which man is exposed and their effects on trace element balances in general. The growing awareness of the importance of minerals in human nutrition must surely encourage more and deeper studies to be undertaken in this area.

REFERENCES

APGAR, J. (1968). Amer. J. Physiol. 215: 160 and 1478.

BAUER-MOFFETT, C. and ALTMAN, J. (1977). Brain Research 119: 249.

DAVIES, N.T., KRISTIC, V. and FLETT, A.A. (1977). Nut. Rep. Int. 15: 207.

DREOSTI, I.E., BUCKLEY, R.A. and RECORD, I.R. (1978). In preparation.

DREOSTI, I.E., FRASER, F.J. and RECORD, I.R. (1978). In preparation.

HAMBRIDGE, K.M., HAMBRIDGE, C., JACOBS, M. and BAUM, J.D. (1972). Pediat. Res. 6: 868.

HARVEY ANDERSON, G., HARRIS, L., RAO, A.V. and JONES, J.D. (1976). J. Nutr. 106: 1166.

HENKIN, R.I. (1971). "Newer Trace Elements in Nutrition" Eds. W. Mertz and W.E. Cornatzer. (Dekker: New York).

HURLEY, L.S. and SWENERTON, H. (1966). Proc. Soc. Exp. Biol. Med. 123: 692.

ISMAIL-BEIGI, F., REINHOLD, J.G., FARAJI, B. and ABADI, P. (1977). J. Nutr. 107: 510.

JAMESON, S. (1976). Acta. Med. Scand. Supplement 593.

MERTZ, W. (1975). "Trace Element Metabolism in Animals - 2" Eds. W.G. Hoekstra, J.W. Suttie, H.G. Gunther and W. Mertz. (University Park Press: Baltimore).

NIELSEN, F.H., SUNDE, M.L. and HOEKSTRA, W.G. (1966). J. Nutr. 89, 35.

PORIES, C.J., STRAIN, W.H. and ROB, C.G. (1971). "Environmental Geochemistry in Health and Disease" Memoir 123, Geological Society of America 72.

PRASAD, A.S., HALSTEAD, J.A. and NADIMI, M. (1961). Amer. J. Med. 31: 532.

SANDSTEAD, H.H. (1973). Amer. J. clin. Nutr. 26: 1251.

SCHWARTZ, K. (1975). "Trace Element Metabolism in Animals - 2" Eds. W.G. Hoekstra, J.W. Suttie, H.E. Gunther and W. Mertz. (University Park Press: Baltimore).

SEVER, L.E. and EMANUEL, I. (1973). Teratology 7: 117.

UNDERWOOD, E.J. (1976). "Trace Elements in Human and Animal Nutrition" 4th ed. (Academic Press: New York).

VALLEE, B.L., WACKER, W.E.C., BARTHOLOMAY, A.F. and ROBIN, E.D. (1956). N. Engl. J. Med. 255: 403.

WANG, J. and PIERSON, R.N. (1975). J. Lab. clin. Invest. 85: 50.

WARKANY, J. and PETERING, H.G. (1973). Amer. J. Mental Deficiency 77: 645.

WHITE, H.S. (1969). J. Amer. dietet. Assoc. 55: 38.