KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Blood Chem Vitamin D Imbalance Review

VITAMIN D:

- Promotes calcium absorption in the gut.
- Maintains calcium and phosphate levels in the blood.
- Regulates cell growth and neuromuscular and immune function.
- Vitamin D in the circulation is converted by hepatic hydroxylase into 25(OH)D, calcidiol, which is what is typically measured on a blood test.
- As needed, 25(OH)D is converted into 1,25(OH)2D, calcitriol.
- Calcitriol increases the level of calcium in the blood by increasing the uptake of calcium from the gut, decreasing renal excretion of calcium, and possibly increasing the release of calcium into the blood from the bone.
- Conversion of 25(OH)D to calcitriol is tightly regulated by parathyroid hormone.
- Parathyroid hormone, or PTH, increases calcitriol formation, helps to increase serum calcium by acting on kidney and bone.
- The two potential ways of increasing calcitriol are increasing the supply of calcidiol through sun exposure, supplements, or diet or increasing demand for calcitriol via parathyroid hormone.
- Different ethnicities may convert calcidiol to calcitriol more effectively, and they require less calcidiol to achieve the necessary amount of calcitriol.
- Another possibility is that nonwhites require less PTH to convert calcidiol to calcitriol

FIVE KEY TAKEAWAYS

1	2	3	4	5
25(OH)D doesn't indicate **biological** vitamin D **activity**	People with **nonwhite ancestry** may be adapted to lower optimal 25(OH)D level	Many people considered **"deficient"** by current lab range may not be	Supplementing these people with vitamin D may be **unnecessary** and **even harmful**	The reference range for 25(OH)D should be **population-specific**

PTH and calcitriol can help clarify when low 25(OH)D is pathological versus normal.

- Low-normal 25(OH)D level and low PTH (below 30) suggests the patient is not vitamin D deficient from a biological perspective and that supplementation, diet, and lifestyle changes aren't required.
- A low or borderline low 25(OH)D with PTH above 30 does suggest biological deficiency.
- The higher the PTH is above 30, the more biologically deficient the person is.

Most people obtain vitamin D from cutaneous production, meaning sun exposure and supplementation, not food sources.

- Dietary vitamin D contributes only 10 to 20 percent.
- Only a few foods such as cold-water fatty fish or shellfish are rich in vitamin D.

VITAMIN D TOXICITY

- Hallmark sign is hypercalcemia due to intestinal calcium hyperabsorption and calcium resorption from bone.
- Excess vitamin D also causes hyperphosphatemia.
- Hypercalcemia and hyperphosphatemia cause mineralization of various soft tissues, and this can lead to kidney stones and increased risk of cardiovascular disease, among other health problems. Vitamin D-intoxicated patients suffer from headache, nausea, vomiting, diarrhea, anorexia, weight loss, polyuria, and polydipsia, and excess vitamin D intake has also been shown to contribute to several documented deaths.

STATUS OF SERUM MARKERS IN VITAMIN D DEFICIENCY AND TOXICITY

Vitamin D status	25(OH)D	1,25(OH)2D	PTH	Calcium	Phosphorus
Toxicity	High	Low, normal, or high	Low or normal	Normal or high	Normal or high
Deficiency	Low	Low, normal, or high	>30	Low or normal	Low or normal

IMPORTANT NOTES

- In most cases of vitamin D toxicity due to supplements, 1,25(OH)2D is not elevated.
- Toxicity leads to hypercalcemia and hyperphosphatemia and depresses calcitriol, so vitamin D toxicity cannot be ruled out in cases of high calcidiol and normal calcitriol.
- When calcidiol or 25(OH)D levels are extremely high, calcitriol levels can fall to undetectable levels because PTH and FGF23 suppress the conversion of calcidiol into calcitriol in an attempt to protect against hypercalcemia and hyperphosphatemia.

- When 25(OH)D is high and 1,25(OH)2D is low, it could actually be vitamin D toxicity, or it could be vitamin D deficiency, so it is important to use other markers such as PTH, serum calcium, and serum phosphorus to clarify the diagnosis.

CONCLUSIONS GIVEN THE RESEARCH AND GIVEN AN EVOLUTIONARY PERSPECTIVE

- Sunlight or UV exposure is the optimal source of vitamin D and accounts for the majority of 25(OH)D serum levels in the absence of supplementation.
- The range of serum 25(OH)D, which the majority of researchers agree, that avoids deficiency or toxicity is between 30 and 60 or 65 ng/mL.
- The 25(OH)D range should likely vary depending on ethnicity, genetics, PTH activity, and nutritional status, especially vitamins A and K2, potassium, and magnesium, as well as fluid intake.
- In the absence of specific ranges, clinicians should use other markers such as PTH, calcitriol, serum calcium, and serum phosphorus to clarify biological vitamin D status.

HYPERPARATHYROIDISM

- High vitamin D 25(OH)D, serum calcium, and PTH.
- 25(OH)D is not always out of the lab range in hyperparathyroidism, and, in fact, it can even be normal or low. In those cases, 25(OH)D deficiency or low levels of 25(OH)D can obscure hyperparathyroidism, which doesn't become evident until vitamin D is repleted through sun exposure or supplements.
- Elevated serum calcium is the most important indicator of hyperparathyroidism.

The functional vitamin D reference range is from 35 to 60 ng/mL.

RECOMMENDED SUN EXPOSURE BY SEASON

The benefits of sunlight go far beyond vitamin D. When human skin is exposed to sunlight, it produces several peptides and hormones that contribute to systemic wellness. When making recommendations to patients about sun exposure, remember that many variables affect the conversion of ultraviolet light to vitamin D, including skin type, season, time of day, latitude, age, and health status, but here are some general guidelines:

- Late fall, winter, and early spring: Spend half as much time as it takes skin to turn pink in the sun three to seven times per week depending on solar angle.
- Late spring, summer, and early fall: Spend half as much time as it takes skin to turn pink in the sun at least three times per week.

Most people who follow the recommendations above for food, including cod liver oil and ultraviolet light exposure, won't need vitamin D supplements. However, following these recommendations is not possible for everyone and in these cases supplementation should be considered.

VITAMIN D SUPPLEMENTATION CONSIDERATIONS

- Take with fat for maximum absorption.
- D3 is better absorbed than D2.
- Dose should be adjusted by weight and inflammatory/gut status, and an increased dose may be needed in obesity and digestive issues/malabsorption.
- Weekly or daily dosing results in a similar increase in serum vitamin D levels; large monthly or semi-annual doses are not recommended.

The only way to know for sure how much vitamin D you need is to test blood levels, change the vitamin D regimen, and then test again three to four months later to determine if it had the desired effect.

NEXT STEPS BASED ON 25(OH)D LEVELS

25(OH)D level (ng/mL)	Suggested action
<25	Begin treatment
25–35	Use PTH to determine whether treatment is necessary
>35	No treatment necessary; continue diet & lifestyle for maintaining adequate vitamin D

In fall or early winter, it may make sense to take a half-teaspoon per day or even a teaspoon per day of cod liver oil and then retest in 60 days to be sure that deficiency isn't developing, given the time of year.

TREATMENT BASED ON OUTCOME OF STEP ONE

25(OH)D level (ng/mL)	Suggested action
<15	1 tsp/d EVCLO, diet/UV exposure, plus 10,000 IU/d D3
15–25	1 tsp/d EVCLO, diet/UV exposure, plus 5,000 IU/d D3
26–35 with PTH >30	1 tsp/d EVCLO, diet/UV exposure
26–35 with PTH <30 >35	No treatment necessary; continue diet & lifestyle for maintaining adequate vitamin D

In all cases, advise them to eat one pound of coldwater fatty fish such as salmon, herring, mackerel, or sardines; six to eight egg yolks per week, pasture-raised. Ultimately, food is the best source of nutrients because there are various cofactors that are required for the absorption of certain nutrients that are present in food that are not present in synthetic supplements.

TREATMENT BASED ON OUTCOME OF STEP TWO

25(OH)D level (ng/mL)	**Suggested action**
<15	1 tsp/d EVCLO, diet/UV exposure, consider D3 injections
15–25	1 tsp/d EVCLO, diet/UV exposure, plus 5,000-10,000 IU/d D3
26–35 with PTH >30	1 tsp/d EVCLO, diet/UV exposure
26–35 with PTH <30 >35	No treatment necessary; continue diet & lifestyle for maintaining adequate vitamin D

Step three is to retest 25(OH)D levels and PTH levels after 60 days. Note that you may need to retest at least twice a year, after spring and in the fall, to determine what their natural 25(OH)D levels are at different times of the year.

The 25(OH)D range for autoimmune disease is 45 to 60 ng/mL. Phototherapy, or UV exposure, is superior to supplementation for patients with autoimmune disease.