The following is an extract from:

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

ENDORSED BY THE NHMRC ON 9 SEPTEMBER 2005

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The Nutrient Reference Values (NRVs) was a joint initiative of the Australian National Health and Medical Research Council (NHMRC) and the New Zealand Ministry of Health (MoH). The NHMRC would like to thank the New Zealand MoH for allowing the use of the NRV material in the development of this website.

VITAMIN A

BACKGROUND

Vitamin A is a fat-soluble vitamin which helps maintain normal reproduction, vision and immune function. It comes in a number of forms (as retinol, retinal, retinoic acid or retinyl ester).

The term vitamin A is used in the context of dietary requirements to include provitamin A carotenoids that are dietary precursors of retinol. Of the many carotenoids in nature, several have provitamin A activity but food composition data are only readily available for α-carotene, β-carotene and β-cryptoxanthin. Preformed vitamin A is found only in animal-derived foods, whereas dietary carotenoids are found primarily in oils, fruits and vegetables.

Vitamin A intakes or requirements are generally expressed in terms of retinol equivalents (RE). One RE is defined as the biological activity associated with 1 μg of all-*trans* retinol. Although there is some ongoing discussion in the literature about the conversion rates for carotenes, 6 μg all-*trans* β-carotene and 12 μg of α-carotene, β-cryptoxanthin and other provitamin A carotenoids have been retained as the conversion figures as being equivalent to 1 RE. These traditional conversion rates align more with the sources of carotenes in the Australian and New Zealand diets. They are also in line with the most recent decision of the FAO, (FAO:WHO 2001) who concluded that the literature to date was insufficient to justify a change in conversion rates.

1 μg Retinol Equivalent	=	1 μg of all-*trans* retinol
	=	6 μg all-*trans* β-carotene
	=	12 μg of α-carotene, β-cryptoxanthin and other provitamin A carotenoids
1 International Unit (IU) retinol	=	0.3 μg Retinol Equivalents

Retinol is required for the integrity of epithelial cells throughout the body (Gudas et al 1994). Retinoic acid regulates the expression of various genes that encode structural proteins, enzymes, extracellular matrix proteins and retinol binding proteins and receptors. Retinoic acid plays an important role in embryonic development, particularly in the development of the spinal cord and vertebrae, limbs, heart, eye and ears (Morris-Kay & Sokolova 1996). It is also required to maintain differentiation of the cornea and conjunctiva, preventing xerophthalmia, as well as for photoreceptor rod and cone cells in the retina (Sommer & West 1996). The retinal form of vitamin A is also required by the eye to change light to neural signals for vision (Saari 1994). Retinol and its metabolites are necessary for maintenance of immune function (Katz et al 1987, Trechsel et al 1985, Zhao & Ross 1995).

An adequate supply of vitamin A also plays a role in preventing morbidity and mortality from infectious disease, particularly in children (Glasziou & Mackerras 1993). Infection and infestation can cause malabsorption of vitamin A (Mahalanabis et al 1979, Sivakumar & Reddy 1972, 1975). The matrix of foods eaten can affect the release of carotenoids from foods, however, processing of food (cutting up, cooking etc) greatly improves availability and thus absorption of carotenoids from foods (Micozzi et al 1992, Tang et al 2000, Torronen et al 1996). Some studies show improved absorption of carotenoids with increased fat intake (Jalal et al 1998, Reddy & Srikantia 1966, Roels et al 1963) but the data are not consistent (Borel et al 1997, Figuera et al 1969).

Positive interactions between iron or zinc status and vitamin A status have been reported in animal studies (Amine et al 1970, Rosales et al 1999) or within human population groups in developing countries (Bloem et al 1989) but the relevance to the Australia and New Zealand population is unclear. Deficiency can result in abnormal dark adaptation, followed by xerophthalmia but is uncommon in Australia and New Zealand. The New Zealand Children's Survey, 2002 (MOH 2003) did, however, state

that a significant proportion of Pacific children and Maori males might be at risk of inadequate intakes. Chronically high levels of alcohol ingestion can negatively affect vitamin A status through an effect on the liver (Wang 1999).

Vitamin A status has been assessed using a variety of indicators including a dark adaptation test (Carney & Russell 1980), a pupillary response test (Stewart & Young 1989), plasma retinol concentration (Underwood 1984), total liver reserves by isotope dilution (Bausch & Rietz 1977, Furr et al 1989), relative dose response methods (Amedee-Manesme et al 1984, 1987, Loerch et al 1979, Mobarhan et al 1981) and/or immune function assessment (Butera & Krakowka 1986, Carman et al 1989, 1992, Cohen & Elin 1974, Friedman & Sklan 1989, Smith et al 1987). However, these methods have limitations in the context of setting EARs for the population. They are too specific (ie only related to visual outcomes), accurate only across a limited intake range or susceptible to confounding (FNB:IOM 2001).

The method used to set the EARs in the current document was thus based on an estimate of the amount of dietary vitamin A required to maintain a given body-pool size in well-nourished subjects (Olson 1987, FNB:IOM 2001). The modifications to this approach that were needed to determine requirements for specific age groups or for pregnancy and lactation are noted below.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	AI	Vitamin A
0–6 months	250 µg/day of retinol (as retinyl esters)	
7–12 months	430 µg/day of retinol equivalents (REs)	

Rationale: The AI for 0–6 months of 250 µg retinol as retinyl esters is calculated from multiplying the average intake of breast milk (0.78 L/day) by the average concentration of retinol present as retinyl esters in human milk, 310 µg/L, (Canfield et al 2003) to give 242 µg retinol, and rounding up. It assumes no contribution from carotenes in breast milk. For 7–12 months, the equivalent calculation is average intake of breast milk (0.6 L/day) x concentration of retinol (310 µg/L) plus a contribution of 244 µg from complementary foods that includes some contribution from carotenes, giving an AI of 430 RE.

Children & adolescents	EAR	RDI	Vitamin A (as retinol equivalents)
All			
1–3 yr	210 µg/day	300 µg/day	
4–8 yr	275 µg/day	400 µg/day	
Boys			
9–13 yr	445 µg/day	600 µg/day	
14–18 yr	630 µg/day	900 µg/day	
Girls			
9–13 yr	420 µg/day	600 µg/day	
14–18 yr	485 µg/day	700 µg/day	

Rationale: No data are available to estimate average requirement of children and adolescents. The computational method used by the US:Canadian DRI committee (FNB:IOM 2001) was adopted for setting the EAR. The RDI was set by using a CV for the EAR of 20% based on calculated half-life values for liver vitamin A and rounded to the nearest 100 µg.

Adults	EAR	RDI	Vitamin A (as retinol equivalents)
Men			
19–30 yr	625 µg/day	900 µg/day	
31–50 yr	625 µg/day	900 µg/day	
51–70 yr	625 µg/day	900 µg/day	
>70 yr	625 µg/day	900 µg/day	
Women			
19–30 yr	500 µg/day	700 µg/day	
31–50 yr	500 µg/day	700 µg/day	
51–70 yr	500 µg/day	700 µg/day	
>70 yr	500 µg/day	700 µg/day	

Rationale: The computational approach of the US:Canadian DRI committee (FNB:IOM 2001) was adopted. This is based on the amount of dietary vitamin A required to maintain a given body-pool size in well-nourished subjects.

The formula used was: Average requirement = A x B x C x D x E x F where:

A = % body vitamin A stores lost per day when ingesting a vitamin A-free diet, B = minimum acceptable liver vitamin A reserve, C = liver weight:body weight ratio, D = reference weight for a specific age group and gender, E = ratio of total body:liver vitamin A reserves and F = efficiency of storage of ingested vitamin A. The RDI was set using a CV of 20% for the EAR, with rounding to the nearest 100 µg.

Pregnancy	EAR	RDI	Vitamin A (as retinol equivalents)
14–18 yr	530 µg/day	700 µg/day	
19–30 yr	550 µg/day	800 µg/day	
31–50 yr	550 µg/day	800 µg/day	

Rationale: Direct studies are lacking. The model used to set the EAR is the US:Canadian DRI approach based on the accumulation of vitamin A in the liver of the fetus during gestation and an assumption that liver contains approximately 50% of the body's vitamin A when liver stores are low, as for newborns. The RDI was set on the basis of a CV of 20% for the EAR with rounding to the nearest 100 µg.

Lactation	EAR	RDI	Vitamin A (as retinol equivalents)
14–18 yr	780 µg/day	1,100 µg/day	
19–30 yr	800 µg/day	1,100 µg/day	
31–50 yr	800 µg/day	1,100 µg/day	

Rationale: An average of 250 µg/day retinol (AI for infants 0–6 months) is added to the EAR for non-pregnant adolescent girls and women. The RDI was set assuming a CV of 20% for the EAR, with rounding to the nearest 100 µg.

UPPER LEVEL OF INTAKE - VITAMIN A AS RETINOL

Infants

0–12 months	600 μg/day

Children and adolescents

1–3 yr	600 μg/day
4–8 yr	900 μg/day
9–13 yr	1,700 μg/day
14–18 yr	2,800 μg/day

Adults 19+ yr

Men	3,000 μg/day
Women	3,000 μg/day

Pregnancy

14–18 yr	2,800 μg/day
19–50 yr	3,000 μg/day

Lactation

14–18 yr	2,800 μg/day
19–50 yr	3,000 μg/day

Rationale: The UL is set based on causality, quality and completeness of available data. The critical adverse event used for women of childbearing age was teratogenicity and for other adults it was liver abnormalities, notably abnormal liver pathology (FNB:IOM 2001). For infants, reports of hypervitaminosis A were used to derive the UL. There was a paucity of evidence for children and adolescents, so the UL was determined by extrapolation from adult data on the basis of relative body weight.

Those with high alcohol intake, pre-existing liver disease, hyperlipidaemia or severe protein malnutrition may be particularly susceptible to excess intake of preformed vitamin A and may not be protected by the UL for the general population.

UPPER LEVEL OF INTAKE - BETA-CAROTENE

The UL for β-carotene cannot be established for supplemental use and does not need to be established for food use.

Rationale: Although β-carotene is a precursor of vitamin A, excess intake has not been associated with vitamin A toxicity in humans as the metabolic conversion of β-carotene is regulated by vitamin A status. Beta-carotene is of low toxicity in both animals and humans. Until recently, β-carotene was thought to be without adverse effect other than a yellowing of the skin that occurred after sustained high intake. However, human studies in the 1990s have indicated that excess intake through supplements (20 mg/day or more) by smokers and subjects previously exposed to asbestos has been associated with an increased risk of lung cancer (ATBC trial 1994, Omenn et al 1996). However, there is insufficient scientific basis to set a precise figure for an UL for β-carotene, as no dose-response relationship for the observed effects is available either from the intervention trials in humans or from appropriate animal models (FNB:IOM 2000, European Commission 2000).

In conclusion, there is insufficient evidence to establish a UL for β-carotene for supplemental use, but high intakes can cause yellowing of the skin and may be harmful to smokers. A UL for β-carotene from food does not need to be established, based on an absence of adverse effects.

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