6 Nutritional and Non-Nutritional Uses of Vitamin B₆

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6.1 Introduction

Nutritional deficiency of vitamin B₆ is essentially unknown, although a significant proportion of the population in developed countries show biochemical evidence of inadequate or marginal vitamin B₆ nutritional status, despite intakes that meet or exceed reference intakes, suggesting that current estimates of requirements may be too low. Furthermore, since estimates of requirement are based on prevention of deficiency, it is relevant to consider whether somewhat higher intakes may be beneficial in terms of promoting optimum nutrition.

Vitamin B₆ has been used to treat a wide variety of conditions, which may or may not be related to inadequate intake. In some conditions use of vitamin B₆ supplements has been purely empirical; in other conditions there is a reasonable physiological or metabolic mechanism to explain why supplements of the vitamin many times greater than average requirements may have therapeutic uses. However, even in such conditions there is little evidence of efficacy from properly conducted controlled trials.

At high levels of intake (in excess of 100 mg/day, compared with reference intakes of 1.5–2 mg/day) vitamin B₆ is neurotoxic, and there have been reports of (partially reversible) sensory nerve damage among people taking supplements of 1000 mg/day.

In June 1997 the UK Department of Health Committee on Toxicity [1] proposed limits on the amounts of vitamin B₆ that may be supplied in supplements. The proposals can be interpreted as an attempt to differentiate between levels of intake that may be considered to be nutritionally relevant and higher levels that can be considered to be for pharmaceutical purposes, to treat a disease or condition:

- up to 10 mg may be sold freely as a nutritional supplement (this is some 6-fold higher than the reference intake, although the figure was derived by extrapolation from toxicological data);
- 10–50 mg/day may only be sold in a pharmacy, where professional advice is assumed to be available;
- over 50 mg/day may only be provided on prescription, since at or above this level of intake there is considered to be a risk of adverse effects, which therefore have to be balanced against the benefits in treating a clinical condition.
The proposals generated very considerable controversy, with arguments both from those who opposed all regulation of nutritional supplements and those who did not oppose regulation, but questioned the scientific evidence on which the limits had been established. In July 1998 the proposed legislation was put in abeyance, pending further examination of the evidence concerning toxicity of the vitamin. This chapter aims to provide an overview of the requirements for vitamin B₆, a summary of the evidence for the pharmacological uses of vitamin B₆ and finally a discussion of drug interactions and toxicity of vitamin B₆.

6.2 Metabolism and Metabolic Functions of Vitamin B₆

Six vitamins have vitamin B₆ metabolic activity: pyridoxine, pyridoxal and pyridoxamine, and their 5'-phosphates (see Fig. 1). The metabolically active coenzyme is pyridoxal 5'-phosphate. In the liver there is rapid oxidation of the other vitamins to pyridoxal, and rapid phosphorylation to pyridoxal phosphate, which is the main circulating vitamin, exported from the liver bound to albumin. Uptake into peripheral tissues is by extracellular dephosphorylation, followed by metabolic trapping inside the cell as pyridoxal phosphate. Pyridoxal phosphate that is not bound to enzymes is rapidly dephosphorylated, and surplus pyridoxal in tissues is oxidised to pyridoxic acid, which is the main urinary metabolite of the vitamin [2].

![Fig. 1. Metabolic interconversion of the vitamin B₆ vitamers](image-url)