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SYMPOSIUM ON 'TRACE ELEMENTS AND HUMAN HEALTH'

Trace element status of the human diet

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At first glance, it could be conceived that a comparison of the intake of a particular nutrient with local recommended dietary intakes could indicate whether or not that intake is appropriate for the physiological well-being of the individual or population being studied. This approach, however, is inadequate because it does not allow for the efficiency with which that particular element is taken up by the intestine and transferred to the body; i.e. what many people term the availability of the element in the diet. The practical aspects of availability will be discussed by Southon *et al.* (1988). Additionally, since the derivation, definition and application of recommended intakes is the justified province of this year's Boyd Orr Lecture I will not consider recommended intakes and their suitability for assessing the adequate status of the diet. Important as they both are, I will not dwell on these areas. I would, however, like to make some additional points about the trace-element composition of human diets; these relate to (1) the potential impact of geochemistry and soil on the mineral content of the diet, (2) the need to consider the dietary content of other nutrients when the dietary adequacy of one particular nutrient is being considered, (3) the effect of altered mineral compositions in synthetic and refined diets, and (4) the effect which supplementation, or fortification, of diets with trace minerals to ensure adequate intakes has on the overall adequacy of the mineral content.

Influence of local geochemical anomalies on the dietary intakes of trace minerals

These effects are most apparent with anionic species of trace elements such as those of fluorine, selenium and iodine. The extensive occurrence throughout the People's Republic of China of a Se-responsive cardiomyopathy known as Keshan disease has been well documented (Chen *et al.* 1980). More recently, Yang *et al.* (1983) described a Se toxicosis affecting some communities in Enshi county of Hubei Province. Their paper described clinical features resembling those seen in other seleniferous regions. It also included findings which illustrate the interactions of various factors in influencing the mobility through the food chain of soil Se. In particular the content of water-soluble Se in the soil was reduced by soil acidity and high humus content; conversely the water-soluble Se was increased in alkaline soils. In turn the Se content of cereals grown on those soils correlated with their content of water-soluble Se. This locally grown produce contributed greatly to the Se burden of the local populations subsisting on them. Variations in the

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Table 1. *Interaction between a molybdenum-rich geochemical environment and human metabolism of copper and molybdenum (from Kovalsky* et al. *1961)*

(Mean values and standard deviations from varying nos. of subjects in each group)

	Dietary intake (mg/24 h)		Blood (μg/1)				Urinary loss (μg/24 h)			
			Cu		Mo		Cu		Mo	
	Cu	Mo	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Mo-rich zone:										
Patients*	5–10	10–15	1130	250	30	80	304	14	29	2
Healthy individuals	5–10	10–15	1380	260	170	80	184	30	28	4
Control zone:										
Healthy individuals	10–15	1–2	1830	200	60	20	120	24	16	3

*Patients had an arthropathy and raised blood uric acid.

human intake of Se elsewhere in the world and the implications for human health will be discussed later in this symposium (Casey, 1988).

The continuingly high prevalence of iodine-deficiency diseases in man highlights the known, but neglected, consequence of geochemical anomalies on the I intake of populations. A recent report (Subcommittee for the Study of Endemic Goitre and Iodine Deficiency of the European Thyroid Association, 1985) has demonstrated that I deficiency diseases are by no means restricted to the Third World where, perhaps, the implementation of supplementation programmes would be limited by socio-economic and logistic factors. Although the risk of goitre and thyroid deficiency has been shown to be reduced by iodination programmes, endemic goitre persists in at least twelve European countries, including some where I prophylaxis is mandatory. The changes reviewed in the report were the grosser features of I deficiency. Now that the subtle effects of suboptimal I status in the mother during gestation on neurological development in the child are appreciated (Connolly *et al.* 1979), it would seem possible that an inadequate dietary intake of I may have more-far-reaching sequelae than has been realized hitherto.

The impact of geochemistry on diet is not restricted entirely to the anionic elements. Some anions may affect indirectly the metabolism of trace cations. The interaction between molybdenum and sulphur in limiting the intestinal uptake of copper in ruminants has been described (Mills, 1980). Less certain, however, is whether or not Mo can affect adversely the metabolism of Cu in non-ruminants including man. An interesting study (Kovalsky *et al.* 1961) from Armenia, summarized in Table 1, suggests that this may be so; it would be valuable to see this study reproduced in the light of recent advances in our understanding of the metabolism of Mo and Cu.

Nutrient inter-relations

It is unlikely with customary dietary sources that nutritional defects affecting the cations would occur in isolation. More probably, associated nutritional deficits would occur. This is a very important but overlooked concept. It was clearly appreciated by Eggleton (1939) who, soon after the first descriptions of the successful induction of zinc deficiency in laboratory animals, proposed that Zn deficiency may contribute to the features of some malnutrition syndromes. His assessments of the Zn content in some

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foodstuffs demonstrated some congruence with that of thiamin and he surmised that Zn status was impaired in patients with beri-beri.

More recently, Golden & Golden (1981) have demonstrated this concept very effectively. They compared the Zn and protein contents of diets as expressed in relation to energy. This comparison demonstrated that, if the recommended dietary allowances were appropriate, it would be virtually impossible for someone to have an inadequate intake of protein without also having a dietary deficiency of Zn. In the foodstuffs which they compared, with the exception of some seafoods, Zn would have become a limiting nutrient before protein. This type of comparison shows nicely that when considering the dietary requirements and recommended allowances of any particular nutrient, and the adequacy of a diet, a rigorous analysis relative to other dietary constituents is necessary.

The preceding comments are a little speculative being based, as they are, on the assumed validity of recommended allowances and on a simple mathematical relation. However, if the nutrients are functionally or metabolically integrated then the interrelation of their nutritional supply becomes more pertinent. For example, an apparently healthy animal, including man, on a barely adequate Zn intake can be precipitated rapidly into clinical Zn deficiency by an increase in the protein intake. Conversely, an adequate supply of essential fatty acids can ameliorate some features of Zn deficiency. In laboratory and farm animals the relative supplies of polyunsaturated fatty acids, Cu and iron can have a most profound influence on the dietary requirement for Se and for vitamin E (Dougherty *et al.* 1981; Dougherty & Hoekstra, 1982). These interactions in particular are not well documented in healthy populations but certainly they may have contributed to the development of Se deficiency in patients on total parenteral nutrition. Other such interdependencies would alter the nutritional requirements of patients on synthetic and refined diets, and may even affect healthy individuals.

An apparently striking dietary interaction has been described between Cu and the carbohydrate source in the diet (Reiser *et al.* 1985). In this, adult male volunteers, being fed, in a cross-over study, on a diet containing 1 mg Cu/d in conjunction with sucrose providing 20% of the dietary energy intake, developed altered Cu metabolism, as evidenced by reduced activity of the erythrocyte enzyme superoxide dismutase (*EC* 1.15.1.1) which did not occur when the carbohydrate source was maize starch.

Refined and other synthetic diets and problems with fortification

The processing of foods can result in considerable loss of trace elements. This has been shown for both sugar and flour. During the refining of molasses to refined sugar an initial mean chromium content of 266 μg/g was reduced to 20 μg/g (Masironi *et al.* 1973). Table 2 is derived from the findings of Schroeder (1971). It demonstrates the extensive loss of manganese, Fe and Zn from wheat flour during milling.

Table 2. *The loss of trace elements (mg/kg) during the milling of wheat flour (Schroeder, 1971)*

	Wheat	White flour
Percentage of wheat	100	72
Chromium	0·05	0·03
Selenium	0·63	0·53
Molybdenum	0·48	0·25
Zinc	35	7·8
Iron	43	10·5
Manganese	46	6·5

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Table 3. *Representative content (μmol/l) and molar ratios* of iron, zinc and copper in infant formulas*

	Fe	Zn		Cu		Total
		Content	Molar ratio	Content	Molar ratio	
Human breast milk (after 1 month lactation)	6.2	20	3·2	5·2	0·8	31·4
Cow's milk and soya-bean protein-derived formula (UK)	120	60	0·5	8	0·08	188
Fe-fortified formula (USA)	215	61	0·3	6·3	0·03	282

*Relative to Fe.

Attempts to compensate for the losses of such nutrients by fortification of products with trace elements can precipitate inter-element imbalances. These may be related to interactions at the level of intestinal uptake and transfer, or such imbalances could also alter the systemic metabolism of nutrients. This is of particular relevance to infant feeding where most infant formulas are supplemented to levels of Fe which are far in excess of those supplied by human breast milk. From the examples in Table 3 it is apparent that such supplementations distort the absolute and relative quantities of the minerals needing to be absorbed and used by the infant. Antagonistic interactions can occur between these elements. Fe can interfere with the intestinal uptake and transfer of Zn (Solomons & Jacob, 1981). However, one study of an infant formula based on cow's milk did not find this interaction, but it detected by balance methodology an improved net intestinal absorption of Cu by infants when the Fe content of the formula was reduced (Haschke *et al.* 1986). A similar approach investigating a soya-bean-based product has recently found enhanced net intestinal absorption of both Cu and Zn following a reduction of the customary Fe fortification of that particular preparation (C. Miller, personal communication). In such reactions, not only are the relative amounts of elements important but no doubt so are the total amount of metals competing for uptake sites. Since the latter amount would be affected by the other dietary constituents it will not be surprising if the extent and nature of inter-element interactions are affected by other dietary constituents. These interactions are not restricted to infant formulas. In a study in Iranian schoolboys of the effect of Fe, and of Fe and Zn supplements on height velocity, the latter supplement was ineffective compared with a placebo whereas the Fe supplement alone increased height velocity. It is possible that the additional Zn impaired the utilization of the Fe (Mahloudji *et al.* 1975).

Notwithstanding the latter study, the precise implications of the interactions for the adequacy of the human diet or for human nutrition and metabolism are not known. Clearly they demonstrate the interdependence of nutrients and the necessity to consider the varied nature of such interactions when assessing the status of the human diet and when devising strategies to improve it.

REFERENCES

Casey, C. E. (1988). *Proceedings of the Nutrition Society* **47**, 55–62.
Chen, X., Yang, G., Chen, J., Chen, X., Wen, Z. & Ge, K. (1980). *Biological Trace Element Research* **2**, 91–107.

Connolly, K. J., Pharoah, P. O. D. & Hetzel, B. S. (1979). *Lancet* **ii**, 1149–1151.
Dougherty, J. J., Croft, W. A. & Hoekstra, W. G. (1981). *Journal of Nutrition* **111**, 1784–1796.
Dougherty, J. J. & Hoekstra, W. G. (1982). *Proceedings of the Society for Experimental Biology and Medicine* **169**, 201–208.
Eggleton, W. G. E. (1939). *Biochemical Journal* **33**, 403–406.
Golden, M. H. N. & Golden, B. E. (1981). *British Medical Bulletin* **37**, 31–36.
Haschke, F., Ziegler, E. E., Edwards, B. B. & Fomon, S. J. (1986). *Journal of Pediatric Gastroenterology and Nutrition* **5**, 768–773.
Kovalsky, V. V., Jarovaja, G. A. & Smavonjan, D. M. (1961). *Zhurnel Obshchei Biologii* **22**, 179–191.
Mahloudji, M., Reinhold, J. G., Haghshenass, M., Ronaghy, H. A., Spivey Fox, M. R. & Halsted, J. A. (1975). *American Journal of Clinical Nutrition* **28**, 721–725.
Masironi, R., Wolf, W. & Mertz, W. (1973). *Bulletin of the World Health Organization* **49**, 322–329.
Mills, C. F. (1980). In *Biological Roles of Copper. Ciba Foundation Symposium* no. 79, pp. 49–69.
Reiser, S., Smith J. C. Jr, Mertz, W., Holbrook, J. T., Scholfield, D. J., Powell, A. S., Canfield, W. S. & Canary, J. J. (1985). *American Journal of Clinical Nutrition* **42**, 242–251.
Schroeder, H. A. (1971). *American Journal of Clinical Nutrition* **24**, 562–573.
Solomons, N. W. & Jacob, R. A. (1981). *American Journal of Clinical Nutrition* **34**, 475–482.
Southon, S., Fairweather-Tait, S. J. & Hazell, T. (1988). *Proceedings of the Nutrition Society* **47**, 27–35.
Subcommittee for the Study of Endemic Goitre and Iodine Deficiency of the European Thyroid Association (1985). *Lancet* **ii**, 1289–1293.
Yang, G., Wang, S., Zhou, R. & Sun, S. (1983). *American Journal of Clinical Nutrition* **37**, 872–881.

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