Vitamin D Deficiency and Related Disorders

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Medscape 5th August 2014

Practice Essentials

Vitamin D deficiency can result from inadequate exposure to sunlight; malabsorption; accelerated catabolism from certain medications; and, in infants, the minimal amount of vitamin D found in breast milk. In children, vitamin D deficiency can result in rickets, which presents as bowing of the legs; in adults, it results in osteomalacia, which presents as a poorly mineralized skeletal matrix.

Essential update: Task force finds lack of evidence to support routine Vitamin D screening in asymptomatic adults

The US Preventive Services Task Force (USPSTF) has released a draft recommendation stating that insufficient evidence exists for or against routine screening of healthy, asymptomatic adults for vitamin D deficiency. The statement points to the ongoing debate over what vitamin D levels should be considered optimal or deficient and notes that, evidence suggests, results vary between different vitamin D tests, as well as between the same tests run at different facilities. The task force also states that in cases of asymptomatic vitamin D deficiency, evidence indicates that treatment will not reduce the risk of cancer, type 2 diabetes, fracture (in persons not otherwise considered to have a high fracture risk), or mortality (in community-dwelling adults).[1, 2]

The USPSTF recommendation is aimed at nonpregnant, community-dwelling primary care patients aged 18 years or older who are asymptomatic for vitamin D deficiency or any disorder treated with vitamin D.

Signs and symptoms

Vitamin D deficiency is often clinically silent. Manifestations are as follows:

- Children are often found to have started walking late or prefer to sit down for prolonged periods
- Adults can experience chronic muscle aches and pains

Physical findings in severe vitamin D deficiency are as follows:

- In children, bowing in the legs
- In adults, periosteal bone pain, best detected with firm pressure on the sternum or tibia

See Clinical Presentation for more detail.

Diagnosis

Measurement of serum 25-hydroxyvitamin D (25[OH]D) is the best test to determine vitamin D status. levels of 25(OH)D are interpreted as follows[3]:

- 21-29 ng/mL (52.5-72.5 mmol/L): Vitamin D insufficiency
- < 20 ng/mL (< 50 mmol/L): Vitamin D deficiency

Although not always required for the diagnosis of vitamin D insufficiency, measurement of the serum parathyroid hormone (PTH) level may help establish the diagnosis of vitamin D insufficiency. PTH levels are often elevated in patients with vitamin D insufficiency, indicating secondary hyperparathyroidism.

Screening for vitamin D deficiency is recommended only in those individuals who are at high risk for vitamin D deficiency, including the following[4]:

- Patients with osteoporosis
- Patients with a malabsorption syndrome
- Black and Hispanic individuals
- Obese persons (body mass index >30 kg/m^2)
- Patients with disorders that affect the metabolism of vitamin D and phosphate (eg, chronic kidney disease)

See Workup for more detail.

Management

Recommended treatment for vitamin D–deficient patients up to 1 year of age is as follows[4]:

- 2000 IU/day of vitamin D_2 or D_3 for 6 weeks *or*
- 50,000 IU of vitamin D_2 or D_3 once weekly for 6 weeks
- When the serum 25(OH)D level exceeds 30 ng/mL, provide maintenance treatment of 400-1000 IU/day

Recommended treatment for vitamin D–deficient patients 1–18 years of age is as follows[4]:

- 2000 IU/day of vitamin D_2 or D_3 for at least 6 weeks *or*
- 50,000 IU of vitamin D_2 once weekly for at least 6 weeks
- When the serum 25(OH)D level exceeds 30 ng/mL, provide maintenance treatment of 600-1000 IU/day

Recommended treatment for vitamin D–deficient adults is as follows[4]:

- 50,000 IU of vitamin D_2 or D_3 once weekly for 8 weeks *or*
- 6000 IU/day of vitamin D_2 or D_3 for 8 weeks
- When the serum 25(OH)D level exceeds 30 ng/mL, provide maintenance treatment

of 1500-2000 IU/day

Recommended treatment for vitamin D–deficient patients who are obese, have a malabsorption syndrome, or are taking medication that affects vitamin D metabolism, is as follows[4]:

- At least 6000-10,000 IU of vitamin D daily
- When the serum 25(OH)D level exceeds 30 ng/mL, provide maintenance treatment of 3000-6000 IU/day

If the 25(OH)D concentration remains persistently low despite several attempts at correction with oral vitamin D, a trial of ultraviolet B light therapy (ie, by tanning lamps) may be considered to improve vitamin D status.

Prevention

Unprotected sun exposure is the major source of vitamin D for both children and adults.[4] Provision of vitamin D from sunlight is as follows:

- Sensible sun exposure, especially between the hours of 10 am and 3 pm, produces vitamin D in the skin that may last twice as long in the blood compared with ingested vitamin D[5]
- Full-body sun exposure producing slight pinkness in light-skinned persons results in vitamin D production equivalent to ingesting 10,000-25,000 IU[6]
- Increased skin pigmentation, aging, and sunscreen use reduce the skin's vitamin D_3 production

Recommended dietary intake of vitamin D for patients at risk of vitamin D deficiency is as follows[4]:

- In infants and children up to 1 year old, at least 400 IU/day, to maximize bone health
- In children and adolescents 1-18 years of age, at least 600 IU/day to maximize bone health
- In adults 19-50 years of age, at least 600 IU/day to maximize bone health and muscle function
- Raising the serum 25(OH)D level consistently above 30 ng/mL may require vitamin D intake of at least 1000 IU/day
- Whether recommended levels of vitamin D intake will provide all the potential nonskeletal health benefits associated with vitamin D is currently unknown

Most dietary sources of vitamin D do not contain sufficient amounts of the vitamin to satisfy daily requirements. The following foods contain the indicated amounts of vitamin D, as reported by the US Department of Agriculture's (USDA's) Nutrient Data Laboratory:

- Fortified milk (8 oz) - 100 IU
- Fortified orange juice (8 oz)[7] - 100 IU
- Fortified cereal (1 serving) - 40-80 IU
- Pickled herring (100 g) - 680 IU

- Canned salmon with bones (100 g) - 624 IU
- Mackerel (100 g) - 360 IU
- Canned sardines (100 g) - 272 IU
- Codfish (100 g) - 44 IU
- Swiss cheese (100 g) - 44 IU
- Raw shiitake mushrooms (100 g) - 76 IU
- Most multivitamins (1 tab) - 400 IU

Background

Vitamin D deficiency in children can manifest as rickets (it is the most common cause of nutritional rickets), which presents as bowing of the legs. Vitamin D deficiency in adults results in osteomalacia, which presents as a poorly mineralized skeletal matrix. These adults can experience chronic muscle aches and pains .(See Presentation and Prognosis.)

Vitamin D is important for calcium homeostasis and for optimal skeletal health. The major function of vitamin D is to increase the efficiency of calcium absorption from the small intestine. Heaney and colleagues demonstrated that maximum calcium absorption occurs at levels of 25-hydroxyvitamin D (25[OH]D) greater than 32 ng/mL. (See Pathophysiology and Etiology.)[9]

Vitamin D also enhances the absorption of phosphorus from the distal small bowel. Adequate calcium and phosphorus absorption from the intestine is important for proper mineralization of the bone. The second major function of vitamin D is involvement in the maturation of osteoclasts, which resorb calcium from the bones. (See Pathophysiology and Etiology.)

The term vitamin D refers to either vitamin D2 or vitamin D3. Vitamin D3, also known as cholecalciferol, is either made in the skin or obtained in the diet from fatty fish. Vitamin D2, also known as ergocalciferol, is obtained from irradiated fungi, such as yeast. Vitamin D2 and vitamin D3 are used to supplement food products or are contained in multivitamins. (See Treatment and Medication.)

Past studies suggested that vitamin D3 may be more effective than vitamin D2 in establishing normal vitamin D stores.[10, 11] However, a study by Holick and colleagues demonstrated that vitamin D2 and vitamin D3 appear to be equipotent in raising 25(OH)D concentrations when they are given in daily doses of 1000 IU.[12]

Physiology

The production of vitamin D3 in the skin involves a series of reactions initiating with 7-dehydrocholesterol. Upon exposure to ultraviolet B (UVB) radiation between the wavelengths of 290-315 nm, 7-dehydrocholesterol is converted to previtamin D3, which is then converted to vitamin D3 after a thermally induced isomerization reaction in the skin.

From the skin, newly formed vitamin D3 enters the circulation by binding to vitamin D binding protein (DBP). In order to become active, vitamin D requires 2 sequential hydroxylations to form 1,25-dihydroxyvitamin D (1,25$[OH]_2$ D).

Vitamin D is initially hydroxylated in the 25 position by the hepatic microsomal and/or mitochondrial enzyme vitamin D 25-hydroxylase. The second hydroxylation occurs in the kidney and is performed by the P450 enzyme 25-hydroxyvitamin D-1 alpha-hydroxylase.

Upon entering the cell, the 1,25$(OH)_2$ D hormone binds to the vitamin D receptor (VDR). The bound vitamin D receptor then forms a heterodimer with the retinoic acid X receptor (RXR). This heterodimer then goes to the nucleus to bind deoxyribonucleic acid (DNA) and increases transcription of vitamin D–related genes.

Pathophysiology

Inadequate circulating 25(OH)D is associated with elevated parathyroid hormone (PTH); this condition is called secondary hyperparathyroidism. The rise in PTH may result in increased mobilization of calcium from the bone, which leads to decreased mineralization of the bone.

Of note, prolonged exposure to the sun does not cause vitamin D toxicity. This is because after prolonged UVB radiation exposure, the vitamin D made in the skin is further degraded to the inactive vitamin D metabolites tachysterol and lumisterol.

Etiology

Vitamin D deficiency can result from the following:

- Inadequate exposure to sunlight - This causes a deficiency in cutaneously synthesized vitamin D; adults in nursing homes or health care institutions are at a particularly high risk[13]
- Vitamin D malabsorption problems - People who have undergone resection of the small intestine are at risk for this condition; diseases associated with vitamin D malabsorption include celiac sprue, short bowel syndrome,[14] and cystic fibrosis[15]
- Minimal amounts of vitamin D in human breast milk - The American Academy of Pediatrics recommends vitamin D supplementation starting at age 2 months for infants fed exclusively with breast milk[16]
- Medications - Some medications are associated with vitamin D deficiency; drugs such as Dilantin, phenobarbital, and rifampin can induce hepatic p450 enzymes to accelerate the catabolism of vitamin D

Epidemiology

Occurrence in the United States

Vitamin D insufficiency is highest among people who are elderly, institutionalized, or hospitalized. In the United States, 60% of nursing home residents[17] and 57% of hospitalized patients[18] were found to be vitamin D deficient.

However, vitamin D insufficiency is not restricted to the elderly and hospitalized population; several studies have found a high prevalence of vitamin D deficiency among healthy, young adults. A study determined that nearly two thirds of healthy, young adults in Boston were vitamin D insufficient at the end of winter.[19]

An analysis of data on 2877 US children and adolescents (age, 6-18 y) from the National Health and Nutrition Examination Survey (NHANES) 2003-2006 indicated that, based on current Institute of Medicine Committee guidelines, about 10.3% of this population (an estimated 5.5 million) had inadequate vitamin D (25(OH)D) levels (< 16 ng/mL), and 4.6% (an estimated 2.5 million) had levels placing them at risk of frank deficiency (< 12 ng/mL).[20, 21] Adolescents (age, 14-18 y) and obese children had the highest risk of 25(OH)D deficiency and inadequacy, and these risks were also higher among girls than boys (of any age and body mass index) and among nonwhite children.[21]

Vitamin D status may fluctuate throughout the year, with the highest serum 25(OH)D level occurring after the summer and the lowest serum 25(OH)D concentrations after winter. A study by Shoben at el demonstrated that mean serum 25(OH)D concentrations can vary as much as 9.5 ng/mL. Factors such as male sex, higher latitude, and greater physical activity levels were found to be associated with greater differences in serum 25(OH)D concentrations in winter and summer.[22]

International occurrence

Similar rates of vitamin D deficiency have been reported in Europe[23] and Canada. A greater prevalence of vitamin D deficiency exists in Middle Eastern countries. A study of 316 young adults aged 30-50 years from the Middle East showed that 72.8% had 25(OH)D values of less than 15 ng/dL (that is, severely deficient). This was significantly more common in women than in men (83.9% vs 48.5%, respectively). The difference between sexes probably reflects the cultural and religious practices leading to less skin exposure in women than in men.[24, 25, 26, 27]

Race-related demographics

Darker skin interferes with the cutaneous synthesis of vitamin D. A study by Holick and coauthors demonstrated that non-Hispanic black subjects require 6 times the amount of UV radiation necessary to produce a serum vitamin D concentration similar to that found in non-Hispanic white subjects.[28] The explanation for the increased radiation necessary to increase vitamin D levels is that melanin absorbs ultraviolet radiation.

The decreased efficacy of vitamin D production by darker-pigmented skin explains the

higher prevalence of vitamin D insufficiency among darker-skinned adults. Dawson-Hughes and colleagues demonstrated that in Boston, 73% of elderly black subjects were vitamin D insufficient, compared with 35% of elderly non-Hispanic whites.[29]

In a large survey of 1500 healthy black women younger than 50 years, 40% were vitamin D deficient (25[OH]D < 16ng/mL), compared with 4% of 1400 white women in that study.[30]

Age-related demographics

Vitamin D production in the skin declines with advancing age, making elderly populations more dependent on dietary vitamin D. For the average older person, higher dietary intake of vitamin D may be required to achieve optimal serum levels of 25(OH)D.[31]

Prognosis

The treatment of vitamin D insufficiency can decrease the risk of hip and nonvertebral fractures.[32, 33] A meta-analysis by Boonen et al of postmenopausal women and of men aged 50 years or older reporting a risk of hip fracture found that oral vitamin D supplementation reduced the risk of hip fractures by 18% when vitamin D and calcium were taken together.[34] Most of the trials that demonstrated the antifracture efficacy of vitamin D used approximately 800 IU of vitamin D3. The minimum 25(OH)D level at which antifracture efficacy was observed was 30 ng/ml (74 nmol/L), suggesting a threshold for optimal levels of 25(OH)D for fracture protection.

Results from another meta-analysis, evaluating the efficacy of oral vitamin D supplementation in the prevention of hip and other nonvertebral bone fractures in individuals aged 65 years or older, indicated that vitamin D offers dose-dependent fracture protection.[35] The analysis, by Bischoff-Ferrari et al, took into account 12 double-blind, randomized, controlled trials (RCTs) for nonvertebral fractures (n = 42,279) and 8 RCTs for hip fractures (n = 40,886), comparing the results obtained from the use of oral vitamin D (with or without calcium) with those derived from the administration of calcium alone and from placebo use.

In this study, doses of more than 400 IU/day were found to reduce fractures by at least 20% in individuals aged 65 years or older.[35] In contrast to the Boonen study, the investigators maintained that these effects were independent of calcium supplementation.

Vitamin D insufficiency contributes to osteoporosis by decreasing intestinal calcium absorption.[9, 36] Treatment of vitamin D deficiency has been shown to improve bone mineral density.[37, 38] An analysis of the Third National Health and Nutrition Examination Survey (NHANES III) demonstrated a positive correlation between circulating 25(OH)D levels and bone mineral density.[39]

Vitamin D supplementation has been associated with a reduction in falls and improved muscle strength in the elderly. A meta-analysis demonstrated that vitamin D supplementation resulted in a reduction in falls of about 22% in ambulatory and institutionalized elderly subjects, as compared with controls.[40, 41] Another meta-analysis

examining muscle strength associated with vitamin D supplementation found significant improvement in reduced postural sway, timed up-and-go test results, and lower extremity strength in a pooled analysis of 13 studies.[42]

Epidemiologic data suggest that vitamin D deficiency places adults at risk for developing cancer[43, 44, 45, 46, 47]; these apparently include breast, colon, and prostate cancer.[48, 49] Several studies using cultured cancer cells in mice models have also supported the notion that vitamin D prevents the growth of cancers.[50] Larger, randomized clinical trials are underway in humans to establish the role of vitamin D in the prevention of cancers.

Vitamin D insufficiency may increase the risk for type I and type II diabetes mellitus.[31, 51] In NHANES III, lower vitamin D status was associated with higher fasting glucose and 2-hour glucose after an oral glucose tolerance test.[52] Furthermore, vitamin D supplementation in adults has been associated with improved insulin sensitivity in several small, case-control studies.[51]

Joergensen et al determined that vitamin D deficiency in type 1 diabetes may predict all causes of mortality but not development of microvascular complications.[53] The contribution of vitamin D deficiency to mortality must be mediated by nonvascular mechanisms.

Low levels of vitamin D have also been linked to increased cardiovascular disease (CVD) biomarkers in older adults. In an observational study of 957 hypertensive older adults, vitamin D deficiency (< 25 nmol/L) was associated with higher levels of biomarkers linked with CVD and conditions such as multiple sclerosis and rheumatoid arthritis.[54, 55] Individuals deficient in vitamin D had significantly higher levels of the inflammatory biomarkers interleukin-6 (IL-6) and C-reactive protein (CRP), and higher IL-6:IL-10 and CRP:IL-10 ratios compared with subjects who had serum vitamin D levels > 75 nmol/L.[54, 55]

A meta-analysis evaluated the effect of vitamin D supplementation (using a mean supplementation dosage of about 500 IU daily) on all-cause mortality in 18 randomized controlled trials and found a 7% relative risk reduction for death.[56] Severe vitamin D deficiency (25(OH)D < 10 ng/mL) has been associated with increased in-hospital mortality in patients admitted for acute coronary syndrome.[57]

A Cochrane Review of 50 randomized, controlled trials that included more than 94,000 individuals, primarily elderly women, found that vitamin D3 supplementation decreased mortality. Other forms of vitamin D, including vitamin D2, calcitriol, and alpha-calcidiol, did not reduce mortality.[58]

History and Physical Examination

History

Vitamin D deficiency is often a silent disease. By definition, rickets occurs in children whose growth plates have not fused. These children are often found to have started

walking late or prefer to sit down for prolonged periods. In adults, vitamin D deficiency results in osteomalacia, which presents as a poorly mineralized skeletal matrix. Adults in these cases can experience chronic muscle aches and pains.[8]

Vitamin D deficiency is the most common cause of nutritional rickets. Rare genetic forms of rickets occur because of defects in vitamin D metabolism. Vitamin D–dependent rickets type I occurs because of a defect in the renal 25-hydroxyvitamin D-1 alpha-hydroxylase that results in decreased $1,25(OH)_2$ D production. Vitamin D–dependent rickets type II occurs when a mutation exists in the VDR.

Physical examination

In children with a severe vitamin D deficiency, the examination may reveal bowing in the legs. In adults with a severe vitamin D deficiency, the examination can reveal periosteal bone pain. This is best detected using firm pressure on the sternal bone or tibia.

Diagnostic Considerations

Conditions to be considered in the differential diagnosis of vitamin D deficiency include the following:

- Lack of dietary intake
- Inadequate sunlight exposure
- Malabsorptive diseases - Celiac sprue, short bowel syndrome, cystic fibrosis
- Use of antiepileptic medications that accelerate vitamin D metabolism - Phenytoin, phenobarbital
- End-stage liver disease

Approach Considerations

Serum 25(OH)D

This is the best test to determine vitamin D status (see Vitamin D3 25-Hydroxyvitamin D). The circulating half-life of 25(OH)D is 2 weeks. A 25(OH)D level of less than 30 ng/mL is considered vitamin D insufficient.[3] A 25(OH)D level of less than 15 or 20 ng/mL have been used to define vitamin D deficiency. Intestinal calcium absorption is optimized at levels above 30-32 ng/mL.[9, 36] Parathyroid hormone levels start to rise at 25(OH)D levels below 31 ng/mL,[59] which is another marker of vitamin D insufficiency.

Parathyroid hormone

Although not always required for the diagnosis of vitamin D insufficiency, a serum PTH may be used to help establish the diagnosis of vitamin D insufficiency. Often, patients with vitamin D insufficiency have a corresponding elevated PTH, indicating secondary hyperparathyroidism. An inverse relationship exists between PTH and 25(OH)D levels.[59] Usually, PTH levels decrease after the correction of a vitamin D insufficiency.

The Endocrine Society, along with the Canadian Society of Endocrinology and Metabolism and the National Osteoporosis Foundation, published a clinical practice guideline in 2011

titled "Evaluation, Treatment and Prevention of Vitamin D Deficiency." The committee recommended screening of only those individuals who are at high risk for vitamin D deficiency, including patients with osteoporosis or a malabsorption syndrome, as well as black and Hispanic individuals, obese persons (BMI >30 kg/m^2), and those with several other medical conditions.

The daily maintenance dose of vitamin D varies by age, but most children and adults generally require 600-2000 IU of vitamin D daily. For vitamin D-deficient children and adults, higher doses of vitamin D given either daily or weekly are recommended, followed by an increase in the daily dose of vitamin D.[4]

In a population-based study, the electronic medical records of more than 1,200,000 members of a health maintenance organization (HMO) were analyzed to determine the upper limit of vitamin D beyond which there is an increased risk of acute coronary syndrome (ACS) or mortality.[60, 61] The lowest risk of mortality and morbidity was reported in members with vitamin D levels in the 20-36 ng/mL range.[61] The hazard ratio increased not only below but also above this range, with adjusted hazard ratios of 1.88 among subjects with vitamin D levels lower than 10 ng/mL, 1.25 among those with levels of 10-20 ng/mL, and 1.13 among those with levels higher than 36 ng/mL ($P < 0.05$).

Follow-up

After correction of their vitamin D status with oral vitamin D, patients should have a repeat test of their 25(OH)D level to confirm that they are in the normal range. If the 25(OH)D concentration remains persistently low despite several attempts at correction with oral vitamin D, a trial of UVB light therapy (ie, by tanning lamps) may be considered to improve vitamin D status.

Sun Exposure

Sensible sun exposure, especially between the hours of 10:00 am and 3:00 pm produces vitamin D in the skin that may last twice as long in the blood compared with ingested vitamin D.[5] If sun exposure produces slight pinkness, the amount of vitamin D produced in response to exposure of the full body is equivalent to ingesting 10,000-25,000 IU.[6] A variety of factors reduce the skin's vitamin D-3 production, including increased skin pigmentation, aging, and the topical application of a sunscreen. A clinical study from Sweden comparing full body irradiation with UVB lamps 3 times a week for 6 weeks to a daily vitamin D_3 supplement of 1,600 IU daily for 6 weeks found UVB therapy to be more efficacious in raising serum 25(OH)D concentrations. This suggests that UVB therapy may be a useful therapeutic approach in selected individuals.[62]

Diet

Individuals who do not have exposure to sunlight are at risk for vitamin D deficiency if they do not ingest adequate amounts of foods that contain vitamin D.

However, most dietary sources of vitamin D do not contain sufficient amounts of the vitamin to satisfy daily requirements. Foods thought to contain high amounts of vitamin D3

are oily fish, such as salmon, mackerel, and blue fish, as well as fortified milk and other dairy products.

A single serving (3.5 oz) of wild-caught salmon has 988 ± 524 IU of vitamin D3, an amount that remains unchanged after baking but that decreases by 50% if the salmon is fried in vegetable oil.[63] In comparison, farm-raised salmon has only 25% of the vitamin D3 content found in the flesh of wild salmon. Blue fish and mackerel have vitamin D3 levels of 280 ± 68 IU and 24 IU, respectively.[63]

Fortified milk may contain less than the stated amount of vitamin D3 on the product (in some cases less than 80% of the amount).[64] Vegetables are not a good source for vitamin D.

The following foods contain the indicated amounts of vitamin D, as reported by the US Department of Agriculture's (USDA's) Nutrient Data Laboratory:

- Fortified milk (8 oz) - 100 IU
- Fortified orange juice (8 oz)[7] - 100 IU
- Fortified cereal (1 serving) - 40-80 IU
- Pickled herring (100 g) - 680 IU
- Canned salmon with bones (100 g) - 624 IU
- Mackerel (100 g) - 360 IU
- Canned sardines (100 g) - 272 IU
- Codfish (100 g) - 44 IU
- Swiss cheese (100 g) - 44 IU
- Raw shiitake mushrooms (100 g) - 76 IU
- Most multivitamins (1 tab) - 400 IU

It should be kept in mind that the potency of vitamin D supplements from different manufacturers can vary widely. In one study, pills from sealed bottles of over-the-counter cholecalciferol supplements (1000 IU, 5000 IU, and 10,000 IU) contained 52-135% of the dose listed on the labels. Analysis of bottles with the same lot number revealed that potency ranged from 57% to 138% of what was on the bottle. Compounded 50,000-IU pills contained 52-105% of the expected dose, and 1000-IU compounded pills contained 23-146%.[65]

Medication Summary

The goals of pharmacotherapy are to correct the vitamin D deficiency, reduce morbidity, and prevent complications.

Over the past 2 years, some controversy has arisen around the issue of adequate vitamin D requirements. The Institute of Medicine’s (IOM) recommendations for daily vitamin D requirements are less than those recommended by the Endocrine Society.[4] This difference may stem from the fact that the IOM targets food fortification and the Endocrine Society targets individual patient care.[66] The daily maintenance dose of vitamin D varies by age.

The Endocrine Society recommends 400 IU for children aged 0-1 year and 600 IU/day for children aged 1-18 years.[4] The Endocrine Society recommends 1500-2000 IU for all men and women older than 18 years, including lactating and pregnant women whose infants are not ingesting vitamin D. Higher doses of vitamin D, given either daily or weekly, are recommended for vitamin D–deficient children and adults, followed by an increase in the daily dose of vitamin D.[4]

Physicians should exercise caution when recommending over-the-counter (OTC) vitamin D supplementation. Some brands may not contain the amount of vitamin D stated on the bottle.

Vitamins, Fat-Soluble

Class Summary

Vitamin D promotes absorption of calcium and phosphorus in the small intestine. It also promotes renal tubule resorption of phosphate.

Ergocalciferol (Calciferol, Drisdol)

Ergocalciferol is the most widely available form of vitamin D. This agent stimulates calcium and phosphate absorption from the small intestine and promotes calcium release from bone into the blood.

Nutritional Supplementation

Adult

Recommended daily allowance (RDA)

19-70 years: 600 IU (15 mcg)/day

Pregnant or lactating women: 600 IU (15 mcg)/day

Osteoporosis

Prophylaxis and treatment

>50 years: 800-1000 IU (20-25 mcg) PO once daily with calcium supplements

Hypoparathyroidism

25,000-200,000 IU (0.625-5 mg) PO once daily with calcium supplements

Vitamin D-Resistant Rickets

12,000-500,000 IU (0.3-12.5 mg) PO once daily

Familial Hypophosphatemia

10,000-60,000 IU (0.25-1.5 mg) PO once daily with phosphate supplements

Paediatric

Dosing Forms & Strengths

RDA

0-12 months: 400 IU (10 mcg) PO once daily

1-18 years: 600 IU (15 mcg) PO once daily

Vitamin D-Resistant Rickets

12,000-500,000 IU (0.3-12.5 mg) PO once daily

Familial Hypophosphatemia

40,000-80,000 IU (1-2 mg) PO once daily with phosphate supplements; may be reduced after stage of growth is complete.

Geriatric

RDA

<70 years: 600 IU (15 mcg) PO once daily

>70 years: 800 IU (20 mcg) PO once daily

Drug Interactions

Contraindicated (1)

- sucroferric oxyhydroxide

Serious - Use Alternative (0)

Significant - Monitor Closely (25)

- aluminum hydroxide
- calcium acetate
- calcium carbonate
- calcium chloride
- calcium citrate
- calcium gluconate
- chlorothiazide
- chlorthalidone

- cholestyramine
- colesevelam
- colestipol
- digoxin
- fosphenytoin
- hydrochlorothiazide
- indapamide
- magnesium citrate
- magnesium hydroxide
- methyclothiazide
- metolazone
- mineral oil
- orlistat
- phenobarbital
- phenytoin
- primidone
- sucralfate

Minor (0)

Adverse Effects

Frequency Not Defined

Arrhythmias

Confusion

Constipation

Dry mouth

Headache

Hypercalcemia

Lethargy

Metallic taste

Muscle or bone pain

Nausea

Sluggishness

Vomiting

Contraindications & Cautions

Contraindications

Hypercalcemia

Hypervitaminosis D

Ergocalciferol (oral): Gastrointestinal (GI), liver, or biliary disease associated with malabsorption of vitamin D analogues

IV administration

Cautions

Ergocalciferol: Use with caution in renal impairment (strong caution), heart disease, kidney stones, arteriosclerosis

Obtain serum calcium twice weekly during titration

Discontinue if patient becomes hypercalcemic

Presence of tartrazine in some products may cause allergic reactions

Vitamin D toxicity may last ≥2 months after therapy is discontinued

Restrict intake in infants with idiopathic hypercalcemia

Concurrent use of cardiac glycosides

Adequate clinical response to vitamin D therapy is dependent on adequate dietary

Pregnancy & Lactation

Pregnancy category: C (ergocalciferol)

Lactation: Drug is distributed into breast milk; use with caution

Pharmacology

Mechanism of Action

Stimulates calcium and phosphate absorption from small intestine; stimulates phosphate resorption at renal tubule; stimulates secretion of calcium into blood from bone

Absorption

Peak effect: 1 month with daily dosing

Metabolism

Metabolized in liver

Elimination

Excretion: Urine