

The clinical pathology of Vitamin D

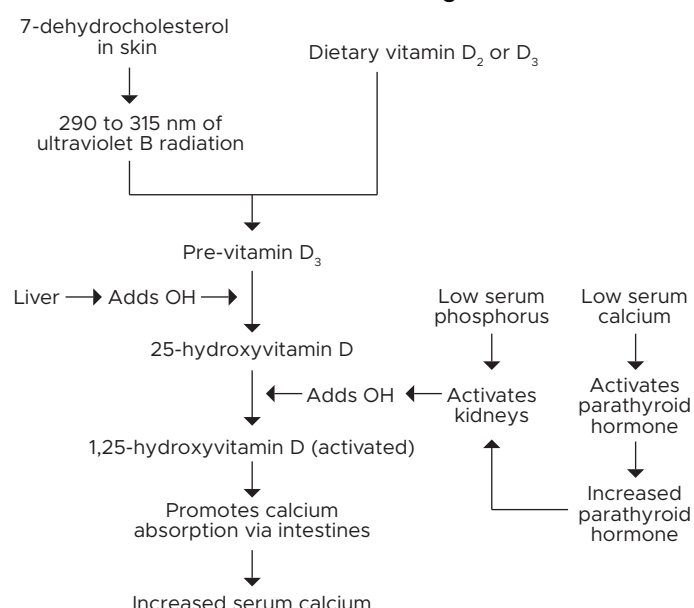
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Since the realisation in the late 19th century that a lack of vitamin (vit) D is the cause of rickets in children, it has become clear that an insufficiency is associated with many other pathologic conditions at all ages. Vit D is not only related to skeletal development and the maintenance of healthy bones; it also plays an important role in immunity, cardiac and neuromuscular functioning, and mood disorders. However, the signs of vit D deficiency are insidious and nonspecific. It can go untreated and is a major concern in general practice.

Definitions

In adults, vit D deficiency is defined as a serum 25-hydroxyvitamin D (25(OH)vit D) level of less than 20 ng/mL (50 nmol/L). Insufficiency is defined as a serum level of 20-30 ng/mL (50-75 nmol/L). In children the lower limit of 'normal' is slightly less owing to the high metabolic turnover of bone tissue.

Fig. 1: Vit D metabolism.



Metabolism (Fig 1)

There are two forms of vit D, D2 (ergocalciferol from yeast and plant sterols) and D3 (cholecalciferol from oily fish and UV B irradiation of cholesterol in the skin). Humans typically obtain 90% of vit D from sunlight.

Laboratory measures

Vit D is usually measured by competitive binding methods, high-performance liquid chromatography (HPLC), and radioimmunoassays (RIA).

Historically, the reference method has been LC-MS/MS, which can measure D2 and D3 separately, however, an RIA is often the method of choice in many reference labs because of its relative ease of use.

In routine labs such as ours, an automated competitive immunoassay for 25(OH) vit D on the ADVIA Centaur platform is used. The assay measures 25(OH) vit D only, which reflects total stores.

There is of course the issue of not directly assessing 1,25(OH) vit D, which is the active form, but current guidelines are clear that 25(OH) vit D is much more reflective of stores and a potential deficiency.

Measures of 1,25(OH) vit D are only relevant for patients on dialysis or end stage renal failure.

Interference

The main cause of assay interference is heterophilic antibodies, which will typically cause an abnormal elevation of the reported concentration.

Haemoglobin and haeme derivatives as well as cholesterol, triglycerides and some artificial supplements may also interfere with detection.

Vitamin D deficiency in non-bone conditions

Vit D deficiency is implicated in many other pathological conditions other than bone disease. The commonest of these are:

1. Cardiovascular: hypertension, elevated BMI, hyperglycaemia.
2. Neoplasia: colorectal cancers appear to be responsive to the antiproliferative effects of 1,25(OH) vit D and a deficiency has been reported to be negatively correlated with prognosis and disease development.
3. Mood disorders: Depression and decreased cognition.
4. Immunity: Autoimmune conditions and sub-optimal immune regulation.

Prevention and Treatment

To prevent vit D deficiency in persons with inadequate sun exposure, the daily recommendation is 200-400 IU for infants, children, and adults younger than 51 years; 400 IU for adults 51 to 70 years of age; and 600 IU for adults older than 70 years. Vit D-deficient adults should be treated with 50,000 IU vit D once a week for 8 weeks or its equivalent of 6000 IU daily, followed by a maintenance dose of 1500–2000 IU daily.

Clinical history and symptomatology

Vit D may manifest in non-specific ways. A high clinical index of suspicion is helpful as a frank deficiency is common in South Africa, particularly in impoverished communities, those with very specific dietary requirements or in individuals who have very limited sun exposure. It is therefore wise to consider the risk factors as well as the potential clinical manifestations of vit D deficiency or insufficiency (Table 1).

Vitamin D toxicity

Vit D is a lipid soluble vitamin (the others being E, A and K) and overconsumption can lead to toxicity. The most common signs and symptoms of this are: headache, metallic taste, nephrocalcinosis, pancreatitis, nausea and vomiting.

Supplementation with vit D should never exceed the following doses per day:

- Infants < 6 months: 1,000IU
- Infants 6-12 months 1,500IU
- Children 1-9 years 3,000IU
- Individuals >10 years 4,000IU

Table 1.

Risk factors for Vit D deficiency	Clinical manifestations
Age older than 65 years or individuals with sedentary lifestyle	Bone discomfort or pain (often throbbing) in lower back, pelvis, lower extremities
Infants who are exclusively breastfed without vitamin D supplementation	Increased risk of falls; history of fractures with or without osteopaenia
Dark skin or clothing that limits sunlight exposure	Muscle aches or weakness
Medications (e.g., anticonvulsants, glucocorticoids) Sedentary lifestyle	Depression or anxiety with or without cognitive impairment
Obesity (BMI > 30)	Autoimmune diseases or history of chronic infections

References

1. Bordelon, P. et al. Am Fam Physician. 2009 Oct 15;80(8):841-846.
2. Aranow, C. J Investig Med. 2011 Aug; 59(6): 881-886.



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