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Nutrient Reference Values for Australia and New Zealand
Including Recommended Dietary Intakes

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COPPER

BACKGROUND

Copper is a component of a number of metalloenzymes including diamine oxidase, monoamine oxidase, lysyl oxidase, ferroxidases, cytochrome *c* oxidase, dopamine beta monooxygenase, alpha-amidating monooxygenase and cupro/zinc superoxide dismutase.

Copper is widely distributed in foods with organ meats, seafood, nuts and seeds being major contributors. Wheat bran cereals and whole grain products are also good sources. Nearly two thirds of the body's copper is found in the skeleton and muscles but the liver is also important in maintaining plasma levels (Olivares & Uauy 1996, Turnlund et al 1998).

Copper is absorbed mainly in the small intestine although some absorption may also occur in the stomach. Absorption varies with copper intake, ranging from more than 50% at intakes below 1 mg/day to less than 20% for intakes above 5 mg/day (Turnlund 1998). The composition of the diet itself has little effect on bioavailability. However, very high levels of zinc or iron, generally taken as supplements, can affect absorption in adults and infants (Botash et al 1992, Lonnerdal & Hernell 1994, Morais et al 1994 Turnlund 1999). Excretion through bile is used to regulate copper balance. Urinary copper excretion is normally very low over a wide range of intakes.

Copper deficiency results in defects in connective tissue that lead to vascular and skeletal problems, and anaemia related to defective iron metabolism. It can also affect the central nervous system (Harris 1997, Turnlund 1999) and the immune and cardiovascular systems, notably in infants (Graham & Cordano 1969, Olivares & Uauy 1996, Turnlund, 1999). Frank copper deficiency is rare in humans but has been seen in certain circumstances in infants (Shaw 1992) and under conditions of total parenteral nutrition (Fujita et al 1989). Symptoms include normocytic, hyperchromic anaemia, leukopenia and neutropenia. Other studies have observed osteoporosis in copper-deficient infants and young children (Higuchi et al 1988) and heart beat irregularities (Milne 1998).

There is no single indicator for the assessment of requirements for copper in humans (FNB:IOM 2001). Serum copper, ceruloplasmin concentration, erythrocyte superoxide dismutase activity, platelet copper, cytochrome *c* oxidase activity, urinary copper, leucocyte copper concentration, lysyl oxidase activity, peptidyl glycine alpha-amidating mono-oxygenase activity, diamine oxidase activity, copper balance and factorial analysis have all been used, but they generally give inconsistent results.

1 mmol copper = 63.5 mg copper

RECOMMENDATIONS BY LIFE STAGE AND GENDER

<i>Infants</i>	AI	Copper
0–6 months	0.20 mg/day	
7–12 months	0.22 mg/day	

Rationale: The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of copper in breast milk, and rounding. The figure used for breast milk was 0.25 mg/L based on the studies of Biego et al (1998), Raiten et al (1998) and Rossipal & Krachler (1998) as outlined in the relevant FNB:IOM document (FNB:IOM 2001). The AI for 7–12 months was set by adding the average intake from human milk to a component for complementary foods. There are no data for copper intake of weaning foods in Australia or New Zealand. Data from the US NHANES survey (FNB:IOM 2001) showed that the median copper intake from weaning foods for children 7–12 months was 0.1 mg/day. At 7-12 months, human milk concentration is 0.20 mg/L or less, such that with a milk volume of 0.6 L, intake from milk is 0.12 mg/day. Thus, total intake is 0.22 mg/day.

<i>Children & adolescents</i>	AI	Copper
All		
1–3 yr	0.7 mg/day	
4–8 yr	1.0 mg/day	
Boys		
9–13 yr	1.3 mg/day	
14–18 yr	1.5 mg/day	
Girls		
9–13 yr	1.1 mg/day	
14–18 yr	1.1 mg/day	

Rationale: As there are no data to set EARs, AIs for children were set using the median intakes from reanalyses using appropriate age-bands of the National Nutrition Surveys of Australia (ABS 1998) and New Zealand (MOH 1999, 2003) weighted on a population basis.

<i>Adults</i>	AI	Copper
Men		
19–30 yr	1.7 mg/day	
31–50 yr	1.7 mg/day	
51–70 yr	1.7 mg/day	
>70 yr	1.7 mg/day	
Women		
19–30 yr	1.2 mg/day	
31–50 yr	1.2 mg/day	
51–70 yr	1.2 mg/day	
>70 yr	1.2 mg/day	

Rationale: It was felt that the small data sets – one in young men, one in men of mixed age and one in postmenopausal women – were insufficient to allow the setting of an EAR and an RDI. An AI was set based on median population intakes from the Australian (ABS 1998) and New Zealand (MOH 1999) National Dietary Surveys weighted on a population basis. As dietary data can underestimate intakes, the highest intake of the adult age groups for the men and women was used to set a figure for all adult males or females.

<i>Pregnancy</i>	AI	Copper
14–18 yr	1.2 mg/day	
19–30 yr	1.3 mg/day	
31–50 yr	1.3 mg/day	

Rationale: There are no data on the needs for copper in pregnancy. Therefore an AI was derived based on the amounts of copper that must be accumulated during pregnancy to account for the fetus and products of pregnancy. Over the course of pregnancy, the additional requirement is about 0.067 mg absorbed copper/day (Widdowson & Dickerson, 1964) or 0.10 mg dietary copper/day. From the available data, it is not possible to assume that absorption efficiency increases in pregnancy to account for this; so 0.10 mg/day was added to the AI for non-pregnant, adolescent girls and women.

Lactation	AI	Copper
14–18 yr	1.4 mg/day	
19–30 yr	1.5 mg/day	
31–50 yr	1.5 mg/day	

Rationale: There are no data to set an EAR for lactating women. The AI was set on the basis of the amount of copper required to replace copper secreted daily in human milk, equivalent to additional absorbed copper of 0.20 mg/day. At the level of the AI, copper bioavailability is about 65–75%, so an additional 0.30 mg/day copper needs to be consumed.

UPPER LEVEL OF INTAKE - COPPER

Infants

0–12 months **Not possible to establish. Source of intake should be milk, formula and food only**

Children and adolescents

1–3 yr **1 mg/day**
 4–8 yr **3 mg/day**
 9–13 yr **5 mg/day**
 14–18 yr **8 mg/day**

Adults+ 19 yr

Men **10 mg/day**
 Women **10 mg/day**

Pregnancy

14–18 yr **8 mg/day**
 19–50 yr **10 mg/day**

Lactation

14–18 yr **8 mg/day**
 19–50 yr **10 mg/day**

Rationale: Human data relating to liver effects were used as the indicator outcome as described in FNB:IOM (2001). A NOAEL of 10 mg/day was identified from the work of Pratt et al (1985) who undertook a 12-week, double blind study in seven adults. Liver function tests were normal. A UF of 1 was applied, as there is no evidence from large international databases to indicate adverse effects at 10–12 mg copper/day in foods and because of the rarity of observed liver damage from copper exposure in humans with normal copper homeostasis. Thus, a UL of 10 mg/day from food and supplements was set for adults.

Given the lack of information, the ULs for children and adolescent were extrapolated from the adult figure on the basis of relative body weight, and rounded down. As there are no data about toxicity in pregnancy and lactation, the ULs for adolescent girls and adult women were also applied to the equivalent pregnant and lactating adolescent girls and women.

These ULs do not apply to individuals with Wilson's disease, Indian Childhood Cirrhosis or Idiopathic Copper Toxicosis.

REFERENCES

- Australian Bureau of Statistics: Department of Health and Aged Care; *National nutrition survey. Nutrient intakes and physical measurements. Australia, 1995*. Canberra: Australian Bureau of Statistics, 1998.
- Biego GH, Joyeux M, Hartemann P, Debry G. Determination of mineral contents in different kinds of milk and estimation of dietary intakes in infants. *Food Addit Contam* 1998;15:775–81.
- Botash AS, Nasca J, Dubowy R, Weinberger HL, Oliphant M. Zinc-induced copper deficiency in an infant. *Am J Dis Child* 1992;146:709–11.
- Food and Nutrition Board: Institute of Medicine. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc*. Washington DC: National Academy Press, 2001.
- Fujita M, Itakura T, Takagi Y, Okada A. Copper deficiency in total parenteral nutrition: Clinical analysis of three cases. *J Parent Enter Nutr* 1989;13:421–42.
- Graham GG, Cordano A. Copper depletion and deficiency in the malnourished infant. *Johns Hopkins Med J* 1969;124:139–150.
- Harris ED. Copper. In: O'Dell BL, Sude RA eds. *Handbook of nutritionally essential mineral elements*. New York: Marcel Dekker, 1997. Pp 231–73.
- Higuchi S, Higashi A, Nakamura T, Matsuda I. Nutritional copper deficiency in severely handicapped patients on a low copper enteral diet for a prolonged period: estimation of the required dose of dietary copper. *J Pediatr Gastroenterol Nutr* 1988;7:583–7.
- Lonnerdal B, Hernell O. Iron, zinc, copper and selenium status of breast-fed infants and infants fed trace element fortified milk-based infant formula. *Acta Paediatr* 1994;83:367–73.
- Milne DB. Copper intake and assessment of copper status. *Am J Clin Nutr* 1998;67:1041S–1045S.
- Ministry of Health. *NZ Food: NZ people. Key results of the national nutrition survey*. Wellington; Ministry of Health, 1999.
- Ministry of Health. *NZ Food: NZ Children. Key results of the 2002 national children's nutrition survey*. Wellington: Ministry of Health, 2003.
- Morais MB, Fishberg M, Suzuki HU, Amancio OM, Machado NL. Effects of oral iron therapy on serum copper and serum ceruloplasmin in children. *J Trop Pediatr* 1994;40:51–2.
- Olivares M, Uauy R. Limits of metabolic tolerance to copper and biological basis for present recommendations and regulations. *Am J Clin Nutr* 1996;63:846S–852S.
- Pratt WB, Omdahl JL, Sorenson JR. Lack of effects of copper gluconate supplementation. *Am J Clin Nutr* 1985;42:681–2.
- Raiten DJ, Talbot JM, Walters JH. Assessment of nutrient requirements for infant formulas. *J Nutr* 1998;128:2059S–2294S.
- Rossipal E, Krachler M. Pattern of trace elements in human milk during the course of lactation. *Nutr Res* 1998;18:11–24.
- Shaw JCL. Copper deficiency in term and preterm infants. In: Fomon SJ, Zlotkin S, eds. *Nutritional anaemias*. New York: Vevey/Raven Press, 1992. Pp 105–17.
- Turnlund JR, Keyes WR, Peiffer GL, Scott KC. Copper absorption, excretion and retention by young men consuming low dietary copper determined by using the stable isotope ⁶⁵Cu. *Am J Clin Nutr* 1998;67:1219–25.
- Turnlund JR. Human whole-body copper metabolism. *Am J Clin Nutr* 1998;67:960S–964S.
- Turnlund JR. Copper. In: Shils ME, Olson JA, Shike M, Ross AC eds. *Modern nutrition in health and disease, 9th ed*. Baltimore: Williams & Wilkins, 1999. Pp 241–52.
- Widdowson EM, Dickerson JWT. Chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral metabolism: an advanced treatise, Vol II. Part A*. New York: Academic Press, 1964. Pp 1–248.