

OBJECTIVE

Appropriate vitamin D testing and supplementation is understood and practiced in Alberta. Specifically that:

- There is NO CLINICAL BENEFIT to test for vitamin D levels in the general population who may be at risk for low vitamin D levels as a result of low dietary intake and/or seasonal (sunlight) variation
- Vitamin D supplementation for this general population should be recommended without a need to screen or monitor vitamin D levels
- Vitamin D testing may be useful for certain clinical conditions, e.g., metabolic bone disorders, abnormal blood calcium, malabsorption syndromes, chronic renal disease, chronic liver disease, and should be referred to and managed by a specialist

TARGET POPULATION

Adults, children and pregnant/lactating women who may be at risk for low vitamin D levels as a result of low dietary intake or seasonal (sunlight) exposure do not require vitamin D testing

EXCLUSIONS

Patients with malabsorption syndromes, renal failure, unexplained bone pain, unusual fractures, and other evidence of metabolic bone disorders may require vitamin D testing determined by specialists managing these conditions

RECOMMENDATIONS

VITAMIN D TESTING^{1,2}

- X **DO NOT** order routine vitamin D testing for the general pediatric population who may be at risk for deficiency from low dietary intake and/or low exposure to sunlight
 - High levels of the biologically less active C-3 epimers of vitamin D levels are found in infants (< 1 year) therefore testing vitamin D levels may be misleading
- X **DO NOT** order routine vitamin D testing for the general adult population who may be at risk for deficiency from low dietary intake and/or low exposure to sunlight
- X **DO NOT** order routine screening for vitamin D deficiency for the general population of pregnant/lactating women from low dietary intake and/or low exposure to sunlight
- ✓ **DO** recommend vitamin D supplementation when indicated as per guidelines (see [Vitamin D Supplementation](#))

- ✓ **DO** refer patients (adults, children, pregnant/lactating women) with clinical conditions known to be or at high risk for vitamin D deficiency (as described above) to a specialist for management and when vitamin D testing may be clinically indicated
- ✓ When clinically indicated, serum 25-hydroxyvitamin D is the best test for determining vitamin D levels

VITAMIN D SUPPLEMENTATION

Vitamin D supplementation for the general adult population in Alberta is safe and necessary therefore supplements can be recommended without testing for deficiency.

RECOMMENDED VITAMIN D SUPPLEMENTATION FOR HEALTHY ALBERTANS³

Healthy Population in Alberta	Vitamin D3 Supplementation	Comments
Infants (breast or formula fed) from birth to adults 70 years old and younger	400 IU/day	Vitamin D supplementation will assist meeting total recommended dietary allowance for vitamin D of 600 IU/day
Adults 71 years of age and older	800 IU/day	Vitamin D supplementation will ensure total recommended dietary allowance for vitamin D of 800 IU/day is met

Table 1 Vitamin D Supplementation for Healthy Albertans

ADULTS REQUIRING ADDITIONAL VITAMIN D SUPPLEMENTATION⁴

Population at Risk of Osteoporosis from Vitamin D deficiency	Vitamin D3 Supplementation	Comments
For adults at lower risk of vitamin D deficiency	Minimum of 400 IU – up to 1000 IU/day	To achieve optimal vitamin D status, daily supplementation with more than 1000 IU may be required
For adults over age 50 at moderate risk of vitamin D deficiency	800 IU – 1000 IU/day	To achieve optimal vitamin D status, daily supplementation with more than 1000 IU may be required
For adults over age 50 at moderate risk of vitamin D deficiency and to prevent osteoporosis and reduce risk of fragility fractures	2000 IU/day	Daily doses up to 2000 IU are safe and do not necessitate monitoring

Table 2 Adults Requiring Additional Vitamin D Supplementation

- The upper limit of intake suggested to be safe for most individuals is 4,000 IU per day (though toxic levels of vitamin D usually require much higher consumption up to 10,000 IU per day).^{5,6,7}
- Weekly dosing regimens (one week of adult dosage taken as a single dose once each week, i.e., 7,000 IU) or monthly dosing regimens (one month of adult dose taken once a month, i.e., 50,000 IU) may be more convenient for some individuals and has been shown to be safe.

OTHER VITAMIN D SUPPLEMENTATION CONSIDERATIONS

- Tripkovic et al⁸ recommends supplementing with vitamin D3 over D2 (note: most over the counter vitamin D supplements available in Canada contain vitamin D3 whereas high dose vitamin D2 is available only by prescription).
- Vitamin D supplements are almost always contraindicated for individuals with hypercalcemia and should be used with caution in people with hyperphosphatemia.

CLINICALLY INDICATED VITAMIN D TESTING

SERUM 25-HYDROXY VITAMIN D

- Serum 25-hydroxyvitamin D is the best test for assessing vitamin D levels in the following clinical scenarios where patient vitamin D levels may be abnormal including:
 - Significant renal or liver disease
 - Osteomalacia, osteopenia or osteoporosis
 - Malabsorption syndromes
 - Hypo or hypercalcemia/hyperphosphatemia
 - Hypo or hyperparathyroidism
 - Prescribed medications that affect vitamin D metabolism such as phenobarbital, carbamazepine, phenytoin and valproate
 - Prescribed medications that might interfere with vitamin D absorption such as cholestyramine, colestipol and orlistat
 - Unexplained increased levels of serum alkaline phosphatase
 - Intake of high dose vitamin D combined with symptoms suggesting vitamin D toxicosis, i.e., hypervitaminosis D

SERUM 1,25-DIHYDROXY VITAMIN D

- The serum 1,25-dihydroxyvitamin D test is rarely of value as a diagnostic tool and should be limited to use by specialists for their patients suspected of having a 1 α -hydroxylase activity abnormality, e.g., deficiency in renal tubule disorders, excessive (ectopic) 1 α -hydroxylase, e.g., sarcoidosis.

- This is most often observed in significant chronic renal failure (i.e., stage 4 or 5 chronic kidney disease) and genetic renal tubule disorders such as X-linked hypophosphatemic rickets.
- The test may be useful for unexplained hyperparathyroidism in patients with seemingly adequate serum levels of 25-hydroxyvitamin D, lymphoma, sarcoidosis, or suspected vitamin D receptor defects.

TESTING BOTH 25-HYDROXY VITAMIN D AND 1,25-DIHYDROXY VITAMIN D

- Other than in very rare and complex clinical cases managed by specialists (e.g., hypercalcemia with reportedly low endogenous levels of 25-hydroxyvitamin D), there is rarely an indication for ordering both 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D on the same specimen at the same time.

VITAMIN D DEFICIENCY

- Specialist consultation should be considered for patients with unexplained bone pain, unusual fractures, hypercalcemia of unexplained origin or other evidence suggesting a metabolic bone disease or malabsorption syndromes including gastric bypass surgery.

VITAMIN D TOXICITY

- Vitamin D toxicity is very rare⁹ and defined as a serum 25-hydroxyvitamin D concentration consistently >500 nmol/L (>200 ng/mL)
- Doses of up to 10,000 IU of vitamin D₃ daily for as long as five months have been shown to be tolerated by adults.¹⁰ Only when vitamin D₃ is ingested in excess of 10,000 IU/d for prolonged periods with normal gut function and concurrent ingestion of excessive calcium would there be a risk for vitamin D toxicity.⁶
- Patients with granulomatous disease are at risk of hypercalcemia due to increased 1 α hydroxylase activity (which converts 25-hydroxyvitamin D to active 1,25-dihydroxyvitamin D). Toxicity has been reported during vitamin D treatment of tuberculosis and in patients with active sarcoidosis.^{3,11} Specialist advice should be sought before initiating vitamin D therapy.
- Excessive intakes of either vitamin D₂ or vitamin D₃ can cause toxicity and lead to hypercalcaemia. The high serum calcium may cause nausea, dehydration and constipation and potentially lead to soft tissue calcification and subsequent renal and cardiovascular damage.
- The recommended test for investigating vitamin D toxicity is a serum calcium (albumin-corrected total calcium or ionized calcium),¹ and only if the calcium level is elevated would vitamin D testing be indicated.

THERAPEUTIC VITAMIN D DOSAGE MONITORING

- Routine monitoring of serum 25-hydroxyvitamin D is only recommended to assess dosage adequacy following supplementation, and ONLY for those clinical conditions managed by specialist, e.g., renal disease, metabolic bone disease, malabsorption syndromes, etc.
- For the general population where therapeutic vitamin D dosage may be recommended, the serum 25-hydroxyvitamin D is not directly associated with vitamin D supplement intake alone due to the complex pharmacokinetics of vitamin D and other confounding (environmental) influences, i.e., variation in dietary and supplemental vitamin D intake and exposure to sunlight. Therefore, monitoring of serum 25-hydroxyvitamin D is not a reliable indicator of ideal vitamin D dosage.

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SUGGESTED CITATION

Toward Optimized Practice (TOP) working Group for Vitamin D. Guideline for vitamin D testing and supplementation in adults. Edmonton, AB: Toward Optimized Practice. 2014 May.

For more information see www.topalbertadoctors.org

GUIDELINE COMMITTEE

The committee consisted of representatives of internal medicine, family medicine and laboratory services.

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