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

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BIOTIN

BACKGROUND

Biotin is a cofactor for four carboxylase enzymes found in mammals – pyruvate carboxylase, methyl-crotonyl-CoA carboxylase, proprionyl-CoA carboxylase and acetyl-CoA carboxylase. The first three of these are mitochondrial and the fourth is both mitochondrial and cytosolic. They are involved in a range of actions including catabolising acetyl CoA, carboxylation of pyruvate, degradation of leucine and carboxylation of proprionyl-CoA. Biotin is found in free and protein-bound forms in food but little is known about its bioavailability. It is found in the protein-bound form in meats and cereals, although it seems to be less bioavailable in the latter (Mock 1996).

There are very few data about the biotin content of foods. Liver is known to be a very concentrated source, providing 100 µg/100 g compared to only 1 µg/100 g in meats and plant foods. Avidin, a protein found in raw egg white, binds biotin in the gut and prevents its absorption (Mock 1996). In the intestines, biotin is transported across the brush border membrane by a biotin carrier, against a sodium ion gradient. It can also be synthesised by intestinal microflora (Bonjour 1991) but it is not clear whether this is an additional potential source in humans. About half the biotin undergoes metabolism to bisnorbiotin and biotin sulfoxide before excretion. Urinary excretion and serum concentrations of biotin and its metabolites increase in similar proportions in response to intravenous or oral administration of large doses (Mock & Heird 1997, Zempleni et al 1997).

Although rare, biotin deficiency has been seen in people who consume raw egg white over long periods (Baugh et al 1968) and in total parenteral nutrition. Symptoms include dermatitis, conjunctivitis, alopecia and CNS abnormalities, including developmental delay in infants (Mock 1996). People with genetic biotinidase deficiency will have increased requirements.

The most useful information about requirements comes from assessment of clinical signs in patients on biotin-free intravenous nutrition, in those eating raw egg white or from the results of biotin bioavailability and pharmacokinetic experiments. The most sensitive end points are decreased biotin excretion and/or increased 3-hydroxyisovalerate excretion (Mock et al 1997a, 2002a).

Evidence about biotin requirements is not sufficient to set an EAR and RDI so AIs were set based on extrapolation from data on infants, and on some population intake data from New Zealand for people over 15 years of age (LINZ 1992).

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Biotin**
0–6 months	**5 µg/day**	
7–12 months	**6 µg/day**	

***Rationale*:** The AI for 0–6 months was set by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of biotin in breast milk (6 µg/L) from the studies of Hirano et al (1992), Paul & Southgate (1978) and Salmentera et al (1985). The AI for 7–12 months was extrapolated from the AI for younger infants using the reference body weight method.

Children & adolescents	AI	Biotin
All		
1–3 yr	**8 µg/day**	
4–8 yr	**12 µg/day**	
Boys		
9–13 yr	**20 µg/day**	
14–18 yr	**30 µg/day**	
Girls		
9–13 yr	**20 µg/day**	
14–18 yr	**25 µg/day**	

***Rationale*:** In the absence of adequate data, the AIs for children and adolescents were extrapolated from those for infants using the relative body weight extrapolation with an allowance for growth, and rounding up. Using a food data base developed by DSIR in New Zealand, population intake data from New Zealand (LINZ 1992) gave a median intake of 37.9 µg/day for males aged 15–18 years and 26.7 µg/day for females aged 15–18 years. There are no population intake data for Australia.

Adults	AI	Biotin
Men		
19–30 yr	**30 µg/day**	
31–50 yr	**30 µg/day**	
51–70 yr	**30 µg/day**	
>70 yr	**30 µg/day**	
Women		
19–30 yr	**25 µg/day**	
31–50 yr	**25 µg/day**	
51–70 yr	**25 µg/day**	
>70 yr	**25 µg/day**	

***Rationale*:** In the absence of adequate data, the AIs for adults were extrapolated from those for infants using relative body weights with an allowance for growth. Use of the DSIR data base, population intake data from New Zealand (LINZ 1992) gave an estimated median intake of 33 µg/day for men 19 years and over and 27 µg/day for women. There are no population intake data for Australian children.

Pregnancy	AI	Biotin
14–18 yr	**30 µg/day**	
19–30 yr	**30 µg/day**	
31–50 yr	**30 µg/day**	

Rationale: Studies by Mock & Stadler (1997) and Mock et al (1997b, 2002b) have raised questions about the adequacy of biotin status in pregnancy. Some studies have detected low plasma concentrations of biotin and its metabolites in pregnancy (Bhagavan 1969, Dostalova 1984) but others have not (Mock & Stadler 1997). Emerging evidence suggests that marginal biotin deficiency is teratogenic (Zempleni & Mock 2000). More evidence is needed to assess whether lower plasma concentrations in pregnancy are a natural consequence of haemodilution or indicate inadequate intake. The AI for pregnancy was increased over that of the non-pregnant mother in line with the additional body size associated with placental and fetal tissues.

Lactation	AI	Biotin
14–18 yr	**35 µg/day**	
19–30 yr	**35 µg/day**	
31–50 yr	**35 µg/day**	

***Rationale*:** The AI in lactation was set to cover the additional amount of biotin secreted in milk (5 µg/day).

UPPER LEVEL OF INTAKE - BIOTIN

There is insufficient evidence of adverse effects in humans or animals to set a UL for any age.

Two rat studies showed effects on inhibition of fetal and placental growth and resorption of fetuses (Paul & Duttagupta 1975, 1976) but both used very high doses of injected biotin without a control group. The data were therefore not useful for setting human ULs. In *ex vivo* experiments, 600 µg biotin produced a significant reduction of 33% or greater in mitogen-induced proliferation and cytokine-response of lymphocytes (Zempleni et al 2001). These biomarkers are indicative of a weakened immune response but are not sufficient to allow the setting of a UL. It is unlikely that current levels of intake would be associated with adverse health effects.

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