10. Vitamin B_6

Physiology and metabolism

Six different chemical forms of vitamin B_6 occur in foods: pyridoxine, pyridoxal, pyridoxamine and their phosphates. They are readily interconvertible in the body, giving rise to the metabolically active coenzyme pyridoxal phosphate.

The principal metabolic function of pyridoxal phosphate is as the coenzyme in reactions of amino acids. It is also required for the enzyme glycogen phosphorylase in muscle and liver, and in the metabolism of polyunsaturated fatty acids and phospholipids, and has a role in the function of steroid hormones, acting to release hormone-receptor complexes from tight nuclear binding, and so terminate the actions of the hormone [1,2].

The phosphate forms of vitamin B_6 are dephosphorylated in the intestinal lumen; pyridoxine, pyridoxal and pyridoxamine are all taken up from the small intestine by an energy-dependent process. The various vitamers are readily converted to pyridoxal phosphate in tissues. Pyridoxal phosphate which is not bound to enzymes in tissues is oxidised to 4-pyridoxic acid, the major metabolite of the vitamin excreted in the urine.

A proportion of the vitamin B_6 in plant foods is biologically unavailable, because it is present as pyridoxine glycosides which are not hydrolysed by intestinal enzymes. While the glycosides may be absorbed, they are not used in the body, but are excreted unchanged in the urine.

Some 80% of the body's vitamin B_6 is associated with the enzyme glycogen phosphorylase in muscle. As glycogen reserves are depleted in prolonged fasting, so the vitamin is released from muscle, and made available for the synthesis of glucose from amino acids in the liver. However, muscle pyridoxal phosphate is not released in vitamin B_6 deficiency, so the muscle reserves cannot be regarded as storage of the vitamin.

Deficiency and excess

Gross clinical deficiency of vitamin B_6 is extremely rare; the vitamin is widely distributed in foods, and intestinal flora synthesise relatively large amounts, some of which may be available.

Much of our knowledge of human deficiency comes from an 'outbreak' in the early 1950s, resulting from an infant milk preparation which had undergone severe heating in manufacture, leading to the formation of a biologically inactive complex between pyridoxal (and pyridoxal phosphate) and lysine in proteins. In addition to abnormalities of the metabolism of tryptophan, methionine and other amino acids, the affected infants convulsed. They responded to supplements of vitamin B_6 [3].

Intakes of vitamin B_6 in excess of 500 mg/day are associated with the development of peripheral sensory neuropathy, which is only partially reversible on return to more appropriate intakes [4]. Similar symptoms have been reported in subjects taking doses of 50-500 mg /day. Intakes of more than 50 mg /day must therefore be regarded as potentially harmful [5].

Requirements

Adults

Although 80% of the body's vitamin B_6 is in muscle, this pool turns over relatively slowly, and requirements are closely related to protein intake. Attempts to estimate requirements by measurement of the turnover of body pools have not yielded useful results, and current estimates are based on changes in tryptophan and methionine metabolism, and the decline in blood concentrations of vitamin B_6 during experimental depletion / repletion studies.

Biochemical indices of vitamin B_6 status decline more rapidly in subjects receiving high protein intakes (80-160g /day) than in those receiving low intakes of protein (30-50g /day). Similarly, restoration of indices of vitamin B_6 nutritional status during repletion occurs faster in subjects receiving lower intakes of protein [6,7,8,9]. Such studies suggest that the average vitamin B_6 requirement is 13 µg/g dietary protein. Allowing for individual variation gives a Population Reference Intake of 15 µg vitamin B_6/g dietary protein, and suggests a Lower Threshold Intake of 11 µg/g protein, although there is no experimental evidence to support this lower figure.

The relationship with protein intake may not be valid at low intakes of protein, or under conditions of restricted food intake, when amino acids will be catabolised for energy-yielding metabolism.

High-oestrogen oral contraceptives cause changes in tryptophan metabolism which have been widely interpreted as indicating vitamin B_6 depletion. However, relatively large intakes of the vitamin are required to normalise tryptophan metabolism in women taking oral contraceptives, and other indices of vitamin B_6 nutritional status are generally unaffected by contraceptives. It seems most likely that the derangement of tryptophan metabolism is due to direct effects of oestrogens or their metabolites on tryptophan metabolism. There is no evidence for an increased requirement for vitamin B_6 in women using oral contraceptives [2].

Children

There is no evidence that children have a requirement for vitamin B_6 different from that for adults, i.e. a Population Reference Intake of 15 µg/g dietary protein. It is reasonable to assume that children in the EC have a diet similar to that of adults, providing some 15% of energy from protein.

Pregnancy

Plasma concentrations of pyridoxal phosphate fall markedly and progressively through pregnancy, although erythrocyte transaminase activation coefficients and excretion of 4-pyridoxic acid are normal. The drop of plasma pyridoxal phosphate appears to be a consequence of the preferential uptake of the vitamin by the fetus, and a normal feature of pregnancy. Supplements of 2.5-4 mg/day are required to maintain the plasma concentration of pyridoxal phosphate at the pre-pregnancy level [10]. This is considered neither necessary or desirable, and the same PRI is proposed for pregnancy as in non-pregnant women – 15 µg/g dietary protein. On the extra protein intake recommended during pregnancy, this will result in an increase in the amount of dietary vitamin B_6.

Lactation

There is no evidence that vitamin B_6 metabolism is changed by lactation, and there appears to be no reason for changing the recommendation from that for non-lactating women – 15 µg /g dietary protein. This will provide vitamin B_6 at a higher level than is secreted in milk, and the extra protein intake recommended during lactation will result in an increase in the amount of dietary vitamin B_6.

The elderly

There is a fall in the plasma concentration of pyridoxal phosphate with increasing age, but erythrocyte transaminase activation coefficients do not show a similar change. There is some evidence of age-related changes in the metabolism of the vitamin [8], but there are no good grounds for believing that ageing increases the vitamin B_6 requirement beyond that for younger adults.

Summary

Vitamin B_6 requirements (expressed in weight of pyridoxine) vary with protein intake in all groups.

Average Requirement	13 µg /g protein intake
Population Reference Intake	15 µg /g protein intake

Average protein intakes in the EC are 15% of energy intake. On this basis, and using average energy requirements, vitamin B_6 requirements of adults can be expressed in mg/d.

Adults	*Males*	*Females*
Average Requirement	1.3	1.0
Population Reference Intake	1.5	1.1

Population Reference Intakes for other groups

Age Group		PRI (mg/d)
	6 - 11 m	0.4
	1 - 3 y	0.7
	4 - 6 y	0.9
	7 - 10 y	1.1
Males	11-14 y	1.3
	15-17 y	1.5
Females	11-14 y	1.1
	15-17 y	1.1
	Pregnancy	1.3*
	Lactation	1.4*

* Based on protein increments in pregnancy and lactation.

High intakes

Intakes greater than 500 mg/d are associated with neurological damage and intakes of more than 50 mg/d are potentially harmful in adults.

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