Review Article

Lack of a Recommended Dietary Allowance for Copper may be Hazardous to Your Health

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The 10th edition of Recommended Dietary Allowances (RDA) did not include an RDA for copper; rather a safe and adequate daily intake was suggested. Criteria, history and uses of RDAs were summarized along with data on dietary intakes, balance and depletion experiments, low (fats and oils, skim milk and yogurt) and high (legumes, mushrooms, nuts and seeds) copper foods and hazards of zinc supplements. Bone disease and cardiovascular disease from diets low in copper have been studied in animals for decades. Men and women fed diets close to 1 mg of copper per day, amounts quite frequent in the US, responded similarly to deficient animals with reversible, potentially harmful changes in blood pressure control, cholesterol and glucose metabolism, and electrocardiograms. Women supplemented with trace elements including copper experienced beneficial effects on bone density. These data exceed similar data on magnesium, selenium and zinc and are sufficient for establishing an RDA.

Ischemic heart disease and osteoporosis are likely consequences of diets low in copper. Numerous anatomical, chemical and physiological similarities between animals deficient in copper and people with ischemic heart disease have been noticed. Association between osteoporosis and low copper status deserves further inquiry. Augmenting low copper diets with high copper foods may be beneficial.

Committees that establish RDAs should return to the traditions of the first nine editions and make recommendations that promote health and nutritional welfare, meet functional needs, prevent disease and promote public welfare.

Key teaching points:

- RDAs traditionally have been set to protect health.
- Essential nutrients without RDAs are neglected in dietary surveys, nutrition information and nutritional research.
- Sufficient evidence exists to establish a RDA for copper.
- Low copper intakes may contribute to ischemic heart disease and osteoporosis.
- Diets low in copper can be improved by appropriate food selection.

INTRODUCTION

The Food and Nutrition Board estimates that the safe and adequate daily intake of dietary copper is 1.5 to 3.0 mg for adults (1 mg of copper is c 16 μmol) [1]. It has been known for some time that intakes this high are unusual [2]. Data are increasingly available to support the belief that rather than estimates of dietary requirements being too high, diets often are too low in copper (below). The Board believes data on copper are sufficient to estimate a range of requirements, but insufficient for developing a Recommended Dietary Allowance (RDA) [1].

DIETS, DEPLETION AND FOODS

The amount of copper in a diet is determined best by chemical analysis. Although there is fair correlation between

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analyzed values and calculated values, calculated values generally are too high, resulting in an over-estimate of intakes [3–5].

Before the lower limit of the estimated safe and adequate daily intake of copper was decreased from 2.0 mg [2] to 1.5 mg [1], data from 10 dietary surveys in which dietary copper was assessed by chemical analysis were used to characterize the US diet as a whole. Normal distribution was assumed; means and standard deviations were used to calculate average frequency of several daily intakes. Fourteen percent of diets exceeded 2.0 mg [6].

Data from the surveys on which these calculations were based were pooled so the shape of the distribution of 849 diets could be defined and to allow comparison of diets to the revised standard [1]. The figure reveals positive skewness, but only 3.2% of the diets exceed 3.0 mg/day; 61% are less than 1.5 mg/day and approximately one-third are less than 1 mg. The middle quartiles ranged from 0.91 to 1.86 mg/day. This distribution is representative of diets made from conventional foods in Belgium, Canada, UK and the US [7].

More than 30 men and women have been depleted of copper carefully with diets made with conventional foods containing 0.65 to 1.02 mg/day. Clinical correlates of insufficiency included hypercholesterolemia [8,9], abnormal electrocardiograms [8,10], decreased glucose clearance [11] and hypertension with sustained hand grip exercise [12]. The copper requirement of obese women during weight loss is even greater [13] than that in the depletion experiments cited. Thus, it is easy for many people to consume diets containing too little copper.

Comparison of our successful and unsuccessful depletion experiments reveals that subjects depleted successfully were more likely to be in negative balance regardless of copper intake than those subjects who could not be depleted within a reasonable time interval [14]. Balance studies often are difficult to interpret [15,16]. As trace element balance seems to be a function of previous intake [17], balance data probably are important only if negative. Some of the other biochemical measurements confirmed depletion. Extrapolation from animal experiments reveals that severe cardiovascular damage would have occurred if the depletion experiments [8–13] had been continued.

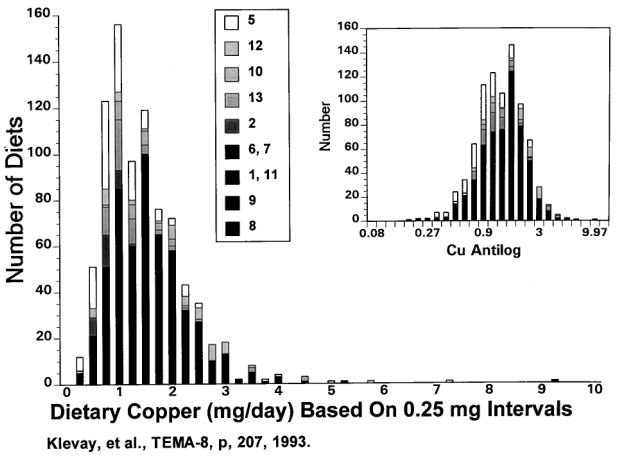

Fig. 1. Frequency distribution of diets from 10 surveys. See reference [7] for details and identity of authors associated with shaded squares. The small insert shows that distribution is normal on logarithmic transformation.

Table 1. Representative Foods Either Low or High in Copper, μg/g

Bottom quartile		Top quartile	
Fats and oils (6)*	0.05	Legumes (178)	2.39
Skim milk (6)	0.05	Ready-to-eat cereals (180)	2.40
Yoghurt (12)	0.08	Mushrooms (181)	2.62
Mayonnaise (17)	0.12	Chocolate (186)	2.86
Jelly and jam (31)	0.19	Seeds (192)	3.30
Whiskey (38)	0.24	Nuts (197)	3.70
Sugar (46)	0.29	Crab (200)	3.90
Corn (42)	0.27	Peanut butter (215)	6.30
Tuna (49)	0.30	Liver (228)	18.2
Lettuce (56)	0.38	Oysters (234)	134

* Numbers in parentheses are ranks; e.g., 6th of 235. Based on data of Lurie et al [21].

Dietary copper can be increased by avoiding foods low in copper and by seeking foods high in copper. Benefits of these maneuvers have already been noticed [18–20].

Lurie et al [21] compiled and evaluated analytical data on 235 foods. I arranged these foods in order of increasing copper based on the grand means thus defining the middle quartile range: 0.43 to 2.31 μg/g. Table 1 contains selected foods from the bottom and top quartiles.

The nutritional concept of empty calories is far from new; few foods are as free of copper as fats and oils. In fact, transition metals are removed by chelation to increase shelf-life of unsaturated oils [22]. Skim milk and yogurt rank slightly higher in copper; it is important to recall that some of the classical copper deficiency experiments were done with milk diets [23–25]. Beer, which ranks below whiskey, contains an unidentified component that promotes copper absorption and retention in animals [26]. Sugar was chosen for deficiency experiments with animals because it is low in copper [27]. Lettuce is low in copper and frequently serves as a carrier of copper-free oil.

The nutritional quality of lettuce salads can be enhanced by adding legumes such as garbanzo beans [28], mushrooms, or nuts and seeds. Not all ready-to-eat cereals are high in copper. As expected from the low rank of corn, corn flakes are the lowest in copper of the 23 cereals we analyzed [29]. Copper in cereals seems to parallel the amount of crude fiber [29]. A chocolate bar with nuts may be a more pleasant nutritional supplement than a tablet or capsule. Although many people consider crab a delicacy, it is high enough in copper to be useful as a supplement. Analytical chemistry will reveal whether or not new peanut butter products low in fat are equivalent in nutritional quality. A small portion of liver can

easily change a diet from deficient to sufficient. Liver is an antidote [30] to the hypercholesterolemic effect of meat in spite of being high in cholesterol and saturated fat. Oysters are so rich in copper that recipes hiding small amounts in other dishes should be developed for those unacquainted with or too busy to use the Rockefeller recipe. It is assumed that the high amount of copper in oysters is sufficient to counteract the potentially inhibiting effect of high zinc. Perhaps the decline in oyster consumption since the last century has not been without harm to the public health [31].

SOME HISTORY

Surprisingly little has been written about criteria which define nutrient essentiality or preferred methods of measuring nutrient requirements. Information on these concepts from the trace element era has been collected [32]. Essentiality can be inferred from low atomic number, biological activity, homeostatic control, low toxicity and ubiquity. However, essentiality is certain only if restricted diets interrupt the life cycle or impair function and supplemented diets prevent pathology or provide relief.

Careful reading of the first nine editions of the Recommended Dietary Allowances reveals that protection of health was implicit among the goals. Although one can infer prevention of deficiency disease, use of phrases like "protection of all body tissues, nutritional welfare, meet functional needs, good nutrition, disease prevention, public welfare, total health, promotion of health, normal function, function and health," etc., seems to imply much more. When asked, members of the lay public translate an interest in nutrition into the desire to live longer and/or better. Although the 10th edition [1] refers to preventing failure of a specific function and mentions it is possible to meet both the RDA and the guidelines published in Diet and Health [33] by consumption of a variety of foods from diverse food groups, this edition [1] seems to decrease the traditional association between the Recommendations and health by stating that data relating diet to risk of chronic disease [33,34] lead to recommendations derived through approaches different from those used in developing RDAs.

The integration of the Food and Nutrition Board into the Institute of Medicine seems to imply emphasis on health and, perhaps, a return to earlier concepts. Indeed the requirement for any nutrient is defined as the "intake that will maintain normal function and health" [35].

PHYSIOLOGY, RISK FACTORS, AND OTHER NUTRIENTS

An RDA for copper should be established. In the depletion experiments cited [8–13] men and women experienced chemical and functional changes. These changes in electrocardiograms, glucose clearance and lipids would not promote health if allowed to persist. They were corrected by copper supplementation without lasting harm, in all probability. Insufficient dietary amounts of magnesium, selenium and zinc, all of which have RDAs, have not been defined by depletion experiments. Evidence of depletion in support of an RDA for copper exceeds that available for these nutrients.

Some nutritionists may consider those who consume diets as low in copper as those used in these experiments as apparently normal, healthy people. However, it is generally agreed that there are many people in the general population with cholesterol levels that are too high and glucose tolerance that is too low. Approximately one-fourth of the deaths in the United States are closely associated with these risk factors.

Adverse effects of zinc supplements on lipid metabolism have been found in more than 75 men and women [6]; experiments with animals confirm that these effects are from the induction of mild copper deficiency [27,36]. There is no other adequate explanation. The lowest effective, supplementary dose of zinc is close to the RDA for zinc (median effective dose 24 mg per day) [37]. Sandstead suggests that 9 mg supplements may be safe [38].

Some uses of the RDAs have been summarized in a recent pamphlet [35]. Essential nutrients without an RDA get less attention in dietary surveys, advice on food selection, food and diet analysis, nutrition information, dietary planning, and nutritional research. For example, studies on osteoporosis generally emphasize calcium and ignore copper although it has been known for decades that diets low in copper can cause osteoporosis [39,40]. Excessive intake of milk may exacerbate, rather than mitigate, this problem [41].

COPPER AND HEALTH

It may seem incongruous to suggest that a diet low in copper can contribute to both osteoporosis and ischemic heart disease, but there is an epidemiologic association between the two illnesses [42–44]. That copper deficiency can produce both cardiovascular and bony pathology has been known for sometime [40,45]; however, cardiovascular experiments are much more numerous than those on bone.

In the two decades since it was suggested that disrupted copper metabolism plays a role in coronary heart disease [27], copper deficiency has been found to be the only nutritional insult that elevates cholesterol, blood pressure and uric acid, has adverse effects on electrocardiograms, impairs glucose tolerance, promotes thrombosis and to which males respond differently than females. Approximately 70 anatomical, chemical and physiological similarities between animals deficient in copper and people with ischemic heart disease have been identified [46,47]. Some mechanisms have been reviewed [48–50].

It has been four decades since bone health was linked to good copper nutriture. Suggestion that the data may relate to

human health is more recent [41]; work on mechanisms is in the earliest stages. For example, osteoblast activity is decreased in both copper deficiency [39,51] and human osteoporosis [52–55]. A supplementation trial with trace elements (including copper) produced beneficial effects on bone density [56]. Decreased levels of copper have been found in people with osteophytic lipping of the thoracic spine [43], ischemic necrosis of the femoral head [57], fractures of femoral neck [58] and decreased lumbar bone density [59].

SUMMARY

The Western diet frequently is low in copper in comparison to suggested standards. Diets containing amounts of copper proved insufficient for men and women in depletion experiments are easily accessible to the general population. These diets can be improved by appropriate food selection. A Recommended Dietary Allowance for copper should be established. Lack of an RDA is based on the mistaken belief that accumulated evidence is insufficient, although the number of successful depletion/repletion studies for copper exceeds those for magnesium, selenium and zinc together and supporting evidence is available. An RDA will improve nutritional advice and planning and will encourage research. The population will not benefit from the *status quo.*

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