



Vitamin D

Insight - November 2018

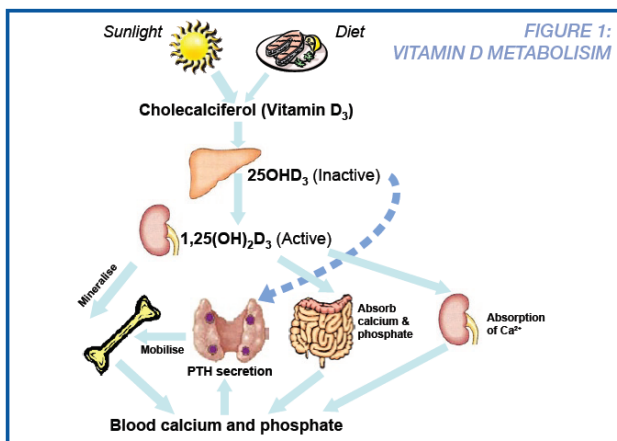
There are a large proportion of Melbournians who are vitamin D deficient which may be in some part due to the success of the Sun Smart message.

Review of Melbourne Pathology Vitamin D results show that 50 percent of results clearly belong to the deficiency category (<50 nmol/L) and deficiency is common across all age groups.

Test for Vitamin D (item no. 66608) is Medicare rebatable for patients at risk.

What does vitamin D do?

Vitamin D is required by the body to regulate blood calcium levels by promoting calcium absorption from food in the intestines and calcium reabsorption in the kidneys. Vitamin D requirements are mainly fulfilled by sunlight exposure which converts 7-dehydrocholesterol to cholecalciferol (vitamin D₃) in the skin (Figure 1). Only small amounts of vitamin D₃ can be derived from the diet. Once formed in the skin or ingested, vitamin D is transported to the liver where it is hydroxylated to 25-hydroxyvitamin D (25OHD). However, 25OHD is biologically inactive and must be converted to 1,25-dihydroxyvitamin D (1,25[OH]₂D) to exert its biological actions.



What is the impact of vitamin D deficiency?

Inadequate sunlight exposure is the major cause of vitamin D deficiency. This triggers parathyroid hormone (PTH) secretion which in turn increases bone resorption. PTH also stimulates renal excretion of phosphate causing phosphate deficiency. Consequently, these combinations result in impaired bone mineralisation leading to bone softening diseases, rickets in children and osteomalacia in adults. It may also contribute to osteoporosis.

There is emerging evidence to suggest that vitamin D deficiency is also associated with a number of chronic diseases including certain cancers, autoimmune diseases and infections.

Who is at risk of vitamin D deficiency?

Groups at risk of vitamin D deficiency include:

- people who are institution/house/office bound
- dark-skinned women particularly if veiled
- people with osteoporosis or hip fracture
- people with gastrointestinal symptoms suggestive of malabsorption
- people who are on certain medications including anticonvulsants and glucocorticoids.

It is also recommended that pregnant women at risk have their 25OHD tested during the first trimester however the Royal College of Pathologists of Australasia recommend that all pregnant women are tested.

BIOCHEMICAL TESTS FOR DIAGNOSIS AND MONITORING OF VITAMIN D DEFICIENCY

Vitamin D

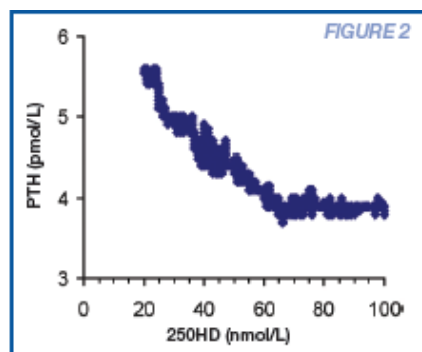
25OHD is a major circulating and storage form of vitamin D and is used to assess vitamin D status. Measurement of 1,25[OH]₂D is not necessary. To monitor treatment response, 25OHD can be measured 2-3 months after commencing supplementation as vitamin D has a long half-life (2-3 weeks).

What cut-off should we use to indicate vitamin D deficiency?

The recommended decision limit for 25OHD is 50 nmol/L. However the Australian guideline also recognises that this limit should be higher in the summer than winter. The typical summer limit may be 60 nmol/L, but may be less in northern Queensland, but higher in Victoria and Tasmania. Deficiency can also be graded as mild, moderate or severe.

25OHD (nmol/L) Vitamin D status

<12.5	Severe deficiency
12.5-24	Moderate deficiency
25-49	Mild deficiency
50-75	Indeterminate
>75	Sufficient



These measurements have been derived through our use of a modern automated method (Diasorin Liaison) for the analysis of 25OHD. We have evaluated the optimal cut-off value for this 25OHD assay using serum PTH as a surrogate marker from

data available in our database (n = 55,714).

Figure 2 shows that when serum 25OHD levels fall below 65 nmol/L PTH begins to rise steadily. This indicates that using our assay, a level of 25OHD below 65 nmol/L is physiologically insufficient. To interpret actual results from individual patients however, we also need to consider assay imprecision. Despite our current 25OHD assay being one of the best assays available, a 25OHD level of 65 nmol/L could fall anywhere between 50 to 75 nmol/L on repeat analysis.

There are three main reasons to consider levels between 50-75 nmol/L as indeterminate; (i) circannual variation, (ii) correlation with PTH and (iii) analytical measurement uncertainty.

PTH

PTH may be used sometimes to evaluate a borderline low 25OHD. An elevated PTH with a low 25OHD confirms vitamin D deficiency. However, a PTH level within reference interval does not exclude vitamin D deficiency. Review of our data showed that only one third of patients with moderately severe vitamin D deficiency (25OHD <25 nmol/L) had PTH raised above the reference interval.

Serum Calcium, Phosphate and Magnesium

Hypocalcaemia and hypophosphataemia may occur in severe vitamin D deficiency although serum calcium and phosphate are usually normal in mild-moderate deficiency.

In people who are on calcitriol (1,25[OH]₂D) supplementation, serum calcium and phosphate are used to monitor treatment as toxicity could result in hypercalcaemia.

Measurement of serum magnesium is sometimes necessary as hypomagnesaemia may blunt the PTH rise in response to vitamin D deficiency.

LFT and UEC

These tests are important to ensure the active form vitamin D (1,25[OH]₂D) can be produced. Occasionally, vitamin D deficiency is detected as a result of isolated mildly raised ALP in LFT.

TREATMENT FOR VITAMIN D DEFICIENCY

Treatment strategies for moderate to severe vitamin D deficiency usually require vitamin D supplementation coupled with advice to increase sun light exposure. Dietary modification alone (even with vitamin-D fortified foods) will not provide adequate amounts of vitamin D. For people who have 25OHD levels in the equivocal range (50-75nmol/L) but are not in the high risk group, it may be advisable to increase sunlight exposure, then to measure 25OHD again in three months.

How much sunlight exposure is required in Melbourne?

It is estimated that to produce about 1000 IU of vitamin D₃, we need to expose 15 percent body surface (hands, arms and face) to sun most days for 6 - 8 minutes in summer or 32 - 52 minutes in winter. People with darker skin may require three to six times more sun light exposure. UV radiation does not transmit through glass, clothing, or broad spectrum sunblocks.

It is important also to strike a balance between risk of vitamin D deficiency and the risk of skin cancer by avoiding deliberate exposure to sunlight in summer between 10am and 2pm (or 11am and 3pm daylight saving time).

Vitamin D supplementation and toxicity

Currently most of the supplements are in vitamin D₃ form (cholecalciferol) in Australia. For adults with moderate to severe deficiency, it is recommended to start vitamin D₃ such as Ostelin or OsteVit-D at 3000-5000 IU per day for at least 6-12 weeks then 1000 IU for ongoing treatment. This treatment is also applicable to women during pregnancy. Vitamin D toxicity due to supplementation is rare. It has been reported that supplementing 10,000 IU per day orally for 90 days in postmenopausal women did not result in adverse effect and monthly doses of 50,000 IU are not uncommon in clinical practice, particularly in nursing homes.

For further information please contact Melbourne Pathology on 9287 7700.



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A University of Melbourne graduate, A/ Prof Sikaris trained at the Royal Melbourne, Queen Victoria, Prince Henry's and Heidelberg Repatriation Hospitals. He obtained fellowships from the Royal College of Pathologists of Australasia (RCPA) and the Australasian

Association of Clinical Biochemists (AACB) in 1992 and 1997 respectively. A/Prof Sikaris was appointed Director of Chemical Pathology at St Vincent's Hospital in 1993 and Medical Director of Dorevitch Pathology in 1998 before starting at Melbourne Pathology in 2003.

He specialises in Prostate Specific Antigen, cholesterol and quality assurance and is Chair of the RCPAQAP Key Incident Monitoring Program for Australasia. A NATA-accredited laboratory assessor, he is also founding Fellow of the RCPA Faculty of Science where he is Principal Examiner in Pathology Informatics.

A/Prof Sikaris is a Principal Fellow of the Department of Pathology at Melbourne University and lectures to undergraduates, GPs and a variety of specialist groups across Australia and overseas. A/Prof Sikaris is also Director of Clinical Support Services for Sonic Healthcare.

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