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Vitamin D: How much do we really need?

by Brenda Yuzdepski, BSP

Learning Objectives:

After completing this lesson, readers will be able to:

1. Understand the importance of vitamin D in bone health as well as other potential health benefits
2. Understand the different forms and sources of vitamin D
3. Understand the absorption, metabolism and excretion of vitamin D
4. Understand Health Canada's daily Recommended Dietary Allowances and upper intake levels for vitamin D
5. Understand vitamin D levels and their relationship to health status
6. Understand the conflicting recommendations regarding optimal daily vitamin D intake and optimal vitamin D blood levels
7. Understand when to refer patients to other members of the healthcare team for further evaluation

Introduction

If ever there was a contest for the most popular nutrient, vitamin D would be considered the odds on favorite. Recently, it seems every week or so, there has been a paper published, a TV report, a magazine article or an Internet blog expounding the benefits of this nutrient. The National Institutes of Health (NIH) has met a number of times in recent years to discuss emerging concerns regarding the inappropriate use of this vital nutrient in the general population. Over the last few years a number of organizations such as the Canadian Cancer Society, Osteoporosis Canada and the Canadian Pediatric Society have published recommended guidelines for vitamin D intake. Recent reports of rickets, the classic vitamin D deficiency disease, and low blood levels of vitamin D being on the rise⁽¹⁾ have created questions regarding if the current Health Canada's recommended dietary allowance guidelines are sufficient to prevent vitamin D deficiency and/or whether further increases in daily vitamin D intake should be recommended

by Health Canada. Consumers are looking to their healthcare professionals for answers regarding how vitamin D may or may not benefit their health. To better understand how to advise these people, one must have an understanding of the basic physiology regarding vitamin D, how it works in the body, what benefits are being shown in research and what dangers can occur with too much of a good thing.

Physiology of Vitamin D

Vitamin D is unique as it is obtained through synthesis in the skin from exposure to sunshine, as well as from dietary intake of fatty fish, eggs or fortified foods such as milk.

Vitamin D₂, also known as ergocalciferol, is synthesized by plants. Vitamin D₃, also known as cholecalciferol or the sunshine vitamin, is synthesized in human skin from 7-dehydrocholesterol after exposure to ultraviolet light.⁽²⁾ In this article, all references to vitamin D indicate vitamin D₃ unless otherwise specified.

In order for vitamin D to become active in the

body it must undergo two metabolic hydroxylation reactions. The first reaction occurs in the liver to form 25-hydroxyvitamin D [25(OH)D] or calcidiol. The second metabolic reaction occurs primarily in the kidney and is stimulated by parathyroid hormone (PTH), resulting in the formation of 1,25-dihydroxyvitamin D [1,25(OH)₂D] or calcitriol, the biologically active form of vitamin D.⁽³⁾ The conversion to 1,25(OH)₂D is regulated by its own concentration, parathyroid hormone (PTH) and serum concentrations of calcium and phosphate.⁽⁴⁾

Levels of vitamin D in the skin reach a plateau in 15–60 minutes of sun exposure. The Mayo Clinic notes as little as 10 minutes of sun exposure daily is thought to be enough to prevent vitamin D deficiency.⁽⁵⁾ However the season of the year, time of day, length of day, cloud cover, smog, latitude, degree of skin pigmentation, amount of body surface exposed, age and sunscreen use are among the factors that influence vitamin D synthesis in the skin by affecting the degree of UV radiation exposure.⁽⁶⁾ Once the plateau is reached, inactive substrates such as lumisterol and tachysterol are produced rather than cholecalciferol.⁽⁷⁾ This is why there are no reports of the development of vitamin D toxicity from sun exposure, although it is possible to develop toxic levels when consuming high doses of vitamin D supplements.

Functions of Vitamin D and Symptoms of Deficiency

Vitamin D is a fat soluble vitamin necessary for bone growth and bone remodeling (the continuous turnover of bone matrix) by specialized bone cells called osteoblasts and osteoclasts. By definition, vitamin D is less of a vitamin and more of a pro-hormone or hormone precursor as it is produced in cells in one part of the body (skin) and then sends out messages that influence cells in other parts of the body such as the bones. It promotes absorption of calcium in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal mineralization of bone.⁽⁸⁾

A vitamin D deficiency can occur when usual intake is lower than recommended levels over time, exposure to sunlight is limited, the kidneys cannot convert vitamin D to its active form or the absorption of vitamin D from the digestive tract is inadequate. Without adequate levels of

TABLE 1 – Dietary Reference Intakes for Vitamin D⁽²²⁾

Age group	Recommended Dietary Allowance (RDA) per day	Tolerable Upper Intake Level (UL) per day
Infants 0-6 months	400 IU (10 mcg)*	1000 IU (25 mcg)
Infants 7-12 months	400 IU (10 mcg)*	1500 IU (38 mcg)
Children 1-3 years	600 IU (15 mcg)	2500 IU (63 mcg)
Children 4-8 years	600 IU (15 mcg)	3000 IU (75 mcg)
Children and Adults 9-70 years	600 IU (15 mcg)	4000 IU (100 mcg)
Adults > 70 years	800 IU (20 mcg)	4000 IU (100 mcg)
Pregnancy & Lactation	600 IU (15 mcg)	4000 IU (100 mcg)

*Adequate Intake rather than Recommended Dietary Allowance

vitamin D, children are at risk of developing rickets or softening of the bones, which can lead to fractures or deformities. Symptoms of deficiency, such as irritability, being easily fatigued and diarrhea, are slow in onset and may take several months to manifest.

Babies with rickets have difficulty sitting and crawling and are slow to walk.⁽⁹⁾

Adults with inadequate levels of vitamin D are at risk for developing osteomalacia (softening of the bones) or osteoporosis (fragile bones). The main symptom of osteomalacia is bone pain, which occurs most often in the hips. Bone tenderness may also occur in the arms, legs and spine. As it progresses, muscle weakness may also develop.⁽²⁾ Osteoporosis, a bone disease, is characterized by low bone mass and deterioration of bone tissue. It is known as “the silent thief” because bone loss occurs without symptoms and as a result the first symptom may be a broken bone.⁽¹⁰⁾

Other symptoms of vitamin D deficiency seen in adults may include chronic back pain,⁽¹¹⁾ diffuse aches and pains,⁽¹²⁾ fatigue and head sweating.⁽¹³⁾

Besides maintaining skeletal muscle balance, vitamin D has many other roles in the human body including neuromuscular and immune function, reducing inflammation⁽⁸⁾ and cancer prevention.⁽⁵⁾ In 2006, using data on over four million cancer patients from 13 different countries, researchers showed a marked increase in some cancer risks in countries with less sun.⁽¹⁴⁾ The authors suggested that increasing the daily intake of vitamin D by 1,000 IU reduced an individual's breast and ovarian cancer risk by 30% and colon cancer risk by 50%.⁽¹⁴⁾

Adequate vitamin D may also be associated with healthy hair follicle growth cycles.⁽¹⁵⁾ Disorders which have been linked to vitamin D deficiency include Alzheimer's

disease,⁽¹⁶⁾ rheumatoid arthritis,⁽¹⁷⁾ multiple sclerosis,⁽¹⁴⁾ sarcopenia (loss of muscle mass and strength),⁽¹⁹⁾ essential hypertension and diabetes mellitus.⁽⁵⁾

Absorption and Excretion

The absorption of vitamin D is enhanced by the presence of fat or bile in the digestive tract; therefore, vitamin D supplements should be taken with food that contains healthy fats such as fish, yogurt, nuts or avocado for best results. Liver disease, pancreatic insufficiency and diseases of the small intestine, such as celiac disease or Crohn's disease, may impair vitamin D absorption and result in suboptimal blood levels. Patients known to be suffering from any of these conditions should be advised to have their vitamin D blood levels checked to ensure adequate levels are being obtained. Studies in infants have suggested that iron deficiency can result in decreased absorption of vitamin D and by correcting the iron deficiency vitamin D absorption improves.⁽²⁰⁾ Vitamin D is primarily excreted in the bile, although some vitamin D metabolites are excreted in the urine.⁽²¹⁾

Intake of Vitamin D

Vitamin D supplements are available in two forms that slightly differ chemically. Vitamin D₂ is manufactured by the UV irradiation of ergosterol in yeast. Vitamin D₃, cholecalciferol, is manufactured by the irradiation of 7-dehydrocholesterol from lanolin and the chemical conversion of cholesterol.⁽²⁾ OTC vitamin D supplements are primarily D₃, as research has noted that vitamin D₂ is less potent and not recommended.⁽⁶⁾

Traditionally, Health Canada recommended that all Canadians over two years of age should follow Canada's Food Guide and consume 500 mL of milk or fortified soy beverages daily. In addition, adults over 50 years of age should

TABLE 2 - Relationship between serum 25-hydroxyvitamin D levels and health status⁽⁶⁾

Serum 25-hydroxyvitamin D (nmol/L)	Health Status
<30	Associated with vitamin D deficiency, leading to rickets in infants and children and osteomalacia in adults
30 – 50	Generally considered inadequate for bone and overall health in healthy individuals
>50	Generally considered adequate for bone and overall health in healthy individuals
>125	Emerging evidence links potential adverse effects to such high levels, particularly > 150 nmol/L

take an additional 400 IU vitamin D supplement daily. Furthermore, all breastfed, healthy term babies should receive a daily supplement of vitamin D of 400 IU beginning at birth and continue until one year of age.⁽²²⁾ Due to the fat soluble nature of vitamin D some researchers have noted the benefits of vitamin D supplementation are seen even when patients take the entire recommended weekly intake amount once per week. Knowing this allows technicians to offer another dosing option for those having difficulty remembering a daily dosing regimen.

Recently, Health Canada adopted new Dietary Reference Intakes (DRIs), which are a comprehensive set of nutrient reference values for healthy populations established by Canadian and American scientists through a review process overseen by the Institute of Medicine (IOM) of the National Academies in the U.S. The new (2010) IOM DRIs for vitamin D in Table 1 have been set assuming minimal sun exposure for all.⁽²²⁾ Note that the Recommended Dietary Allowances (RDAs) in Table 1 refer to total daily vitamin D intake from all sources. In many instances, supplements may not be needed to achieve these intakes. In addition, total vitamin D intake should remain below the daily Tolerable Upper Intake Level (UL) to avoid possible adverse effects.

Health Canada is currently making use of an expert advisory committee to consider the impact the new DRIs on Health Canada's current dietary and other guidance on vitamin D intake for Canadians. They will communicate relevant new information in a timely manner in order to advise Canadians regarding the use of vitamin D.

Several groups suggest higher daily intakes than the RDAs recommended by Health Canada. The Canadian Cancer Society has made recommendations

regarding increasing daily consumption of vitamin D for Canadian adults, in consultation with their healthcare provider, to 1,000 international units (IU) each day during the fall and winter. They also recommend adults at higher risk of having lower vitamin D status such as the older population, individuals with dark skin, those who do not go outside often or individuals who wear clothing that covers most of their skin should consider taking 1,000 IU vitamin D year round.⁽²³⁾

In July 2010, the Osteoporosis Canada's new guidelines recommended adults under the age of 50 without osteoporosis or conditions affecting vitamin D absorption take 400 to 1,000 IU. They go on to recommend individuals over 50 can safely take between 800 and 2,000 IU daily without medical supervision.⁽¹⁰⁾

In October 2010 the Canadian Pediatric Society reaffirmed their 2007 position regarding vitamin D noting accumulation of evidence suggests a much higher intake is necessary during pregnancy. A daily dose of 4,000 IU vitamin D maintained vitamin D sufficiency in the mother and also raised vitamin D in breast milk to the point at which there was no further need of infant supplementation.⁽²⁴⁾ They also noted experimental doses of up to 10,000 IU daily for five months in pregnancy did not elevate levels into the toxic range.⁽²⁵⁾

The IOM, on the other hand, feels that the current evidence is inconsistent and does not clearly demonstrate a cause-and-effect relationship between vitamin D intake and outcomes such as cancer, diabetes, cardiovascular disease and immunity, unlike the scientific data available for the role of calcium and vitamin D in skeletal health. As a result, the IOM based the daily recommended intakes on the amount of vitamin D required to improve skeletal health outcomes.

Measuring Vitamin D Levels

The serum concentration of 25-hydroxyvitamin D or calcidiol, measured in nmol/L, is typically used to determine a patient's vitamin D status as it reflects the amount of vitamin D produced in the skin as well as vitamin D acquired from the diet and supplements.⁽²⁾ It does not, however, indicate the amount of vitamin D stored in body tissues. The level of serum 1, 25-dihydroxy-vitamin D is not usually used to determine vitamin D status as it is tightly regulated by parathyroid hormone, calcium, and phosphate; such that it does not decrease significantly until vitamin D deficiency is already well advanced.⁽⁶⁾

Anything that diminishes the transmission of solar UVB radiation to the earth's surface or anything that interferes with the penetration of UVB radiation into the skin will affect the cutaneous synthesis of vitamin D.⁽²⁾ Vitamin D deficiency or insufficiency in northern latitudes occurs primarily during winter months; however, elderly and institutionalized individuals are at risk throughout the year. Other high-risk groups include breast-fed infants, who may not get enough vitamin D from breast milk alone,⁽²²⁾ women in cultures who are heavily veiled when outside, sunscreen use and dark skin pigmentation also reduce skin synthesis of vitamin D and can result in lower serum levels.⁽²⁾ Obesity is associated with vitamin D deficiency, and it is believed to be due to the sequestration of vitamin D by the large body fat pool.⁽²⁵⁾

Other reasons that have been associated with vitamin D deficiency include individuals with a milk allergy, lactose intolerance, ovo-vegetarianism and veganism.⁽⁶⁾ Medications including anti-seizure medications and glucocorticoids and fat malabsorption are also common causes of deficiency.⁽²⁷⁾

There is some disagreement by various groups regarding the exact levels of 25-hydroxyvitamin D levels needed for good health. Table 2 outlines vitamin D serum levels and associated health status, as established by the IOM based on a review of data on vitamin D needs. The IOM states that 50 nmol/L is the serum 25(OH) D level that is adequate to cover the needs of 97.5% of the population.⁽⁶⁾ The Canadian Health Measures Survey (2010) found that most Canadians have adequate concentrations of vitamin D: only about 5% of men and 3% of women aged six to 79 were considered to

be vitamin D-deficient by their current standards of measurement.⁽²⁸⁾

Despite the recommendations by the IOM, a study released in August 2010 estimated the economic burden and premature death rate in Canada attributable to low serum 25(OH) D levels. If the mean serum 25(OH) D level was increased to 105 nmol/L, the study estimated that the annual death rate could fall by 37,000 deaths, representing 16.1% of annual deaths, and the economic burden could be reduced by 6.9% or \$14.4 billion less the cost of the program. The authors of the August 2010 study have recommended that Canadian health policy leaders consider measures to increase serum 25(OH) D levels for all Canadians.⁽²⁹⁾

Excessive Vitamin D

As noted earlier vitamin D deficiency is associated with a number of symptoms which could potentially decrease one's quality of life however it is important to remember one can have too much of a good thing. Excessive amounts of vitamin D appears to cause abnormal functioning and premature aging.^(16,17,30,31)

Vitamin D toxicity can cause non-specific symptoms such as anorexia, weight loss, increased urination and heart arrhythmias. It can also lead to a rise in calcium blood levels, which can lead to vascular and tissue calcification.⁽⁶⁾ As previously mentioned, there have been no reported cases of excessive vitamin D from sun exposure, due to formation of inactive substrates. It is unlikely intake of vitamin D from food could cause toxic blood levels of vitamin D. Toxicity is much more likely to occur from high intakes of dietary supplements containing vitamin D,

especially from multiple sources. Recommending the discontinuation of supplementation during winter holidays in sunny climates would also be prudent to avoid potential toxicity.

In order to reduce the risk of toxicity, patients should be instructed to calculate their total daily intake from all sources including sun exposure, fortified foods and nutritional supplements. If the patient has any concerns, advise them to see their physician and have their 25-hydroxyvitamin D serum level checked to make sure they are within the recommended range.

Role of the Pharmacy Technicians

It is important the pharmacy technician keep abreast of the changing recommendations of this essential nutrient. By bookmarking the Canadian Cancer Society, Osteoporosis Canada and Health Canada websites to the appropriate places, technicians will have easy access to the most up to date information on vitamin D intake for any discussion with the pharmacist on their team or with patients when necessary. Using this CE information, technicians will be able to more easily identify patients who are at high risk for vitamin D deficiency and be able to help the pharmacist suggest the appropriate vitamin D intake for individual patients for optimal health. Technicians can also regularly remind patients of the many health benefits by listing a few benefits of taking adequate amounts of vitamin D on a regular basis. By asking patients if they have vitamin D at home, technicians can open a dialogue to reiterate the importance of this nutrient. Techs should also remind patients to take their vitamin D with food containing healthy fat for best absorption,

calculate their total daily intake from all sources and to have their serum 25-hydroxyvitamin D levels checked if they are concerned.

With all the conflicting information and recommendations from a variety of different organizations, it is also important for pharmacy techs to be on the lookout for individuals who have a philosophy of "a little is good so a lot is better." Techs can relay to these individuals that further research is required to establish optimal intake and in the interim, patients should get at least Health Canada's daily RDA and should not exceed the daily upper limit without their physician's guidance. It is also important for techs to remember to take adequate doses of vitamin D themselves.

Conclusion

Most vitamin D experts agree the medical profession has not fully appreciated the full role of vitamin D in the maintenance of optimal health despite a large body of recent evidence indicating that suboptimal levels of vitamin D contribute to the development of various chronic diseases. Patients should be reminded of the importance of an adequate intake of vitamin D not only for bone health but for overall wellness especially during winter months. It is also important to remind patients too much vitamin D may be dangerous. If they have any concerns regarding their vitamin D status advise them to discuss the appropriateness of testing their serum 25-hydroxyvitamin D blood levels in order to help guide future recommendations.

References are available at www.CanadianHealthcareNetwork.ca, CE section, Quick search CCCEP # 1065-2011-211-I-T

QUESTIONS

Please select the best answer for each question or answer online at www.CanadianHealthcareNetwork.ca for instant results.

- The conversion of vitamin D to 1,25(OH)₂D is regulated by all of the following except:
 - its own concentration
 - parathyroid hormone (PTH)
 - serum concentrations of calcium and phosphate
 - high oral doses of Vitamin D3
- A study released in August 2010 estimated that increasing the mean

serum 25-hydroxyvitamin D blood level to 105 nmol/L the annual death rate could fall by how much?

- 134,000
- 65,000
- 37,000
- 15,000

3. Vitamin D is best taken with foods that contain healthy fats such as fish, nuts or avocado

- True
- False

4. The Canadian Cancer Society feels which supplemental dose of vitamin D will help reduce the risk of cancer and have the least potential for harm

- 400 IU daily
- 1,000 IU daily
- 20 mcg daily
- 800 mcg daily

5. Health Canada's daily Recommended Dietary Allowances for Canadians are based on which of the following:

QUESTIONS (Continued)

- a) Skeletal health
b) Immunity
c) Cardiovascular disease prevention
d) Diabetes treatment

6. The following are possible causes of vitamin D deficiency, except:

- a) Intake lower than recommended
b) Limited sunlight exposure
c) Decreased absorption from digestive tract
d) Increased conversion in kidneys
e) Breastfeeding (the child being breastfed)

7. Symptoms of vitamin D toxicity may include the following, except:

- a) Anorexia b) Weight loss
c) Decreased urination
d) Heart arrhythmias

8. The recommended dietary allowance outlined by Health Canada for Canadians between the ages of 9 to 70 is

- a) 15 mcg b) 1,000 IU
c) 800 mg d) 600 mcg

Please select the best answer for each question or answer online at www.CanadianHealthcareNetwork.ca for instant results.

9. Vitamin D3 is also known as which of the following?

- a) Cholecalciferol
b) Ergocalciferol
c) 7-dehydrocholesterol
d) PTH

10. Which of the following statements regarding vitamin D supplementation is false?

- a) Absorption is enhanced by the presence of fat or bile, therefore it should be taken with food
b) Serum 25-hydroxyvitamin D levels are typically used to determine vitamin D status
c) Vitamin D toxicity can result from too much sun exposure
d) Breast fed babies are at higher risk for vitamin D deficiency

11. In order for vitamin D to become active in the body it must undergo which metabolic reaction?

- a) Sulfation b) Hydroxylation
c) Methylation d) Oxidation

12. The following is not an early

symptom of rickets

- a) Constipation b) Easily fatigued
c) Irritability d) Diarrhea

13. Sources of vitamin D include all of the following except:

- a) UV light b) Milk
c) Fatty fish d) Pork

14. Which of the following statements about vitamin D is not true?

- a) It is a fat soluble vitamin
b) It is a hormone precursor
c) It promotes absorption of calcium in the gut
d) It promotes osteomalacia in adults

15. Disorders which have been linked to vitamin D deficiency include which of the following:

- a) Alzheimer's
b) Rheumatoid arthritis
c) Sarcopenia
d) None of the above
e) All of the above

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Vitamin D: How much do we really need?

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