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Vitamin D and Aging

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Abstract

Aging affects the formation of 1,25-dihydroxyvitamin D (1,25[OH]₂D; calcitriol), the active form of vitamin D. Production of 1,25(OH)₂D is reduced by 50% as a result of an age-related decline in renal function, although serum 1,25(OH)₂D levels are maintained in part by secondary hyperparathyroidism. Aging also causes a decrease in calcium absorption that precedes the decrease in 1,25(OH)₂D by 10 to 15 years. Because 1,25(OH)₂D is dependent on an adequate supply of the substrate vitamin D, the development of vitamin D deficiency leads to further reduction in the formation of 1,25(OH)₂D. Measurement of the metabolite 25OHD provides the most widely used assessment of vitamin D deficiency. A serum 25OHD level lower than 10 ng/mL (25 nmol/L) represents vitamin D deficiency and leads to a reduction in serum 1,25(OH)₂D. Vitamin D deficiency, is uncommon in North America, probably because of supplementation of dairy products and other foods with vitamin D. Sunlight exposure increases serum 25OHD levels by about 10 ng/mL during the months of April through September, resulting in low serum 25OHD for about 3 to 4 months in winter, with 2 additional months of low levels in more northern latitudes, such as Canada, and 2 fewer months in the southern states. Vitamin D supplementation in the winter can prevent vitamin D deficiency. Vitamin D insufficiency has been defined by the Institute of Medicine as a serum 25OHD level lower than 20 ng/mL (and >10 ng/mL). A serum 25OHD level lower than 20 ng/mL is associated with an increased fracture rate and increased rate of bone loss and treatment. Although other diseases have been associated with low serum 25OHD levels, the evidence for a causative role has not yet been established. Treatment of elderly people with vitamin D 800 IU daily will increase serum 25OHD levels to higher than 20 ng/mL and reduce fractures; this is particularly important in institutionalized people.

Keywords

Vitamin D metabolism; Aging; Vitamin D insufficiency; Vitamin D treatment

VITAMIN D METABOLISM

Vitamin D is derived from diet and sunlight and is not biologically active. Vitamin D must be sequentially converted into 25-hydroxyvitamin D (25OHD) in the liver by the enzyme CYP2R1 and then into 1,25-dihydroxyvitamin D (1,25[OH]₂D) in the kidney by the CYP27B1 enzyme (1-hydroxylase) (Fig. 1). Both 1,25(OH)₂D and 25OHD are carried in the circulation by vitamin D-binding protein (DBP).

The active hormonal form of vitamin D is 1,25(OH)₂D, which binds to the vitamin D receptor (VDR) together with the retinoid X receptor to activate specific genes in target

organs.¹ VDR is present in many tissues besides bone, and certain cells, such as immune and osteoprogenitor cells, also contain the 1 α hydroxylase enzyme as part of an intracrine and paracrine system. The regulation of the 1 α hydroxylase enzyme is tightly maintained so as to keep serum 1,25(OH) $_2$ D levels constant. Production of 1,25(OH) $_2$ D is upregulated by parathyroid hormone (PTH) and low serum phosphorus and inhibited by fibroblast growth factor (FGF-23), which also regulates serum phosphorus levels. The enzyme CYP24 hydroxylase converts 25OHD to the nonactive metabolite 24,25(OH) $_2$ D in the kidney, thereby limiting the production of 1,25(OH) $_2$ D. Local formation of 24,25(OH) $_2$ D is also induced in many target tissues through negative feedback by 1,25(OH) $_2$ D.

1,25(OH) $_2$ D is essential for the efficient absorption of dietary calcium and phosphorus and for mineralization of bone. Recently, 1,25(OH) $_2$ D has been recognized to have a multitude of other biologic functions. Studies suggest that it is unlikely that serum 25OHD has an independent physiologic function that is not fulfilled by 1,25(OH) $_2$ D.

EFFECT OF AGE ON VITAMIN D AND CALCIUM METABOLISM

The following are effects of age on vitamin D and calcium metabolism:

- Decreased calcium absorption
- Intestinal resistance of calcium absorption to circulating 1,25(OH) $_2$ D
- Decreased VDR
- Decreased renal production of 1,25(OH) $_2$ D by the aging kidney
- Decreased skin production of vitamin D
- Substrate deficiency of vitamin D

Decreased Calcium Absorption

Malabsorption of calcium occurs as part of aging and starts at approximately age 65 to 70 years.^{2,3} As a result, it leads to negative calcium balance, secondary hyperparathyroidism, increased bone loss, and osteoporosis. Because of malabsorption of calcium, there is a decreased ability to adapt to a low-calcium diet by increasing fractional calcium absorption.⁴ Although several independent dietary factors affect calcium absorption, such as protein intake, sodium intake, or glucose, the main regulator is 1,25(OH) $_2$ D acting through the VDR and synthesizing genes and proteins involved in calcium transport.⁵ Deletion of the VDR results in malabsorption of calcium.⁶ Calcium absorption occurs by both an active saturable system and a passive diffusion transport system. Active transport of calcium occurs through transcellular and paracellular pathways in the duodenum and jejunum, whereas passive paracellular absorption is the main process of calcium absorption throughout the intestine.⁷ At the molecular level, the calcium-binding protein calbindin-D $_{9k}$ and an epithelial calcium channel transient receptor potential vanilloid type 6 (TRPV6) were initially thought to mediate the diffusion of calcium across the gut.⁷⁻⁹ However, in TRPV6/Calbindin-D $_{9k}$ double knockout mice, calcium absorption still responds to 1,25(OH) $_2$ D administration, challenging this mechanism.¹⁰ The tight junction proteins Claudins-2 and Claudins-12 facilitate paracellular calcium transport and are upregulated by 1,25(OH) $_2$ D via the VDR receptor.¹¹ In summary, part of the change in calcium absorption with aging may be because of abnormalities in the transport proteins that are regulated by 1,25(OH) $_2$ D.

Intestinal Resistance of Calcium Absorption to Circulating 1,25(OH) $_2$ D

In young healthy people, there is a positive correlation between calcium absorption and serum 1,25(OH) $_2$ D, but in older people and patients with osteoporosis, the calcium

absorption response is lower relative to serum $1,25(\text{OH})_2\text{D}$ than in young people (Fig. 2), suggesting intestinal resistance to endogenous circulating $1,25(\text{OH})_2\text{D}$.^{12,13} However, administration of a small oral dose of calcitriol $0.25\text{ }\mu\text{g}$ twice daily to elderly people completely normalizes malabsorption of calcium, suggesting that calcitriol may have a first-pass effect on intestinal transport.¹⁴

Decreased VDR

Aging may affect the intestinal concentration of VDR to cause a decrease in calcium absorption, as demonstrated in aging rats.¹⁵ There have been 2 studies of intestinal VDR performed on biopsies in humans. A small study of 9 subjects older than 65 years Vitamin D and Aging 321 showed a decrease in intestinal VDR concentration with age but no change in serum $1,25(\text{OH})_2\text{D}$.¹⁶ In a similar study of 41 women older than 65, 10 of whom were older than 75, there was no difference in intestinal VDR concentration compared with 59 women younger than 35.¹⁷

Decreased Renal Production of $1,25(\text{OH})_2\text{D}$ by the Aging Kidney

As renal function declines with age, there is a decrease in the activity of the renal enzyme 1 hydroxylase that converts 25OHD into $1,25(\text{OH})_2\text{D}$. Serum $1,25(\text{OH})_2\text{D}$ levels are inversely related to serum creatinine and glomerular function rate (GFR) and a GFR of 50 mL/min is a level that affects $1,25(\text{OH})_2\text{D}$ production.¹⁸ Because many people older than 80 have a GFR less than 50 mL/min, decreased production of $1,25(\text{OH})_2\text{D}$ in this age group is common. To examine the effect of age and GFR on the 25OHD - $1,25(\text{OH})_2\text{D}$ axis, we infused PTH for 24 hours in women of different ages. The increase in serum $1,25(\text{OH})_2\text{D}$ was about 50% lower in the older subjects, indicating decreased renal responsiveness to PTH with age (Fig. 3).¹⁹

Measurement of serum $1,25(\text{OH})_2\text{D}$ in elderly people shows the impact clinically of declining renal production. In a study of women aged 80 to 95 years who were residents of nursing homes and had normal 25OHD levels, the serum $1,25(\text{OH})_2\text{D}$ levels were much lower than in women aged 65 to 75 years (Fig. 4). In summary,

- There is an age-related decrease in calcium absorption that is partly dependent and partly independent of $1,25(\text{OH})_2\text{D}$.
- Serum $1,25(\text{OH})_2\text{D}$ levels decrease as a result of an age-related decline in renal function.
- Reduced levels of serum $1,25(\text{OH})_2\text{D}$ likely further reduce calcium absorption, causing secondary hyperparathyroidism and increased bone resorption.
- Secondary hyperparathyroidism persistently stimulates renal $1,25(\text{OH})_2\text{D}$ production until the kidney can no longer respond effectively.

Decreased Skin Production

Aging reduces vitamin D production in skin. There is a decrease in the concentration of 7-dehydrocholesterol in the epidermis in old compared with young individuals and a reduced response to UV light, resulting in a 50% decrease in the formation of previtamin D3.²⁰

Substrate Deficiency of Vitamin D

All age-related changes in vitamin D metabolism are magnified if there is concomitant vitamin D deficiency, because it limits the substrate supply for 25OHD and ultimately $1,25(\text{OH})_2\text{D}$. Substrate deficiency is a common problem in the elderly and is important to recognize because it is preventable and treatable. There may be deficiency of vitamin D

either from diet or from lack of sunlight, and the decrease in serum 25OHD further limits 1,25(OH)₂D production, especially when there is also renal dysfunction. Serum 1,25(OH)₂D levels decrease when serum the 25OHD level falls below 10 ng/mL in both younger²¹ and older²² people.

VITAMIN D NUTRITION IN THE ELDERLY

Vitamin D is a unique nutrient because its requirement is met from diet and skin. The dietary intake of vitamin D can be estimated from dietary food tables and is usually between 100 and 400 IU daily. Dietary surveys in North America in the National Health and Nutrition Examination Survey (NHANES) show that dietary intake of vitamin D is low, averaging 200 IU daily (Table 1), and, unless one eats a lot of fish with high vitamin D content, daily intake is unlikely to exceed 400 IU daily. Vitamin D intake increases with age because elderly people consume more multivitamins that contain vitamin D.^{23,24}

The production of vitamin D in skin cannot be measured directly; however, the change in serum 25OHD gives an estimate of the effect of sun if diet remains constant. In the Midwest at latitude 40°, serum 25OHD increases by 50% from 20 to 30 ng/mL in summer²⁵; this change is equivalent to a daily oral vitamin D dose of 2000 IU daily. The UV spectrum is effective only when the sun is more than 30° above the horizon. Below that level, ground pollution filters out the UV rays. In the Midwestern section of North America, effective UV light occurs only between late April and early September. Effective UV exposure time is 2 months less in Canada and 2 months more in Florida. Vitamin D supplementation should be increased in winter.

VITAMIN D NUTRITIONAL STATUS: VITAMIN D DEFICIENCY/ INSUFFICIENCY

It is now recognized that serum 25OHD is the best measure of vitamin D nutritional status because it represents input from diet and skin. In the past, vitamin D *deficiency* was defined as a serum 25OHD level lower than 10 ng/mL because both 1,25(OH)₂D and calcium absorption decline at this threshold.^{21,22} In 2003, the World Health Organization defined vitamin D *insufficiency* as serum 25OHD lower than 20 ng/mL and normal as 20 to 30 ng/mL.²⁶ The Institute of Medicine (IOM) reiterated that recommendation in 2011.²⁴ The Endocrine Society suggested an alternative, defining insufficiency as lower than 30 ng/mL and normal as higher than 30 ng/mL.²⁷ Why does it matter if the recommended cutoff for insufficiency is 20 ng/mL or 30 ng/mL? The reason is that meeting this target serum 25OHD changes the Recommended Dietary Allowance (RDA).

If a serum 25OHD lower than 20 ng/mL is used as a cutoff for vitamin D *insufficiency*, then surveys worldwide show that vitamin D insufficiency occurs in many people and more in the elderly. In the North American survey NHANES, 24% had serum 25OHD lower than 20 ng/mL and 8% had serum 25OHD lower than 10 ng/mL.²⁸ However, if one takes into account the within-person variability of the accuracy of the test, the variance of the population data reduces the prevalence of insufficiency to 19%.²⁹ In another North American study of 490 free-living and nursing home elderly women, approximately 28% of women screened in winter had serum 25OHD levels lower than 20 ng/mL and 4% had serum 25OHD lower than 10 ng/mL.¹³ In a multicenter study from Europe and Australia, 80% of 80-year-old institutionalized women had serum 25OHD levels lower than 20 ng/mL,³⁰ and in a national survey from Ireland of 1500 people, 40% had serum 25OHD levels lower than 20 ng/mL in winter and 36% in summer.³¹

If a serum 25OHD lower than 10 to 12 ng/mL is used as a cutoff for vitamin D *deficiency*, then the prevalence in free-living people varies from 4% to 33% depending on location, whereas in institutionalized elderly, the proportion is much higher at 45% to 86%.³² The higher prevalence in institutionalized elderly suggests that lack of sun exposure is the most important factor, as diets are intrinsically low in vitamin D. In Denmark, average serum 25OHD levels were only 3 ng/mL in women covering their body and face with a Burka. Compared with 8 ng/mL in women without, even though dietary vitamin D was 600 IU daily.³³

WHY WAS A SERUM 25OHD LEVEL LOWER THAN 20 NG/ML AND NOT LOWER THAN 30 NG/ML SELECTED TO DEFINE INSUFFICIENCY?

The IOM determined in their 2011 report that much of the data that related serum 25OHD levels higher than 30 ng/mL to diseases other than bone was based on association studies and was not supported by clinical trials.²⁴ The IOM selected a serum 25OHD level of 20 ng/mL to define vitamin D insufficiency, whereas a serum 25OHD level of 30 ng/mL was suggested to define insufficiency in an Endocrine Society guideline.²⁷

The data presented in the Endocrine Society guideline to support a sufficiency level of 30 ng/mL were based on 2 laboratory test-based premises. First, serum PTH was used as a biomarker to define vitamin D insufficiency, with a threshold serum 25OHD of 30 ng/mL used because high levels of PTH decreased and reached a plateau at that level; however, this was based on a selected dataset of 3 studies.²⁷ An additional 70 Vitamin D and Aging 325 studies that were not analyzed did not confirm the 30 ng/mL plateau.³⁴ A recent study of 350,000 PTH/serum 25OHD samples from a laboratory database showed no evidence of a plateau in serum PTH even at a serum 25OHD of 100 ng/mL.³⁵ In addition, up to 50% of people with a very low serum 25OHD of 5 to 15 ng/mL have low serum PTH.³⁶ Thus, the value of serum PTH as an absolute indicator of vitamin D insufficiency is questionable. Second, it was suggested that calcium absorption reaches a maximum at 32 ng/mL, although this was based on modeled, not actual data. Two other studies of calcium absorption show that absorption reaches a maximal threshold at serum 25OHD levels between 5 and 10 ng/mL.^{22,37} Thus, neither the PTH plateau nor calcium absorption tests support a 30 ng/mL threshold.

The data that IOM cites as support for a serum 25OHD level of 20 ng/mL are based on a number of studies with bone outcomes. Several prospective cohort studies relate serum 25OHD lower than 20 ng/mL to an increase in hip fracture rates,²⁴ with no significant increase in hip fractures when serum 25OHD exceeds 20 ng/mL. An analysis of bone markers and serum 25OHD showed that bone resorption markers decrease and plateau at a serum 25OHD level of 18 ng/mL.³⁴ Subsequently, a large study of rates of bone loss in men (the Mr Os study) showed increased bone loss in the hip only in the groups with serum 25OHD lower than 20 ng/mL.³⁸

To estimate what dosage of vitamin D was needed to exceed a serum 25OHD level of 20 ng/mL, the IOM performed an analysis of various individual dose studies of vitamin D and showed that a dosage of 600 to 800 IU daily would exceed a serum 25OHD level of 20 ng/mL.²⁴ This result has been determined experimentally in a recent dose-ranging study and the findings are identical (Fig. 5).³⁹ This study is the first to show that serum 25OHD is regulated and is most likely attributable to formation of 24,25(OH)₂D, the inactive metabolite. Formation of 24,25(OH)₂D is the essential step preventing vitamin D intoxication from a high intake, another regulatory step in skin prevents vitamin D intoxication from sunlight. Because serum 25OHD levels plateau at a mean serum 25OHD level of 45 ng/mL, it would appear that the homeostatic vitamin D system does not need

higher levels in healthy people. If reaching a serum 25OHD level higher than 20 ng/mL is the objective, then 600 to 880 IU will achieve this point in 97.5% of people, satisfying the criteria for the RDA, and 400 IU will meet the needs of 50% of the population (Estimated Average Requirement [EAR]).

Other supporting data were derived from fracture studies. A vitamin D dosage of 800 IU with calcium was shown to be effective in reducing fractures in the most recent meta-analysis performed for the IOM.⁴⁰ Thus, the evidence suggests that an 800 IU vitamin D dosage with calcium increases serum 25OHD to higher than 20 ng/mL and reduces fractures, and that it is not necessary to exceed a serum level of 30 ng/mL for bone efficacy. The preceding discussion applies only to the calcium and bone and may not apply to other diseases of interest, such as cancer and diabetes. Only clinical trials using different vitamin D dosages together with measurement of serum 25OHD can provide an answer in the future.

In Europe, the issue of severe vitamin D deficiency is more of a problem because average serum 25OHD levels are much lower, at approximately 10 to 15 ng/mL. In a recent study of bone biopsies performed at autopsy, 97.5% of cases of osteomalacia occurred at a serum 25OHD level lower than 20 ng/mL.⁴¹ Interestingly, most bone biopsies did not show osteomalacia at serum 25OHD levels lower than 5 ng/mL for unclear reasons, although it is possible that in many of these cases, a high dietary intake of calcium and phosphorus prevented osteomalacia. The evidence-based recommendations by the IOM for the new dietary reference intakes (DRIs) are provided in Table 2.

TOXICITY OF VITAMIN D

Vitamin D intoxication can occur at dosages of more than 20,000 IU daily over the long term or a serum 25OHD level of 200 ng/mL, overwhelming the 24,24(OH)₂D inactivation step. The resultant hypercalcemia suppresses PTH, acting as a second regulatory step against developing vitamin D intoxication by decreasing 1,25(OH)₂D production. However, if the high vitamin D dosage is continued, it appears that at very high levels, serum 25OHD can bind to the VDR and simulate the effect of 1,25(OH)₂D.

Most data on vitamin D intoxication are derived from case studies of accidental vitamin D overdosing. In deriving a Tolerable Upper Limit (TUL) for vitamin D, the IOM agreed that 20,000 IU daily or more would increase the chance of vitamin D intoxication, and that because of safety concerns and reports that serum 25OHD levels higher than 50 ng/mL were associated with increased mortality rates,^{42,43} 4000 IU should represent the TUL. The TUL should not be confused with the recommended dose. It is possible that the TUL is less in older people, those with impaired renal function, or those who take calcium supplements.

EFFECT OF VITAMIN D AND CALCIUM ON OSTEOPOROSIS AND FRACTURES

Osteoporosis is one of the common diseases of aging. Management of osteoporosis using vitamin D and calcium has been in practice for almost 30 years. However, the role of vitamin D and calcium in fracture prevention is an area of controversy, with varying results of meta-analyses depending on their criteria for inclusion. The most recent meta-analysis was based on an analysis performed for the IOM report,⁴⁰ although it was essentially the same as a previously reported analysis, because only 2 more studies were included.⁴⁴

There have been 12 studies of vitamin D plus calcium and 5 of vitamin D alone compared with a placebo or calcium control group. In the vitamin D plus calcium trials, there was a difference between community free-living adults and institutionalized individuals in the

findings. In the community trials, the effect of vitamin D plus calcium reduction on fractures was nonsignificant, with a relative risk of 0.89 (95% confidence interval 0.76–1.04). In the institutional studies, there was a significant reduction in hip fractures of almost 30%, with a relative risk of 0.71 (95% confidence interval 0.57–0.89). The vitamin D dose varied from 300 to 800 IU across studies, but the 800 IU dose was most commonly used and the calcium dose was usually 1000 mg; therefore, vitamin D 800 IU and calcium 1000 mg are the standard daily recommended doses.

ARE THE EFFECTS OF VITAMIN D AND CALCIUM ON FRACTURES RELATED TO SERUM 25OHD?

Most evidence suggests that a serum 25OHD higher than 20 ng/mL is sufficient for skeletal health. This conclusion is based on 5 large studies totaling 6562 subjects that show a higher rate of hip fracture in women and men with serum 25OHD lower than 20 ng/mL.⁴⁵ The evidence linking clinical nonvertebral fractures to low serum 25OHD differs between men and women and by ethnicity. In men, nonhip fractures are more frequent only in those with serum 25OHD lower than 20 ng/mL.⁴⁶ In white women, nonhip fractures are significantly lower in groups with serum 25OHD of higher than 20 ng/mL compared with lower than 20 ng/mL.⁴⁷ However, the opposite is found in African American and Asian women, namely fracture events are more common in the groups when serum 25OHD is higher than 20 ng/mL compared with lower than 20 ng/mL. These results are based on cohort studies and the accuracy of reporting fractures is approximately 80%. Larger prospective studies are needed to confirm these results.

Evidence to link a specific serum 25OHD threshold to treatment with vitamin D is not clear. In half the studies, the baseline serum 25OHD level was higher than 20 ng/mL, and efficacy does not appear to differ whether the baseline starts above or below 20 ng/mL. Another issue is that almost all studies used a single dose, so that a threshold dose cannot be defined. Furthermore, meta-analyses that try to define a threshold response based on serum 25OHD measurements are challenging because serum 25OHD values have been performed with different assays over 30 years and no external independent standards were common to these assays.

FALLS

Although there has been a claim that vitamin D reduces falls, these studies have been affected by the same problems as fracture studies, including small numbers, variable duration from 6 weeks to 1 year, differing doses of vitamin D, and variation in amounts of calcium supplements. The analytic design of a meta-analysis that showed a positive effect of vitamin D on falls has been questioned, and the IOM analysis of the same data did not a significant effect of vitamin D on falls.²⁴ An adequately powered trial is required to answer this question definitively. There is some evidence that calcitriol reduces falls, especially in older people with a GFR less than 60 mL/min,^{48–50} and it may be that in those older than 80 years, reduced conversion of vitamin D to calcitriol reduces the effect of vitamin D on falls.

SUMMARY

Age-related changes affect vitamin D metabolism and reduce the nutritional status of the elderly. A vitamin D supplement is recommended in the elderly. The optimal total calcium intake is unclear. In the absence of adequate safety data, it is suggested that total calcium intake be limited to 1000 to 1200 mg daily, because of a 35% incidence of hypercalciuria or hypercalcemia in women taking low doses of vitamin D who have a total calcium intake of 1200 mg daily.³⁹ Increasing calcium from dietary sources may be safer than supplements,

and requires increasing the intake of dairy products or other vitamin D and calcium-fortified foods. The RDA value is listed on every food and vitamin either as the actual amount or as a percentage of the RDA. For example, if the RDA for vitamin D is 800 IU and a multivitamin contains 1000 IU, the multivitamin provides 125% of the RDA. It has been common practice to supplement dairy products in the United States, Canada, and Scandinavian countries. In North America, milk is fortified with 400 IU per quart. An 8-oz glass of milk provides 80 IU of vitamin D and 250 mg calcium. Evidence suggests that vitamin D and calcium nutrition can be improved in the elderly by increasing the vitamin D intake to 800 IU daily together with calcium 1000 mg daily. This combination is a simple inexpensive strategy that can reduce fractures in institutionalized individuals by 30%.

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KEY POINTS

- There are age-related changes that affect vitamin D metabolism and increase the requirement for vitamin D in the elderly.
- The optimal total calcium intake is unclear. Increasing calcium from dietary sources may be preferred to supplements, and requires increasing the intake of dairy products and calcium-fortified foods.
- Evidence suggests that vitamin D and calcium nutrition can be improved in the elderly by increasing the vitamin D intake to 800 IU daily together with calcium 1000 mg daily. This combination is a simple, inexpensive strategy that can reduce fractures in independent living by ~12 percent and in institutionalized individuals by 30%.

Fig. 1.
Vitamin D metabolism.

Relationship between serum 1,25(OH)₂D and calcium absorption

mean regression line and confidence limits are shown for each group.

Fig. 2.

Calcium absorption is lower in elderly (*red*) compared with young (*yellow*) women for any given serum 1,25 dihydroxyvitamin D level. (Data from Kinyamu HK, Gallagher JC, Prah JM, et al. Association between intestinal vitamin D receptor, calcium absorption, and serum 1,25(OH)₂D in normal young and elderly women. *J Bone Miner Res* 1996;11:1400–5.)

Fig. 3.
Decreased renal production of serum 1,25(OH)₂D with age after PTH stimulation.

Serum 1,25 dihydroxyvitamin D in three groups of women

Fig. 4.

Serum 1,25(OH)₂D levels in women of different ages. (Data from Kinyamu HK, Gallagher JC, Balhorn KE, et al. Serum vitamin D metabolites and calcium absorption in normal and elderly free-living women and in women in nursing homes. *Am J Clin Nutr* 1997;65:790–7.)

Fig. 5.
Dose response of vitamin D on serum 25OHD.

Table 1

Vitamin D intake and serum 25 hydroxyvitamin D (25OHD) for the United States, 2005–2006

Age Group (y)	Vitamin D Intake (IU/d) (mean ± SE)		Serum 25OHD ng/mL (mean ± SE)
	Diet Alone ^a	Total Intake ^b	
Males			
14–18	244 ± 16	276 ± 20	24 ± 0.6
19–30	204 ± 12	264 ± 16	23 ± 0.5
31–50	216 ± 12	316 ± 12	24 ± 0.4
51–70	204 ± 12	352 ± 16	24 ± 0.5
>70	224 ± 16	428 ± 28	24 ± 0.4
Females			
14–18	152 ± 8	200 ± 20	24 ± 0.7
19–30	144 ± 12	232 ± 12	25 ± 0.8
31–50	176 ± 12	308 ± 20	23 ± 0.5
51–70	156 ± 16	404 ± 40	23 ± 0.4
>70	180 ± 8	400 ± 20	23 ± 0.4

^aData for foods.^bData for food + supplements.

Adapted from Bailey RL, Dodd KW, Goldman JA, et al. Estimation of total usual calcium and vitamin D intakes in the United States. *J Nutr* 2010;140(4):817–22; and Institute of Medicine. Dietary reference intakes for calcium and vitamin D. Washington, DC: The National Academies Press; 2011. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK56072>.

Table 2

Calcium and vitamin D intake recommendations for those older than 50 years

Vitamin D	EAR IU/d	RDA IU/d
Men, 51–70 y	400	600
Women, 51–70 y	400	600
Men + women >70 y	400	800
Calcium	EAR mg/d	RDA mg/d
Men, 51–70 y	800	1000
Women, 51–70 y	1000	1200
>70 y	1000	1200

EAR, Estimated Average Requirement; RDA, Recommended Dietary Allowance.

Data from Institute of Medicine. Dietary reference intakes for calcium and vitamin D. Washington, DC: The National Academies Press; 2011.
Available at: <http://www.ncbi.nlm.nih.gov/books/NBK56072>.