



ALL YOU NEED TO KNOW ABOUT VITAMIN B12

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Introduction

Attempts to cure pernicious anaemia led to the isolation and identification of vitamin B12 in 1948. It was understood that this fatal condition was caused by the lack of a factor in gastric secretions (intrinsic factor) and the lack of a food factor (extrinsic), which was subsequently found to be vitamin B12.

Recent continuing research has revealed important issues and implications associated with vitamin B12 deficiency, previously, not well understood.

Function

Vitamin B12 is involved in two critical enzymatic reactions:

- The methylmalonyl mutase reaction that is integral to the maintenance of myelin in the nervous system through fatty acid synthesis pathways; and
- The methionine synthetase reaction, which is required for DNA formation and synthesis, and hence cell division.

There is also an integral relationship between vitamin B12 and Folate pathways, such that a deficiency in one can mimic or mask a deficiency in the other. (Klee 2000)

Causes of deficiency

There are six main causes of vitamin B12 deficiency:

Dietary inadequacy – The Recommended Daily intake (RDI) is 2.4 ug/day.
(Yates 1998)

Impaired absorption

Intrinsic factor or gastric related, or

Ileal malabsorption

Inadequate utilisation

Increased requirement (E.g. pregnancy or hyperthyroidism)

Increased excretion (E.g. alcoholism)

Increased destruction (E.g. by large doses of vitamin C)

The increased destruction of vitamin B12 by vitamin C is a significant cause of deficiency. Ascorbic acid supplements in doses over 100mg/day impairs absorption and utilisation of vitamin B12 and may convert it into biologically unavailable analogue forms. (Herbert 1996a)

Consequences and symptoms of deficiency

Symptoms of deficiency are shown in Table 1.

Table 1 - Symptoms of vitamin B₁₂ deficiency

NEUROLOGICAL	HAEMATOLOGICAL	OTHER
Paraesthesia	Shortness of breath	Sore tongue, mouth
Unsteadiness	Anaemia	Weight loss
Leg weakness	Macrocytosis	Loss of appetite
Muscle tenderness	Hyper segmented neutrophils	Tiredness
Memory loss	-	General weakness
Psychiatric changes Dementia	-	Hair loss

(Bower 1995)

It is important to note that dementia associated with low vitamin B12 reserves is fully reversible if treated within two years of onset. Dementia of longer than two years duration is permanent. (Cunha 1995, Bopp-Kistler 1999, Ho 1999)

Many physicians have waited until the MCV is elevated to alert them of a vitamin B12 (or folate) problem. This approach will miss many cases of deficiency, as MCV is not elevated in many cases. While any MVC result greater than 96fL should be investigated, vitamin B12 deficiency without anaemia and without megaloblastic changes is common. (Rana 1998, Delva 1997, Zittoun 1999)

Recent reports have identified an increased risk of breast cancer in postmenopausal women who were deficient in vitamin B12 during their teens. (Wu 1999, Choi 1999) Further, a link between low maternal vitamin B12 during pregnancy, and an increased risk of brain tumours in their children when they reach puberty has been reported. (McNeil 1997)

Reference range

The usual method of deriving a reference range (Mean +/- 2SD) results in a vitamin B12 reference range of around 130-850 pmol/L. This is an unsafe range as many in the population exhibit neurological symptoms of deficiency at much higher concentrations. The lowest concentration to be considered normal is 221 pmol/L. (Herbert 1996b)

At risk groups

Well-recognised groups that are at risk of becoming vitamin B12 deficient are vegetarians (who consume less than 20 servings of vitamin B12 containing foods/week) and particularly vegans, who must supplement their diet. For vegetarians, the only sources of vitamin B12 are dairy products and eggs, and fortified soymilk alternatives. For vegans, only fortified soy beverages and tablet supplements are available. Some people have been confused reading about B12 in USA publications and on the Internet. In USA almost everything is fortified with B12, and information on American foods cannot be translated to Australia or NZ. Vitamin B12 is not found in mushrooms, and 'natural sources' such as Spirulina and Tempeh contain analogues of the vitamin with no physiological activity and may impair the absorption of useful forms.

Other less recognised at-risk groups, include those that are HIV/AIDS positive, the pregnant and the elderly. Preliminary research analysing pathology result data from one Sydney obstetrician, has revealed that 40% of his pregnant patients have vitamin B12 concentrations below the recommended range (221 pmol/L)

Diagnosis of deficiency

Any patient history of vegetarianism, or others in at-risk groups, should alert physicians to look for symptoms of vitamin B12 deficiency. Serum vitamin B12 is a useful screening test, but a test reflecting body reserves of vitamin B12 is valuable. Two such tests are available. Methylmalonic acid (MMA) and Homocysteine are available, with Homocysteine the simpler test. In vitamin B12 and Folate deficiency, Homocysteine is elevated. Results greater than 10 umol/L should trigger investigation of vitamin B12 and Folate status.

The cause of deficiency (dietary or malabsorption due to either pernicious anaemia (IF related) or intestinal malabsorption) can be identified by the Schillings test. If the Schillings test is abnormal, Anti-intrinsic factor antibodies, Anti-parietal cell antibodies and a gastrin assay can confirm a diagnosis of pernicious anaemia,

Treatment of deficiency

In most cases of dietary deficiency, dietary advice to increase the consumption of vitamin B12 containing foods and include a supplement should suffice. In serious cases of deficiency (serum vitamin B12 <150 pmol/L), a course of IM injections (1000ug) should be considered. When serum concentrations have returned to normal, long-term oral supplements can be trialled, and continued if serum concentrations are maintained. If serum levels cannot be maintained with oral supplements, ongoing IM injections should be considered.

The use of high dose (1000ug/day) oral vitamin B12 is gaining popularity. This avoids the discomfort of injections, and is effective even in cases of pernicious anaemia, utilising the Law of Mass Action. (Kuzminski 1998, Lederle 1991).

Both Cyanocobalamin (Cytamen) and Hydroxocobalamin (Neo Cytamen) are equally effective. Foods supplemented with vitamin B12 are also an effective source of the vitamin for those who have normal absorption.

Conclusions

The capacity to prevent and cure pernicious anaemia and other the symptoms of vitamin B12 deficiency with vitamin B12 is one of Medicine's great success stories. The need for early recognition of the condition and effective long term monitoring and treatment is mandated by the serious potential outcomes that can result from a deficiency.

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Dr Hokin is the Director of Pathology at Sydney Adventist Hospital, a position he has held since 1985. His major research interest focuses on vitamin B12 deficiency issues in at-risk groups.