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

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RIBOFLAVIN

BACKGROUND

Riboflavin is a water-soluble vitamin. The bioactive forms of riboflavin are the oxidised and reduced forms of flavin adenine dinucleotide (FAD and FADH₂, respectively) and flavin mononucleotide (FMN and FMNH₂, respectively) (FNB:IOM 1998, McCormick 2000, Thurnham 2000). They function as co-enzymes for key reactions in the catabolism of fuel molecules (eg β -oxidation of fatty acids, Krebs cycle), and in certain biosynthetic pathways (eg fatty acid synthesis). Riboflavin and its derivatives are important for the body's handling of some other nutrients including conversion of vitamin B-6 to its bioactive form, pyridoxal phosphate; conversion of tryptophan to niacin and conversion of methylenetetrahydrofolate (MTHF) to methylTHF by the enzyme methylenetetrahydrofolate reductase (MTHFR).

As methylTHF is essential for the conversion of homocysteine to methionine, riboflavin deficiency can result in raised plasma levels of homocysteine that are associated with increased cardiovascular risk. A cross-sectional study (McNulty et al 2002) suggested that this association is much more likely to occur in individuals with the TT genetic variant of MTHFR (ie homozygous for the C677T polymorphism), which is found in about 12% of humans, than those with the CT or CC variants. Powers (2003) also noted that riboflavin deficiency is often associated with anaemia, which may result from problems in the body's handling of iron.

The metabolism of riboflavin is tightly controlled and depends on the riboflavin status of the individual (Lee & McCormick 1983). Riboflavin is converted to coenzymes mostly in the small intestine, liver, heart and kidney (Brown 1990, Darby 1981). Surplus riboflavin is excreted in urine, either as riboflavin itself (about two-thirds of total excretion) or as a range of metabolites. In deficiency, only small amounts are excreted.

Most of the riboflavin in our foods occurs as the nucleotides FAD/FADH₂ and FMN/FMNH₂ in a complex of food protein (Merrill et al 1981, Nicholalds 1981). This is released as free riboflavin by digestive enzymes in the small intestine and absorbed into the bloodstream. The major sources are milk and milk products and fortified breads and cereals. The bioavailability of riboflavin is high, probably about 95% (Zempleni et al 1996), but our capacity to absorb riboflavin from the small intestine is only moderate.

The classic disease of riboflavin deficiency is ariboflavinosis, which manifests in growth disturbances, seborrhoeic dermatitis, inflammation of the oral mucosa and tongue, cracks at the corner of the mouth and normocytic anaemia (Wilson 1983).

A range of indicators has been used to assess riboflavin status. These include clinical assessment of the classic physical symptoms of deficiency indicating severe deficiency, urinary excretion of riboflavin, erythrocyte flavin levels and determination of the erythrocyte glutathione reductase activity coefficient (EGRAC) in which erythrocyte glutathione reductase is assayed in the presence and absence of added FAD to establish an in vitro activity coefficient. This value provides an indirect indicator of cellular FAD levels and, by extrapolation, an indicator of whole body riboflavin status. Unfortunately, different studies have used different reference ranges for EGRAC. All of these methods are reasonably satisfactory indicators (Hustad et al 2002), however erythrocyte flavin has not been widely used.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

<i>Infants</i>	AI	Riboflavin
0–6 months	0.3 mg/day	
7–12 months	0.4 mg/day	

Rationale: The AI for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of riboflavin in breast milk (0.35 mg/L) from the studies of Roughead & McCormick (1990) and WHO (1965), and rounding (FNB:IOM 1998). The FNM: IOM found that the AI estimate using intake data for thiamine for 7–12 months were unreasonably high when compared to extrapolation data from either younger infants or adults. The AI for 7–12 months was derived from estimating requirements on a body weight basis from the value for younger infants of 0.35 mg/day and from adults, using a metabolic weight ratio, including consideration for growth (0.35 mg/day) and rounding.

<i>Children & adolescents</i>	EAR	RDI	Riboflavin
All			
1–3 yr	0.4 mg/day	0.5 mg/day	
4–8 yr	0.5 mg/day	0.6 mg/day	
Boys			
9–13 yr	0.8 mg/day	0.9 mg/day	
14–18 yr	1.1 mg/day	1.3 mg/day	
Girls			
9–13 yr	0.8 mg/day	0.9 mg/day	
14–18 yr	0.9 mg/day	1.1 mg/day	

Rationale: As there are limited data specific to these age groups, EARs were derived from the adult recommendations using a metabolic body weight ratio estimate including an allowance for growth. The RDI was set assuming a CV of 10% for the EAR.

<i>Adults</i>	EAR	RDI	Riboflavin
Men			
19–30 yr	1.1 mg/day	1.3 mg/day	
31–50 yr	1.1 mg/day	1.3 mg/day	
51–70 yr	1.1 mg/day	1.3 mg/day	
>70 yr	1.3 mg/day	1.6 mg/day	
Women			
19–30 yr	0.9 mg/day	1.1 mg/day	
31–50 yr	0.9 mg/day	1.1 mg/day	
51–70 yr	0.9 mg/day	1.1 mg/day	
>70 yr	1.1 mg/day	1.3 mg/day	

Rationale: The EARs for adults from 19–70 years were based on a series of studies addressing clinical deficiency signs and biochemical markers, including EGRAC, in relation to measured dietary intake (Belko et al 1983, Bessey et al 1956, Boisvert et al 1993, Brewer et al 1946, Davis et al 1946, Horwitt et al 1949, 1950, Keys et al 1944, Kuizon et al 1992, Roe et al 1982, Sebrell et al 1941, Williams et al 1943). The RDI was derived assuming a CV of 10% for the EAR (FNB:IOM 1998).

As energy expenditure decreases with age, it would be expected that the EAR for older people may also decrease. However two studies question this assumption. Boisvert et al (1993) showed that for elderly Guatemalans, normalisation of EGRAC was achieved with 1.3 mg/day riboflavin and that a sharp increase in urinary riboflavin occurred at intakes above 1.0–1.1 mg/day, suggesting that needs were similar to those of younger adults.

A well-controlled UK study of free-living (ie not in residential care) elderly people over 65 years (Madigan et al 1998) showed that in a population where nearly all subjects had intakes above 1.3 mg/day for men and 1.1 mg/day for women, 12% were deficient (>1.4 EGRAC) and a further 33% had low riboflavin status. Thus the EAR for the elderly was set at 1.3 mg/day for men and 1.1 mg/day for elderly women. The RDI was set assuming a CV of 10% for the EAR.

Pregnancy	EAR	RDI	Riboflavin
14–18 yr	1.2 mg/day	1.4 mg/day	
19–30 yr	1.2 mg/day	1.4 mg/day	
31–50 yr	1.2 mg/day	1.4 mg/day	

Rationale: In pregnancy, an additional requirement of 0.3 mg/day is estimated based on increased growth in maternal and fetal tissues and an increase in energy expenditure (FNB:IOM 1998). This added to the requirement for non-pregnant women to give an EAR of 1.2 mg/day. The RDI was set assuming a CV of 10% for the EAR.

Lactation	EAR	RDI	Riboflavin
14–18 yr	1.3 mg/day	1.6 mg/day	
19–30 yr	1.3 mg/day	1.6 mg/day	
31–50 yr	1.3 mg/day	1.6 mg/day	

Rationale: In lactation it is assumed that 0.3 mg/day of riboflavin is transferred into milk. Use of riboflavin for milk production is estimated as 70% (WHO 1965) meaning that 0.4 mg/day is required. This amount is added to the EAR recommended for non-pregnant, non-lactating women and the RDI is set by assuming a CV of 10% for the EAR.

UPPER LEVEL OF INTAKE - RIBOFLAVIN

The upper level of intake cannot be estimated.

No adverse events have been associated with riboflavin consumption as food or supplements so no upper level of intake can be set. Studies using large doses of riboflavin have been undertaken, but they were not designed to assess adverse effects systematically (Schoenen et al 1998, Stripp 1965, Zempleni et al 1996). The only evidence of adverse effects comes from in vitro studies indicating a potential increase in photosensitivity to ultraviolet radiation (Ali et al 1991, Floersheim 1994, Spector et al 1995).

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