
The Epidemic of Vitamin D Deficiency

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A 37-year-old woman was referred to our endocrine clinic for management of her long-standing hypothyroidism. Her main complaints were muscle aches and pains that started about a year ago. The symptoms progressed to generalized muscle weakness. She described difficulty in getting out of her chair and in climbing stairs. She had an extensive work-up done by her neurologist and rheumatologist, including nerve-conduction studies and a muscle biopsy. The evaluation was normal, and she was diagnosed with fibromyalgia.

She had gastric bypass surgery in 1998 and lost 150 pounds since the operation. She also has had lactose intolerance and a compression fracture without trauma. Her weight was 314 pounds. She had proximal muscle weakness. The rest of her physical examination was normal. Serum laboratory values are listed in Table 1. Based on the laboratory values, she was diagnosed as having severe vitamin D deficiency. She was started on 50,000 IU of vitamin D2 (Ergocalciferol) once a week for 6 months. Now her 25 hydroxyvitamin D level is 40 ng/mL, and her muscle strength has improved.

DISCUSSION

Epidimology of Vitamin D Deficiency

Vitamin D deficiency is an epidemic affecting people of all ages but especially the elderly. Once peak bone mass is attained, adults with vitamin D deficiency will lose 0.25-0.5% of their skeletal mass per year.¹ The prevalence of vitamin D deficiency is 36% in healthy adults aged between 18-29 yrs. It is estimated that 25-54% of nursing

home residents,² 57% of medicine inpatients,³ and 49% of rehabilitation inpatients have low vitamin D levels.⁴ This can have important consequences since vitamin D is necessary for bone health, muscle strength and function, and overall well-being. Some experts estimate that there are over 1 billion people in the world with vitamin D deficiency.

CME INFORMATION

TARGET AUDIENCE

This CME article is intended for primary care physicians, general internists, endocrinologists, general surgeons, orthopedic surgeons, neurologists, rheumatologists, and physical medicine and rehabilitation physicians.

EDUCATIONAL OBJECTIVES

After reading the article, the healthcare provider should recall the production, absorption, and metabolism of vitamin D, its effects on various tissues, the clinical manifestations of its deficiency, and how to screen for and to treat vitamin D deficiency.

Estimated time to complete this activity is 1 hour.

CREDIT

The LSMS Educational and Research Foundation designates this educational activity for a maximum of one (1) *AMA PRA Category 1 Credit*TM. Physicians should only claim credit commensurate with the extent of their participation in the activity.

DISCLOSURE

Dr. Faiz has nothing to disclose.
Dr. Panunti has nothing to disclose.
Dr. Andrews has nothing to disclose.

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Clinical Presentation of Vitamin D Deficiency

Vitamin D deficiency occurs in people lacking sun exposure and/or vitamin D containing foods (Figure, Table 2). Deficiency is seen in areas distant from the equator and is more pronounced in winter.⁵ Since vitamin D is necessary for efficient calcium and phosphorus absorption from the gut, it plays an important role in bone health. Vitamin D deficiency causes a secondary hyperparathyroidism that increases bone resorption and leads to osteomalacia. Osteomalacia cannot be distinguished from osteoporosis on bone densitometry by the T-score alone. In addition to the well known effects on bone, patients can present with non-specific musculoskeletal complaints such as fatigue and myalgias. In fact, fibromyalgia-like symptoms are common in vitamin D deficiency and can be treated successfully by vitamin D replacement.⁶ There also can be proximal muscle weakness leading to difficulty arising from chairs or walking up steps. Improving vitamin D status can decrease the risk of falls, and lower extremity neuromuscular function improves with increasing vitamin D levels above 32 ng/dL.⁷ Several laboratory values may be abnormal in vitamin D deficiency and thereby provide clues to its diagnosis (Table 3).

How to Screen for Vitamin D Deficiency

After metabolism in the liver 25 hydroxyvitamin D is transported by binding protein to adipose tissue, the major storage site for vitamin D. For this reason 25 hydroxyvitamin D is the best measure of body storage of vitamin D in vitamin D deficient patients. Over the

Table 1. Serum laboratory values.

Patient (Normal)
TSH : 4.0 µIU/mL (0.4-4.0)
FreeT4: 1.12 ng/dL (0.71-1.51)
Calcium: 8.6mg/dL (8.7-10.5)
Phosphorus: 3.1 mg/dL (2.7-4.5)
Magnesium 2.4 mg/dL (1.6-2.4)
Alkaline phosphatase: 243 U/L with bone fraction 206 and liver fraction 34 (45-130)
Intact PTH: 216 pg/mL (7.0-58.0)
25 hydroxyvitamin D level 8.7 ng/mL (25-80)
1,25 dihydroxyvitamin D 74 pg/mL (22-67)
Creatinine 0.8 mg/dL (0.5-1.4)
AST 13 U/L (0-31)
ALT 15 U/L (0-31)

Table 2. Who should be screened for vitamin D deficiency?

1. Women with osteoporosis since more than one-half of postmenopausal women with osteoporosis have vitamin D deficiency.⁸
2. Nursing home patients and people with inadequate sunlight exposure.
3. Patients with malabsorption including those with gastric bypass surgery, celiac disease, cystic fibrosis, short bowel, or chronic pancreatitis.
4. Patients with chronic kidney disease.⁹
5. Patients with chronic musculoskeletal pain.⁶

years, the optimal serum level of 25 hydroxyvitamin D has changed and is still evolving. It used to be the amount necessary to prevent rickets and osteomalacia, but now we rely on other parameters including gut absorption of calcium. Currently the lowest acceptable serum level of 25 hydroxyvitamin D is 30-32 ng/mL. This level is required to maximize calcium absorption from the gut.¹⁰ Also, below this level the parathyroid hormone (PTH) level will begin to rise and may adversely affect bone health.¹¹ There are

Table 3. Common laboratory abnormalities consistent with vitamin D deficiency.

- a. Elevated plasma alkaline phosphatase (bone specific).
- b. Low serum calcium (although it is usually normal since the PTH often increases in vitamin D deficiency and will increase calcium level.)
- c. Low 24-hour urine calcium excretion.
- d. High serum parathyroid hormone levels.

studies that show that this value may need to be higher since bone mineral density (BMD) values continue to rise with increasing vitamin D levels to above 40 ng/mL.¹² Although 1,25 dihydroxyvitamin D is the active hormone, we do not rely on its serum level to diagnose vitamin D deficiency for many reasons. The level often is normal in early vitamin D deficiency due to the parathyroid effect which will increase the 1 alpha hydroxylase activity in the kidney to maintain normal levels of 1,25 vitamin D. Also, 1,25 vitamin D production is regulated tightly and therefore variable. Currently we recommend obtaining a serum level of 25 hydroxyvitamin D (normal >30 ng/mL).

Treatment

There is no standard recommendation about the exact way to replete vitamin D stores. Various experts use different doses and preparations. The starting level and target level help determine treatment. D3 preparations are more effective than D2 preparations.

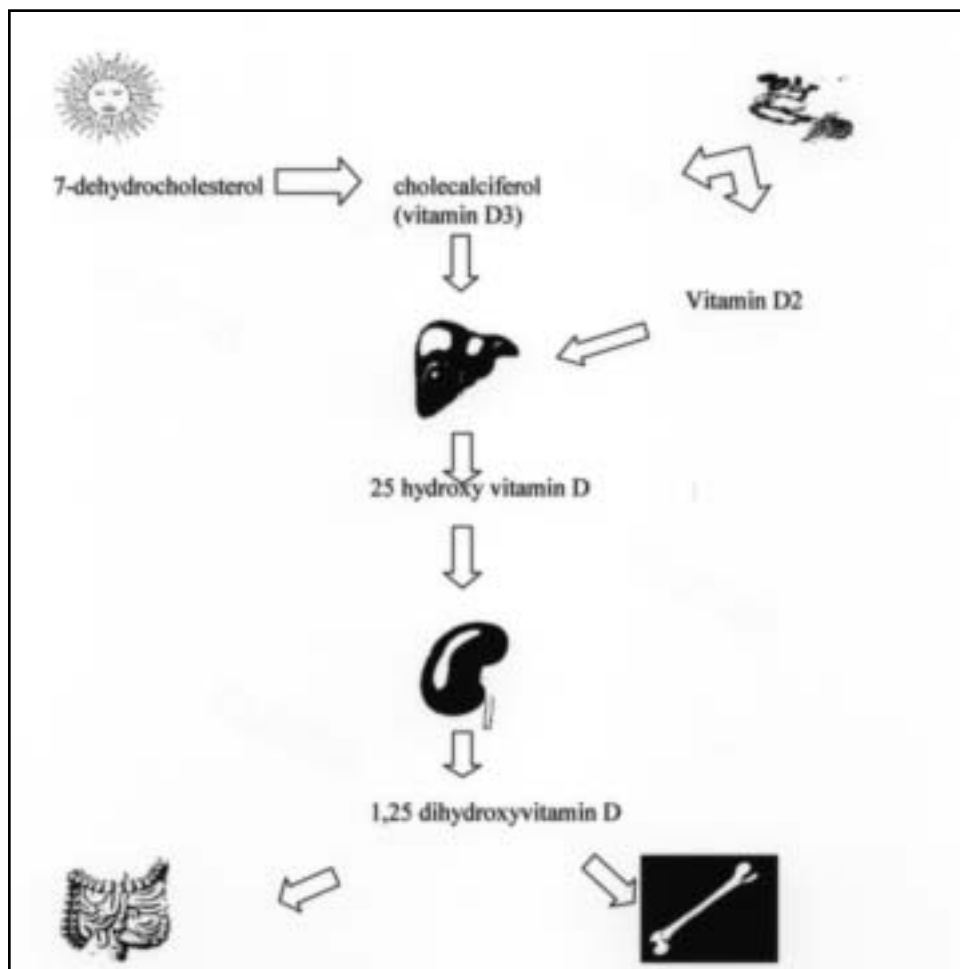


Figure. Vitamin D is produced in the skin by UV-B irradiation to produce vitamin D3, or it is absorbed from the gut as either vitamin D2 or D3. It is then hydroxylated in the liver to 25-hydroxyvitamin D [25(OH)D]. This is followed by 1 α -hydroxylation in the renal proximal tubule to form 1,25-dihydroxyvitamin D. Active vitamin D increases gut absorption of calcium and phosphorous and mobilizes calcium stores from bone.

Current recommendations by the Food and Nutrition Board of the Institute of Medicine for daily vitamin D intake are 200 international units (IU) from birth to age 50 years, 400 IU from age 51 to 70 years, 600 IU for ages over 70 years, and 800 IU for patients who are homebound or institutionalized.¹³ However studies indicate that these recommendations may be too low and that the minimum daily intake of vitamin D for adults should be 800 to 1,000 IU per day.^{14,15} These recommendations, however, are for maintaining stores and not for repleting those deficient in vitamin D. So for our patients with vitamin D deficiency we recommend ergocalciferol 50,000 IU weekly for one month and then monthly until 25 hydroxyvitamin D stores are replete. After the level is >30 ng/dL, the recommended daily amount can be resumed.

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LSBME NEWS:

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2007 Schedule

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May 4	New Orleans (Westbank)
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CME QUESTIONS

Read the preceding CME article and complete the registration, evaluation, and answer form on page 55 to earn CME credit. Mail or fax the registration, evaluation, and answer form to the Educational and Research Foundation. Answers must be postmarked or faxed prior to January 31, 2008. Participants must attain a minimum score of 75% to receive credit.

Choose the one answer that is most correct for each question.

1. A typical patient with vitamin D deficiency can present with all of the following except:
 - a. Chronic muscle aches
 - b. Osteoporosis
 - c. Hypercalcemia
 - d. Malabsorption
2. A 40-year-old woman with a history of celiac disease presents with chronic muscle pain for about a year. She has a history of a lumbar spine fracture 2 years ago with low bone mineral density. What test should you do next?
 - a. Lumbar spine radiograph
 - b. Serum TSH level
 - c. Serum 1,25 dihydroxyvitamin D level
 - d. Serum 25 hydroxyvitamin D level
3. In vitamin D deficiency you can see all of the following laboratory abnormalities except:
 - a. A high serum PTH level
 - b. A high 24-hour urine calcium excretion
 - c. A low serum phosphorus level
 - d. A low serum calcium level
4. A 30-year-old woman with cystic fibrosis comes to see you because of high serum levels of alkaline phosphatase and high PTH and a 25 hydroxyvitamin D level in serum of 8.7ng/mL. What serum level of 25 hydroxyvitamin D should you achieve with replacement therapy?
 - a. 12 ng/mL
 - b. 18 ng/mL
 - c. 30 ng/mL
 - d. 95 ng/mL