Test Definition: DHVD

1,25-Dihydroxyvitamin D, S

Overview

Useful For

As a second-order test in the assessment of vitamin D status, especially in patients with renal disease

Investigation of some patients with clinical evidence of vitamin D deficiency (eg, vitamin D-dependent rickets due to hereditary deficiency of renal 1-alpha hydroxylase or end-organ resistance to 1,25-dihydroxyvitamin D)

Differential diagnosis of hypercalcemia

Method Name

Extraction/Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum

Advisory Information

The 25-hydroxyvitamin D test (25HDN / 25-Hydroxyvitamin D2 and D3, Serum) in serum the preferred initial test for assessing vitamin D status and most accurately reflects the body's vitamin D stores. In the presence of renal disease or hypercalcemia, testing of 1,25-dihydroxy vitamin D (DHVD) might be needed to adequately assess vitamin D status.

Specimen Required

Patient Preparation: Fasting (4-hour preferred but not required)

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: At least 1.5 mL

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-General Request (T239)

-Renal Diagnostics Test Request (T830)

Specimen Minimum Volume

1.2 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	7 days	
	Frozen	28 days	
	Ambient	7 days	

Clinical and Interpretive

Clinical Information

Vitamin D is a generic designation for a group of fat-soluble, structurally similar sterols, which act as hormones. In the presence of renal disease or hypercalcemia, testing of 1,25-dihydroxy vitamin D (DHVD) might be needed to adequately assess vitamin D status. The 25-hydroxyvitamin D (25HDN) test (25HDN / 25-Hydroxyvitamin D2 and D3, Serum) in serum is otherwise the preferred initial test for assessing vitamin D status and most accurately reflects the body's vitamin D stores.

Vitamin D compounds in the body are exogenously derived by dietary means; from plants as 25-hydroxyvitamin D2 (ergocalciferol or calciferol) or from animal products as 25-hydroxyvitamin D3 (cholecalciferol or calcidiol). Vitamin D may also be endogenously derived by conversion of 7-dihydrocholesterol to 25-hydroxyvitamin D3 in the skin upon ultraviolet exposure.

25HDN is subsequently formed by hydroxylation (CYP2R1) in the liver. 25HDN is a prohormone that represents the main reservoir and transport form of vitamin D, being stored in adipose tissue and tightly bound by a transport protein while in circulation. Biological activity is expressed in the form of DHVD, the active metabolite of 25HDN. 1-Alpha-hydroxylation (CYP27B1) occurs on demand, primarily in the kidneys, under the control of parathyroid hormone (PTH) before expressing biological activity. Like other steroid hormones, DHVD binds to a nuclear receptor, influencing gene transcription patterns in target organs.

25HDN may also be converted into the inactive metabolite 24,25-dihydroxyvitamin D (24,25D) by (CYP24A1) hydroxylation. This process, regulated by parathyroid hormone (PTH), might increase DHVD synthesis at the expense of the alternative hydroxylation (CYP24A1) product 24,25D. Inactivation of 25HDN and DHVD by CYP24A1 is a crucial process that prevents over production of DHVD and resultant vitamin D toxicity.

DHVD stimulates calcium absorption in the intestine and its production is tightly regulated through concentrations of serum calcium, phosphorus, and PTH. DHVD promotes intestinal calcium absorption and, in concert with PTH, skeletal calcium deposition, or less commonly, calcium mobilization. Renal calcium and phosphate reabsorption are also promoted, while prepro-PTH mRNA expression in the parathyroid glands is downregulated. The net result is a positive calcium balance, increasing serum calcium and phosphate levels, and falling PTH concentrations.

In addition to its effects on calcium and bone metabolism, DHVD regulates the expression of a multitude of genes in many other tissues including immune cells, muscle, vasculature, and reproductive organs.

DHVD levels are decreased in hypoparathyroidism and in chronic renal failure. DHVD levels may be high in primary hyperparathyroidism and in physiologic hyperparathyroidism secondary to low calcium or vitamin D intake. Some patients with granulomatous diseases (eg, sarcoidosis) and malignancies containing nonregulated 1-alpha hydroxylase in the lesion might have hypercalcemia that appears vitamin D mediated with normal or high serum phosphate (hyperphosphatemia) and hypercalcemia (both of which might be severe) in addition to low PTH and absent parathyroid hormone-related peptide (PTHRP). Assessment of 24,25D might also be required in patients with hypercalcemia that does not appear to be driven by PTH or PTHRP, and may be helpful in assessment of patients with loss of function inactivating *CYP24A1* mutations. Differential diagnostic considerations include vitamin D intoxication and CYP24A1 deficiency.

Reference Values

Males:

<16 years: 24-86 pg/mL

> or =16 years: 18-64 pg/mL

Females:

<16 years: 24-86 pg/mL

> or =16 years: 18-78 pg/mL

For SI unit Reference Values, see https://www.mayocliniclabs.com/order-tests/si-unit-conversion.html

Interpretation

1,25-Dihydroxyvitamin D (DVHD) concentrations are low in chronic renal failure and hypoparathyroidism.

DVHD concentrations are high in sarcoidosis and other granulomatous diseases, some malignancies, primary hyperparathyroidism, and physiologic hyperparathyroidism.

DVHD concentrations are not a reliable indicator of vitamin D toxicity; normal (or even low) results may be seen in such cases.

Cautions

No significant cautionary statements.

Supportive Data

The new, 1,25-dihydroxyvitamin D liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay correlates well with the current immunoassay:

-LC-MS/MS=0.95 RIA (pg/mL) + 2.5 pg/mL; correlation coefficient=0.822

-Inter-assay precision: 7 to 12% CV (19 to 287 pg/mL)

-Interferences: C-3 epimers (EPI) of 1,25 dihydroxyvitamin D3 3.0%

Clinical Reference

1. Endres DB, Rude RK: Vitamin D and its metabolites. In Tietz Textbook of Clinical Chemisty. Third edition. Edited by CA Burtis, ER Ashwood. Philadelphia, WB Saunders Company, 1999, pp 1417-1423

2. Bringhurst FR, Demay MB, Kronenberg HM: Vitamin D (calciferols): metabolism of vitamin D. In Williams Textbook

of Endocrinology. Ninth edition. Edited by JD Wilson, DW Foster, HM Kronenberg, PR Larsen. Philadelphia, WB Saunders Company, 1998, pp 1166-1169

Performance

Method Description

Deuterated stable isotopes are added to sample as internal standard. 1,25-Dihydroxyvitamin D and the internal standard are extracted. The extracts are then further purified by solid phase extraction (SPE) and affinity extraction. Extracts are then derivatized and analyzed by chromatography-tandem mass spectrometry using multiple reaction monitoring.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; 3 p.m.

Analytic Time

2 days

Maximum Laboratory Time

4 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

82652

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
DHVD	1,25-Dihydroxyvitamin D, S	62290-2

Test Definition: DHVD

1,25-Dihydroxyvitamin D, S

Result ID	Test Result Name	Result LOINC Value
8822	1,25-Dihydroxyvitamin D, S	62290-2