

GUIDELINES & PROTOCOLS

ADVISORY COMMITTEE

Vitamin D Testing Protocol

Effective Date: October 1, 2010

Scope

This laboratory protocol describes the appropriate use of vitamin D testing within the general adult (≥ 19 years) population in British Columbia (BC). Patients with malabsorption syndromes, renal failure, unexplained bone pain, unusual fractures, and other evidence of metabolic bone disorders are excluded from this protocol. Recommended vitamin D supplementation is discussed and a patient handout is included.

Routine Diagnostic Testing

- Routine serum vitamin D testing or screening for vitamin D deficiency is not recommended.
- Routine serum vitamin D testing during vitamin D supplementation is not recommended.

Population at Risk

The BC population is at risk of low vitamin D levels from autumn to spring. There is no clinical utility in performing vitamin D tests on patients who are thought to be at risk for sub-optimal vitamin D levels and who would benefit from vitamin D supplementation.

Vitamin D Supplementation without Testing

Because vitamin D supplementation in the general adult population is safe, it is reasonable to advise supplementation without testing. Routine testing of vitamin D levels [25-hydroxyvitamin D or 25(OH)D] is not medically necessary prior to or after starting vitamin D supplementation.

Utilization and Cost of Serum Vitamin D Testing in BC

Utilization of vitamin D testing [as 25(OH)D] in BC has increased ten-fold in the past five years. Medical Service Plan expenditures are approximately \$3 million annually for outpatient vitamin D testing with a cost per test of \$93.63 in 2009.

Measuring serum vitamin D as 1,25-dihydroxyvitamin D [$1,25\text{-(OH)}_2\text{-D}$] is seldom indicated, except in selected patients with advanced renal failure, mineral and/or bone diseases. Specialist consultation should be considered for patients with malabsorption, unexplained bone pain, unusual fractures or other evidence suggesting metabolic bone disorder.

Sun Exposure and Vitamin D Synthesis by Skin

The amount of vitamin D produced by the skin is dependent on the surface area exposed, skin pigmentation, age, season, latitude and use of sun block. During winter months in Canada there is insufficient ultraviolet (UV) radiation in sunlight for adequate vitamin D production.¹ Adequate vitamin D can be made in the body during careful exposure of the arms and legs to sunlight for 10-15 minutes per day in the summer months. However, the risk of skin cancer due to sun exposure and tanning beds must be considered.

Dietary Sources of Vitamin D

Vitamin D can be obtained from dietary sources (e.g., salmon, mackerel, tuna, egg yolk), fortified foods (e.g., cow, soy or rice milk), and supplements. There are no plant sources that provide a significant amount of vitamin D naturally. (See Patient Guide)

Vitamin D Supplementation

During the Canadian autumn, winter and spring, the adult population is unlikely to achieve adequate vitamin D levels through diet and sunlight only. Consideration should be given to supplementation during those seasons. The two major forms of vitamin D supplements are available as D₂ (ergocalciferol) or D₃ (cholecalciferol). Vitamin D₃ has been shown to be three times more effective than vitamin D₂ at increasing serum 25(OH)D levels and maintaining these levels over a longer period of time.^{2,3,4} As a result, D₂ dosage must be tripled to achieve the same benefit.

Osteoporosis Canada recommends supplementing with vitamin D₃ over vitamin D₂.⁴ Most over the counter supplements available in Canada contain vitamin D₃ whereas high-dose Vitamin D₂ is available only by prescription. There is good evidence that supplementation with at least 800 international units (IU) of vitamin D₃ per day, combined with calcium, is required to reduce the risk of fragility fractures, therefore 800 – 1000 IU daily is recommended (although the optimum daily requirement of vitamin D₃ is not known).^{4,5,6} Weekly dosing (one week's adult dose of vitamin D₃ taken as a single weekly dose, i.e. 7000 IU) or monthly dosing (one month's adult dose of vitamin D₃ taken once a month, i.e. 30,000 IU) may be more convenient for some patients and has been shown to be safe.^{1,4,7} At this time, high doses of vitamin D₃ once a year is not recommended as recent evidence has shown possible increased fracture risk.⁸

Vitamin D Toxicity

Vitamin D toxicity is uncommon.^{3,6,9} Daily doses of up to 10,000 IU of vitamin D₃ for up to five months has not been shown to cause harm in adults.^{10,11} Any harm that would occur from excessive vitamin D ingestion is mediated by hypercalcemia. Therefore, if there is a strong clinical suspicion of vitamin over-use (e.g. patients with eating disorders), then the recommended test is serum calcium (albumin-corrected total calcium* or ionized calcium).¹² Only if the calcium level is elevated would a serum vitamin D measurement be indicated.

Physiology

Vitamin D is a fat-soluble vitamin that is naturally present in very few foods.¹³ It stimulates intestinal calcium and phosphate absorption, and is important in maintaining adequate calcium levels for bone mineralization, bone growth and remodelling.¹⁴ Vitamin D deficiency has been linked to a wide variety of common diseases including cancer, diabetes, and cardiovascular disease. Vitamin D is reported to be involved in the regulation of cell growth and metabolism, modulation of immune function, and reduction of inflammation.^{15,16}

For humans there are two sources of vitamin D: vitamin D₂ (ergocalciferol) is derived from plants, and D₃ (cholecalciferol) is produced in the skin by action of UV light on 7-dehydrocholesterol. (See Figure 1) Vitamin D₂ is only one-third as effective as vitamin D₃ in raising levels of 25(OH)D.¹⁷

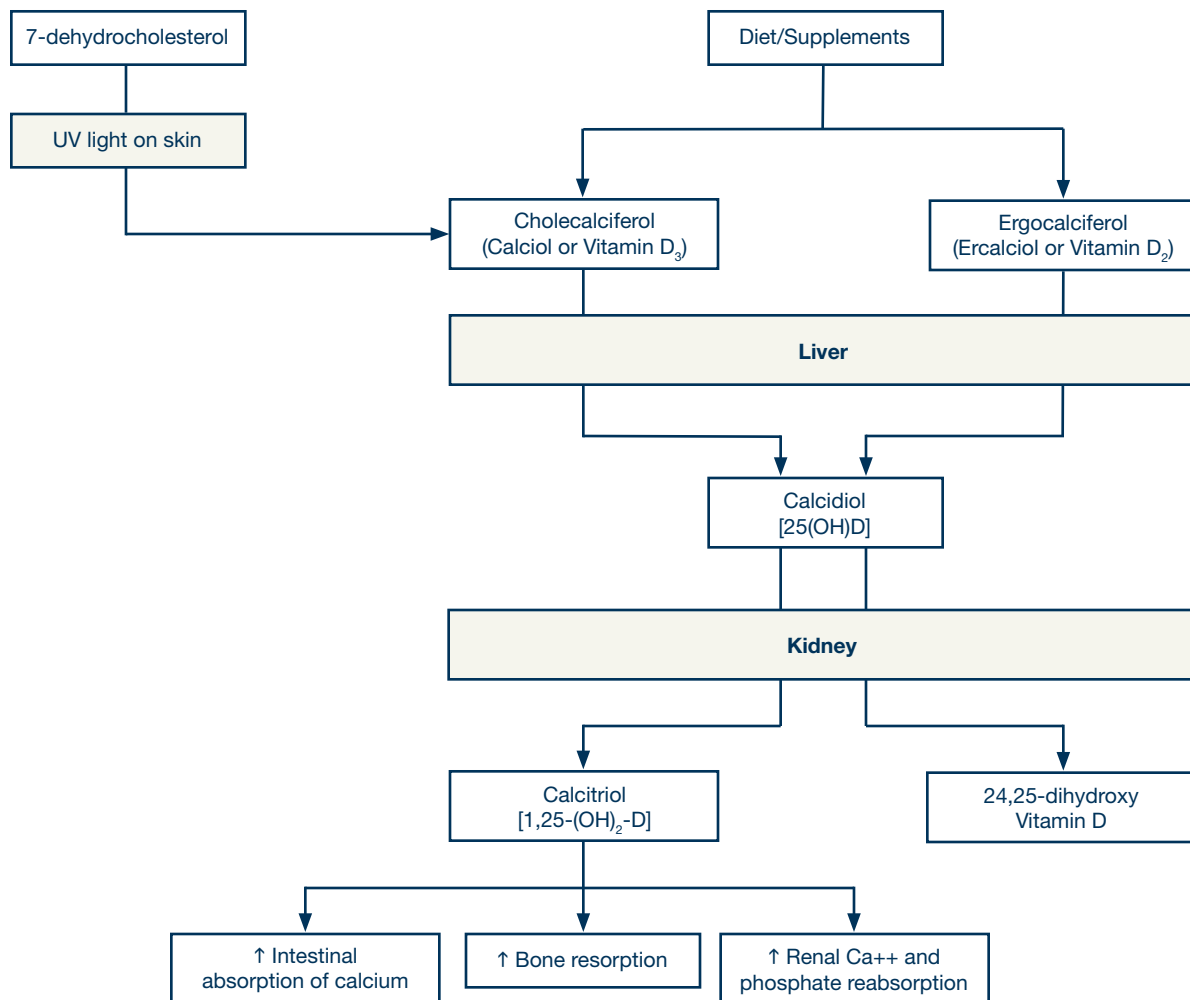
Both D₂ and D₃ are hydroxylated in the liver to 25(OH)D, the major circulating form of vitamin D (metabolically inactive). It undergoes further hydroxylation in the kidney to the active metabolite, 1,25-(OH)₂-D or calcitriol. Calcitriol stimulates intestinal calcium absorption, decreases parathyroid hormone secretion, enables parathyroid hormone-mediated mineral absorption within the kidney, stimulates osteoclastic bone resorption and osteoblasts, decreases production of collagen, influences muscle function, stimulates cell differentiation and modulates the immune system.

Aging brings with it a reduction in the efficiency with which the skin synthesizes vitamin D and a reduction in the kidney's ability to convert vitamin D to its active form.¹⁸ Increased skin pigmentation and use of high efficiency sun blockers also reduce skin synthesis of vitamin D.¹

Because serum 25(OH)D concentration represents both skin production (D₃) and oral intake (D₂ or D₃) of vitamin D, it may be used to determine the adequacy of vitamin D production and intake.¹⁹ Consensus has been reached that a 25(OH)D level that is less than 25 nmol/litre indicates vitamin D deficiency. The optimum level of serum vitamin D, if one exists, has not been determined.

* Corrected Ca = Ca.measured + (40-alb) X 0.02, [Ca in mmol/L; albumin in g/L]

Figure 1: Pathways of vitamin D synthesis*



* Adapted from Janssen HC, Samson MM, Verhaar HJ. Vitamin D deficiency, muscle function, and falls in elderly people. *American Journal of Clinical Nutrition* 2002;75:611-615.

References

- White JH. Vitamin D signalling, infectious diseases, and regulation of innate immunity. *Infection and Immunity* 2008;76:3837-3843
- Compendium of Pharmaceuticals and Specialties: The Canadian Drug Reference for Health professionals. Toronto, Ontario;2010.
- Briot K, Audran M, Cortet B, et al. Vitamin D: skeletal and extra skeletal effects; recommendations for good practice. *Presse Med.* 2009;38:43-54.
- Hanley DA, Cranney A, et al. Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada. [published online ahead of print July 12, 2010]. *CMAJ* 2010. Accessed July 12, 2010, www.cmaj.ca/cgi/rapidpdf/cmaj.091062v2?ijkey=78c43e1d0629c7b1e050f9318ab60caf30b1ec63&keytype=tf_ipsecsha
- Tang BM, Eslick GD, Nowson C, et al. Use of calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. *Lancet* 2007;370:657-66.
- Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. *JAMA.* 2005;293:2257-64.
- Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. *BMJ.* 2003;326:469-75.
- Sanders KM, Stuart AL, et al. Annual High Dose Oral Vitamin D and Falls and Fractures in Older Women: A Randomized Controlled Trial. *JAMA.* 2010;303(18):1815-1822.
- Cranney A, Horsley T, O'Donnel S, et al. Effectiveness and safety of vitamin D in relation to bone health. Agency for Healthcare Research and Quality. c2007 [cited 2010 Feb 10]. Available from: www.ahrq.gov/downloads/pub/evidence/pdf/vitaminD/vitad.pdf

10. Vieth R. Vitamin D toxicity, policy and science. *J Bone Miner Res.* 2007;22:S2;V64-V68.
11. Heaney RP, Davies KM, et al. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. *Am J Clin Nutr.* 2003;77(1):204-210.
12. Jones G. Pharmacokinetics of vitamin D toxicity. *Am J Clin Nutr.* 2008;88:582S-6S.
13. Holick MF. Vitamin D deficiency. *N Engl J Med.* 2007;357:266-81.
14. Pedersen JI. Vitamin D requirement and setting recommendation levels – current Nordic view. *Nutr Rev.* 2008;66:S165-S169.
15. Ontario Medical Advisory Secretariat, Ministry of Health and Long-term Care. Clinical utility of vitamin D: an evidence-based analysis. Ontario Health Technology Assessment Series. 2009; In press.
16. National Institute of Health. Dietary Supplement Fact Sheet: Vitamin D. c2009 [updated 2009 Nov 13; cited 2010 Feb 10]. Available from: <http://dietary-supplements.info.nih.gov/factsheets/vitamind.asp>
17. Armas LAG, Hollis BW, Heaney RP. Vitamin D2 is much less effective than vitamin D3 in humans. *J Clin Endocrinol Metab.* 2004;89:5387-91.
18. Need AG, Morris HA, Horowitz M, et al. Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. *Am J Clin Nutr.* 1993;58:882-5.
19. Institute of Medicine. Vitamin D. In: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington, DC: National Academy Press 1997; p. 250-87.

Resources

HealthLink BC: www.healthlinkbc.ca

Telephone - Anywhere in BC call 8-1-1, Translation services are available in over 130 languages on request. TTY (Deaf and hearing-impaired) call 7-1-1.

List of Abbreviations

25(OH)D - 25	- hydroxyvitamin D
1,25-(OH) ₂ -D	- 1,25-dihydroxyvitamin D
UV	- ultraviolet
IU	- international units

Associated Documents

Vitamin D: A Patient Guide for Adults

This guideline is based on scientific evidence current as of the Effective Date.

The guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

Contact Information

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DISCLAIMER

The Clinical Practice Guidelines (the “Guidelines”) have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problems.

VITAMIN D

A Patient Guide for Adults

Do I need vitamin D?

Vitamin D is important for everyone. Vitamin D plays an important role in helping the body to absorb calcium through the small intestine. Our bodies need calcium to help make and maintain healthy bones, muscles and teeth. Too little vitamin D may be linked to a variety of common diseases.

How much do I need?

For most adult women and men at least 800 to 1,000 international units (IU) per day are recommended. Getting too much vitamin D is rare. Talk to your doctor or pharmacist about how much vitamin D is right for you. More information on different vitamin D supplements is found below.

Do I need a blood test to check my vitamin D level?

Testing your level of vitamin D is NOT needed.

Where can I get vitamin D from?

Vitamin D is made in the skin when it is exposed to sunlight. A small amount is found in some vitamin supplements and foods.

Vitamin D can be made in the body after careful exposure of the arms and legs to sunlight 10-15 minutes per day in the summer months. The amount of sunlight needed to make enough vitamin D varies, depending upon the person's age, skin colour, sun exposure, and other medical problems. In Canada it is hard to get enough vitamin D from sunlight during the fall, winter and spring.

Another source of vitamin D is food. It can be found in some fish, cod-liver oil, and (to a lesser extent) eggs. In Canada, some vitamin D is added to cow, soy, and rice milk. To get enough vitamin D from milk, you would need to drink 10 cups a day. This chart shows some food sources of vitamin D.

Type of Food	Estimated Vitamin D Content (Approximate Content)
Naturally present in food	
Fresh salmon	100-250 IU per 100 g or 3.5 oz (farmed) 600-1000 per 100 g or 3.5 oz (wild)
Mackerel	80-250 IU per 100 g or 3.5 oz (canned)
Cod liver oil	400-1000 IU per 5 ml or 1 teaspoon
Tuna	41-105 IU per 100 g or 3.5 oz (canned) 380-690 IU per 100 g or 3.5 oz (fresh)
Sardines	70-360 IU per 100 g or 3.5 oz (canned)
Egg yolk	20-25 IU vitamin each
Mushrooms	18 IU per 100 g or 3.5 oz (white button) 96 IU per 100 g or 3.5 oz (cooked shiitake)

Vitamin D-fortified foods (Canada)	
Cow's milk	100 IU per 250 ml or 1 cup
Soy or rice milk	80 IU per 250 ml or 1 cup
Some orange juices	100 IU per 250 ml or 1 cup
Margarine	25 IU per 5 ml or 1 teaspoon

Supplements

Other than in summer, vitamin D from the sun or from food is often not enough for our body's needs. Most BC adults would benefit from a vitamin D supplement of at least 800-1,000 IU per day.

Vitamin D supplements come in many different forms. The most common are vitamin D₂ (ergocalciferol) and vitamin D₃ (cholecalciferol). Vitamin D₃ is recommended and is the most common form available over the counter in pharmacies.

Supplements may be taken weekly or monthly if it is more convenient than daily.

For example, a vitamin D₃ dose of 1000 IU per day may also be taken as a single weekly dose of 7,000 IU or as a single monthly dose of 30,000 IU. Your doctor or pharmacist can help you decide how much and how often to take your vitamin D supplements.

More information

- HealthLink BC – health and diet information for British Columbians www.healthlinkbc.ca or telephone 8-1-1
Translation services are available in over 130 languages on request. For deaf and hearing-impaired assistance (TTY) call 7-1-1.