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

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VITAMIN B_6

BACKGROUND

Vitamin B_6 comprises six compounds – pyridoxal, pyridoxine, pyridoxamine and their respective 5' phosphates (see table below). It acts as a coenzyme in the metabolism of amino acids, glycogen and sphingoid bases. The most common form in human tissue is the 5'-phosphate form of pyridoxal (PLP) most of which is found in muscle bound to phosphorylase. The second most common is the 5'-phosphate form of pyridoxamine (PMP). Plant foods contain primarily pyridoxine (PN) and its 5'-phosphate (PNP), sometimes in the form of a glucoside.

Absorption in the gut involves phosphatase-mediated hydrolysis and transport of the non-phosphorylated form to the mucosal cells. Quite large doses of PLP and PMP are well absorbed (Hamm et al 1979). PN glucoside is less well absorbed. Most of the absorbed non-phosphorylated vitamin B_6 goes to the liver where conversion to the phosphorylated form occurs. The major excretory product is 4-pyridoxic acid that accounts for about half the B_6 compounds in urine (Shultz & Leklem 1981).

FORMS AND EQUIVALENCE OF VITAMIN B_6 COMPOUNDS

Units of measurement			
Pyridoxine (PN)	1g = 5.9 mmol	1mmol = 170 mg	Three naturally inter-convertible forms in the tissues
Pyridoxal (PL)	1g = 6.0 mmol	1mmol = 167 mg	
Pyridoxamine (PM)	1g = 6.0 mmol	1mmol = 168 mg	
Pyridoxal-5-phosphate (PLP)	1g = 4.1 mmol	1mmol = 247 mg	Principal active form
4-Pyridoxic acid (4-PA)	1g = 5.5 mmol	1mmol = 183 mg	Principal excretory form
Pyridoxine hydrochloride (PN.HCl)	1g = 4.9 mmol	1mmol = 206 mg	Usual form of supplements

Vitamin B_6 is found in a wide range of foods including organ meats, muscle meats, breakfast cereals, vegetables and fruits. Bioavailability is generally in the region of 75% in a mixed diet (Tarr et al 1981). It has been proposed that vitamin B_6 requirements may be increased at higher protein intake (Baker et al 1964, Hansen et al 1996a, Linkswiler 1978), although other studies have not shown this (Pannemans et al 1994). Nevertheless, protein intake is generally taken into consideration in setting requirements for vitamin B_6.

Clinical deficiency is rare. The symptoms of deficiency include seborrhaeic dermatitis (Mueller & Vilter 1950), microcytic anaemia (Snyderman et al 1953), convulsions (Bessey et al 1957, Coursin 1954) and depression and confusion (Hawkins & Barsky 1948).

Indicators used to assess requirements have ranged from measures of vitamin concentrations in plasma, blood cell or urine to functional measures such as erythrocyte aminotransferase saturation by pyridoxal 5'-phosphate or tryptophan metabolites. Most of these indicators change with dietary intake, but there is little information about what level would indicate a deficiency state. A review (Lui et al 1985) suggested that plasma PLP is probably the best single indicator as it reflects tissue stores.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**		**Vitamin B_6**
0–6months	**0.1 mg/day**		
7–12 months	**0.3 mg/day**		

***Rationale*:** The AI for 0–6 months is calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of vitamin B_6 present in human milk (0.13 mg/L) based on the studies of West & Kirksey (1976). For 7–12 months, the AI was extrapolated from that of the younger infants using a metabolic weight ratio (FNB:IOM 1998).

Children & adolescents	**EAR**	**RDI**	**Vitamin B_6**
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**	**1.0 mg/day**	
14–18 yr	**1.1 mg/day**	**1.3 mg/day**	
Girls			
9–13 yr	**0.8 mg/day**	**1.0 mg/day**	
14–18 yr	**1.0 mg/day**	**1.2 mg/day**	

***Rationale*:** As there are few data on children and adolescents, the EARs were set based on the adult EARs adjusted for metabolic body weight and growth (FNB:IOM 1998). In the absence of information on the standard deviation of requirement, the RDI was set assuming a CV of 10% for the EAR.

Adults	**EAR**	**RDI**	**Vitamin B_6**
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	**1.4 mg/day**	**1.7 mg/day**	
>70 yr	**1.4 mg/day**	**1.7 mg/day**	
Women			
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	**1.3 mg/day**	**1.5 mg/day**	
>70 yr	**1.3 mg/day**	**1.5 mg/day**	

***Rationale*:** Clinical deficiency is rarely seen at intakes below 0.5 mg/day, but various depletion-repletion studies suggest an average daily requirement of 1.1 mg/day in younger men for maintenance of tissue stores, although the range of study results was quite wide (Baker et al 1964, FNB:IOM 1998, Linkswiler 1978, Miller & Linkswiler 1967, Miller et al 1985, Selhub et al 1993, Yess et al 1964). For younger women, the average requirement seems to be similar (Brown et al 1975, FNB:IOM 1998, Hansen et al 1996a,b, 1997, Huang et al 1998, Kretsch et al 1995). The EAR appears to be higher for older people (Madigan et al 1998) and men have higher requirements than women. The increase due to age and gender appears to be about 0.2 to 0.3 mg of food vitamin B_6 per day. RDIs for all groups were set assuming a CV of 10% for the EAR.

Pregnancy	EAR	RDI	Vitamin B_6
14–18 yr	1.6 mg/day	1.9 mg/day	
19–30 yr	1.6 mg/day	1.9 mg/day	
31–50 yr	1.6 mg/day	1.9 mg/day	

***Rationale*:** The EAR in pregnancy was based on additional requirements shown by studies of changes in plasma concentrations in pregnancy, fetal sequestration data and supplemental studies (Cleary et al 1975, Hamfelt & Tuvemo 1972, Contractor & Shane 1970, Shane & Contractor 1980, Lumeng et al 1976) that suggested that an additional allowance of 0.5 mg/day was justifiable. Because of the approximation of this figure, the adolescent EAR was set at the same level as that for older women. The RDI was set assuming a CV of 10% for the EAR.

Lactation	EAR	RDI	Vitamin B_6
14–18 yr	1.7 mg/day	2.0 mg/day	
19–30 yr	1.7 mg/day	2.0 mg/day	
31–50 yr	1.7 mg/day	2.0 mg/day	

***Rationale*:** The vitamin B_6 in breast milk varies according to maternal vitamin B_6 levels. The amount of vitamin B_6 required to increase breast milk by a small increment is much higher than that increment. Accordingly, the additional requirement in lactation is higher than that suggested by the amount secreted in milk (Borschel et al 1986, West & Kirksey 1976). To ensure a breast milk vitamin B_6 concentration of 0.13 mg/L, five times that amount must be consumed in addition to the EAR of 1.1 mg for non-lactating women. Because of the approximation of the estimate, the adolescent EAR was set as for older women. The RDI is set assuming a CV of 10% for the EAR.

UPPER LEVEL OF INTAKE - VITAMIN B_6 AS PYRIDOXINE

Infants	
0–12 months	**Not possible to establish; source of intake should be breast milk, formula or food only**
Children and adolescents	
1–3 yr	**15 mg/day**
4–8 yr	**20 mg/day**
9–13 yr	**30 mg/day**
14–18 yr	**40 mg/day**
Adults 19+ yr	
Men	**50 mg/day**
Women	**50 mg/day**
Pregnancy	
14–18 yr	**40 mg/day**
19–50 yr	**50 mg/day**
Lactation	
14–18 yr	**40 mg/day**
19–50 yr	**50 mg/day**

***Rationale*:** The ULs were set using results of studies involving long-term oral administration of pyridoxine at doses of less than 1g/day (Berger & Schaumburg 1984, Bernstein & Lobitz 1988, Dalton 1985, Dalton & Dalton 1987, Del Tredici et al 1985, FNB:IOM 1998, Parry & Bredesen 1985). A NOAEL of 200 mg/day was identified from the studies of Bernstein & Lobitz (1988) and Del Tredici et al (1985). These studies involved subjects who had generally been on the supplements for 5 to 6 months or less. The study of Dalton and Dalton (1987), however, suggested that symptoms might take substantially longer than this to appear. In this latter retrospective survey, subjects who reported symptoms had been on supplements for 2.9 years on average. Those reporting no symptoms had taken supplements for 1.9 years. Symptoms disappeared 6 months after cessation of supplements. Given these findings, a UF of 4 was used to derive the UL based on the limitations of the data involving pyridoxine doses of less than 500 mg/day (Berger & Schaumburg 1984, Parry & Bredesen 1985, Dalton 1985, Dalton & Dalton 1987, FNB:IOM 1998) and the limited duration of the studies. The UL for adults was thus set at 50 mg/day. The same figure was set for pregnancy and lactation as there is no evidence of teratogenicity at this level. The UL was set based on metabolic body size and growth considerations for all other ages and life stages except infancy. It was not possible to set a UL for infants, so intake is recommended in the form of food, milk or formula.

REFERENCES

Baker EM, Canham JE, Nunes WT, Sauberlich HE, McDowell ME. Vitamin B_6 requirement for adult men. *Am J Clin Nutr* 1964;15:59–66.

Berger A, Schaumburg HH. More on neuropathy from pyridoxyl abuse. *N Engl J Med* 1984;311:986–7.

Bernstein A, Lobitz CS. A clinical and electrophysiologic study of the treatment of painful diabetic neuropathies with pyridoxine. In: Leklem JE, Reynolds RD, eds. *Clinical and physiological applications of vitamin B_6. Current topics in nutrition and disease.* New York: Alan R. Liss, 1988. Pp 415–23.

Bessey OA, Adam DJ, Hansen AE. Intake of vitamin B_6 and infantile convulsions: a first approximation of requirements of pyridoxine in infants. *Paediatrics* 1957;20:33–44.

Borschel MW, Kirksey A, Hanneman RE. Effects of vitamin B_6 intake on nutriture and growth of young infants. *Am J Clin Nutr* 1986;43:7–15.

Brown RR, Rose DP, Leklem JE, Linkswiler H, Arand R. Urinary 4-pyridoxic acid, plasma pyridoxyl phosphate and erythrocyte aminotransferase levels in oral contraceptive users receiving controlled intakes of vitamin B_6. *Am J Clin Nutr* 1975;28:10–9.

Cleary RE, Lumeng L, Li TK. Maternal and fetal plasma levels of pyridoxal phosphate at term: adequacy of vitamin B_6 supplementation during pregnancy. *Am J Obstet Gynecol* 1975;121:25–8.

Contractor SF, Shane B. Blood and urine levels of vitamin B_6 in the mother and fetus before and after loading of the mother with vitamin B_6. *Am J Obstet Gynecol* 1970;107:635–40.

Coursin DB. Convulsive seizures in infants with pyridoxine-deficient diet. *JAMA* 1954;154:406–8.

Dalton K. Pyridoxine overdose in premenstrual syndrome. *Lancet* 1985;i:1168–9

Dalton K, Dalton MJT. Characteristics of pyridoxine overdose neuropathy syndrome. *Acta Neurol Scand* 1987;76:8–11

Del Tredici AM, Bernstein AL, Chinn K. Carpel tunnel syndrome and vitamin B_6 therapy. In: Reynolds RD, Leklem JD, eds. *Vitamin B_6: its role in health and disease. Current topics in nutrition and disease.* New York: Alan R. Liss,1985. Pp 459–62.

Food and Nutrition Board: Institute of Medicine (FNB:IOM). *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic acid, Biotin and Choline.* Washington, DC: National Academy Press,1998.

Hamfelt A, Tuvemo T. Pyridoxyl phosphate and folic acid concentration in blood and erythrocyte aspartate aminotransferase activity during pregnancy. *Clin Chim Acta* 1972;41:287–98.

Hamm MW, Mehansho H, Henderson LM. Transport and metabolism of pyridoxamine and pyridoxamine phosphate in the small intestine of the rat. *J Nutr* 1979;109:1552–9.

Hansen CM, Leklem JE, Miller LT. Vitamin B_6 status of women with a constant intake of vitamin B_6 changes with three levels of dietary protein. *J Nutr* 1996a;126:1891–901.

Hansen CM, Leklem JE, Miller LT. Vitamin B_6 status indicators decrease in women consuming a diet high in pyridoxine glucoside. *J Nutr* 1996b;126:2512–8.

Hansen CM, Leklem JE, Miller LT. Changes in vitamin B_6 status indicators of women fed a constant protein diet with varying levels of vitamin B_6. *Am J Clin Nutr* 1997;66:1379–87.

Hawkins WW, Barsky J. An experiment on human vitamin B_6 deprivation. *Science*, 1948;108:284–6.

Huang Y-C, Chen W, Evans MA, Mitchell ME, Shultz TD. Vitamin B_6 requirement and status assessment of young women fed a high-protein diet with various levels of vitamin B_6. *Am J Clin Nutr* 1998;67:208–20.

Kretsch MJ, Sauberlich HE, Skala JH, Johnson Hl. Vitamin B_6 requirement and status assessment: young women fed a depletion diet followed by a plant-or animal-protein diet with graded amounts of vitamin B_6. *Am J Clin Nutr* 1995;61:1091–101.

Linkswiler HM. Vitamin B_6 requirements of men. In: *Human vitamin B_6 requirements: proceedings of a workshop*. Washington, DC: National Academy of Sciences, 1978. Pp 279–90.

Lui A, Lumeng L, Aronoff GR, Li T-K. Effect of oral contraceptives on the plasma concentration of pyridoxyl phosphate. *Am J Clin Nutr* 1985;27:326–33.

Lumeng L, Clearey RE, Wagner R, Pao-Lo Y, Li TK. Adequacy of vitamin B_6 supplementation during pregnancy: a prospective study. *Am J Clin Nutr* 1976;29:1376–83.

Madigan SM, Tracey F, McNulty H, Eaton-Evans J, Coulter J, McCartney H, Strain JJ. Riboflavin and vitamin B-6 intakes and status, and biochemical response to riboflavin supplementation, in free-living elderly people. *Am J Clin Nutr* 1998;68:389–95.

Miller LT, Leklem JE, Shulktz TD. The effect of dietary protein on the metabolism of vitamin B_6 in humans. *J Nutr* 1985;115:1663–72.

Miller LT, Linkswiler H. Effect of protein intake on the development of abnormal tryptophan metabolism by men during vitamin B_6 depletion. *J Nutr* 1967;93:53–9.

Mueller JF, Vilter RW. Pyridoxine deficiency in human beings being induced by desoxypyridoxine. *J Clin Invest* 1950;29:193–201.

Pannemans DL, van den Berg H, Westerterp KR**.** The influence of protein intake on vitamin B-6 metabolism differs in young and elderly humans. *J Nutr* 1994;124:1207–14.

Parry GJ, Bredesen DE. Sensory neuropathy with low-dose pyridoxine. *Neurology* 1985;35:1466–8.

Selhub J, Jacques PF, Wilson PWF, Rush D, Rosenberg H. Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. *JAMA* 1993;270:2693–8.

Shane B, Contractor SF. Vitamin B_6 status and metabolism in pregnancy. In: Tryfiates GP, ed. *Vitamin B_6 metabolism and role in growth*. Westport, CT: Food & Nutrition Press, 1980. Pp 137–71.

Shultz TD, Leklem JE. Urinary 4-pyridoxic acid, urinary vitamin B_6 status and dietary intake in adults. In: Leklem JE, Reynolds RD, eds. *Methods in vitamin B_6 nutrition*. New York: Plenum Press, 1981. Pp 250–65.

Snyderman SE, Holt LE, Carretero R, Jacobs K. Pyridoxine deficiency in the human infant. *Am J Clin Nutr* 1953;1:200.

Tarr JB, Tamura T, Stokstad EL. Availability of vitamin B_6 and pantothenate in an average American diet in man. *Am J Clin Nutr* 1981;62:802–8.

West KD, Kirksey A. Influence of vitamin B_6 intake on the content of the vitamin in human milk. *Am J Clin Nutr* 1976;29:961–9.

Yess N. Price J, Brown RR, Swan PB, Linkswiler H. Vitamin B6 depletion in man: urinary excretion of tryptophan metabolites. *J Nutr* 1964;84:229–36.