Vitamin D Testing

Indications for Ordering

• Use to diagnose vitamin D insufficiency and monitor response to vitamin D therapy
• Testing is recommended only for patients at risk for vitamin D insufficiency

Test Description

Vitamin D, 25-Hydroxy
• Quantitative chemiluminescent immunoassay
• Tests for combined D2 and D3 forms of vitamin D, 25-hydroxy

Vitamin D, 1, 25-Dihydroxy
• Quantitative chemiluminescent immunoassay

25-Hydroxyvitamin D2 and D3 by Tandem Mass Spectrometry, Serum
• Quantitative high performance liquid chromatography-tandem mass spectrometry (LC-MS/MS)

Tests to Consider

Typical testing strategy

Screening
• Vitamin D, 25-Hydroxy

Hypercalcemia and/or renal failure
• See Related tests

Monitoring therapy
• Vitamin D, 25-Hydroxy – preferred test
• 25-Hydroxyvitamin D2 and D3 by LC-MS/MS – may be useful in individuals who are not responding to supplementation

Primary tests
Vitamin D, 25-Hydroxy 0080379
• Preferred screening test for vitamin D deficiency
• Preferred test to monitor response to supplementation

Vitamin D, 1, 25-Dihydroxy 0080385
• May be useful for evaluating calcium metabolism in individuals with hypercalcemia or renal failure in addition to Vitamin D, 25-Hydroxy testing
• Test is not appropriate for diagnosing vitamin D insufficiency

25-Hydroxyvitamin D2 and D3 by Tandem Mass Spectrometry, Serum 2002348
• May be useful for individuals with vitamin D insufficiency/deficiency who are not responding to supplementation
• Not the test of choice for initial evaluation of vitamin D insufficiency; Vitamin D, 25-hydroxy is preferred

Related tests
Parathyroid Hormone, Intact with Calcium 0070172
• Preferred test to diagnose calcium disorders suspected to be a result of parathyroid dysfunction

Parathyroid Hormone-Related Peptide (PTHrP) by LC-MS/MS, Plasma 2010677
• Aid in the diagnosis and monitoring of treatment for hypercalcemia

Renal Function Panel 0020144
• Screen kidney function for renal failure in individuals at risk for vitamin D deficiency

Disease Overview

Vitamin D Deficiency

Prevalence
• African American – 82.1% (may be less if weakly bound to vitamin D, 25-hydroxy)
• Hispanics – 69.2%
• Overall – 42%

Symptoms/signs
• Bone/joint pain
• Decreased bone mineral density (BMD)
• Nontraumatic fractures
• Hypercalcemia
  o Nausea, coma, vomiting, diarrhea, headache, polydipsia and polyuria, hypertension, nephrolithiasis, and metastatic calcifications

Diagnostic issues
• Vitamin D deficiency associated with
  o Rickets
  o Osteomalacia
  o Osteoporosis
• Other conditions thought to be associated with vitamin D deficiency
  o Autoimmune disease
  o Cancer
  o Cardiovascular disease
Physiology

- Refer to vitamin D metabolism diagram below
- Vitamin D, 25-Hydroxy – prohormone
  - Synthesized in the skin
  - Absorbed from diet when exposed to sunlight
  - Stored in the liver
- Vitamin D, 1, 25-Dihydroxy
  - Converted from vitamin D, 25-hydroxy by the kidneys
    - Conversion under control of the parathyroid hormone
  - Directs calcium absorption from the small intestine and reabsorption from bones
- Chronic vitamin D deficiency causes a secondary hyperparathyroidism
  - Excretion of phosphorus by the kidneys
  - Calcium reabsorbed from bones
  - Leads to decreased bone mineral density, osteomalacia, rickets (in children), and osteoporosis

Screening/detection

Screening recommended for at-risk populations
- African American and Hispanic ethnicities
- Body mass index (BMI) greater than 30 kg per m²
- Chronic kidney disease
- Granuloma-forming disorders
- Hepatic failure
- Hyperparathyroidism
- Malabsorption
- Medication that impairs vitamin D metabolism (eg, antiseizure medications, glucocorticoids, AIDS medication, antifungals, cholestyramines)
- Advanced age with history of falls or nontraumatic fractures
- Osteomalacia
- Osteoporosis
- Pregnancy and lactation
- Rickets
- Some lymphomas

Etiology

Major causes of vitamin D deficiency (The Endocrine Society Clinical Practice Guideline, 2011)
- Inadequate exposure to sunlight (sunscreen or dark skin)
- Obesity
- Fat malabsorption syndrome (eg, celiac disease)
- Bariatric surgery
- Nephrotic syndrome (vitamin D bound to albumin)
- Drug catabolism (HIV and anticonvulsants)
- Granuloma-forming disorders, lymphomas, and primary hyperparathyroidism

Laboratory Findings

<table>
<thead>
<tr>
<th>Clinical Disorder</th>
<th>25(OH)D</th>
<th>1,25(OH)2D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D deficiency</td>
<td>D</td>
<td>D, N, I</td>
</tr>
<tr>
<td>Severe hepatocellular disease</td>
<td>D</td>
<td>D, N</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>D</td>
<td>D, N</td>
</tr>
<tr>
<td>Renal failure</td>
<td>N</td>
<td>D</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>N</td>
<td>D</td>
</tr>
<tr>
<td>Hypoparathyroidism</td>
<td>N</td>
<td>D, N</td>
</tr>
<tr>
<td>Pseudohypoparathyroidism</td>
<td>N</td>
<td>D, N</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>N</td>
<td>D, N</td>
</tr>
<tr>
<td>Vitamin D dependent rickets, type I (pseudo vitamin D deficiency rickets)</td>
<td>N, I</td>
<td>D</td>
</tr>
<tr>
<td>Vitamin D-dependent rickets, type II (pseudo vitamin D deficiency rickets)</td>
<td>N, I</td>
<td>D</td>
</tr>
<tr>
<td>D = decreased, N = normal, I = increased</td>
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<td></td>
</tr>
</tbody>
</table>

Test Interpretation

Vitamin D, 25-Hydroxy

**Reference Ranges for Adults and Children**

<table>
<thead>
<tr>
<th></th>
<th>0-17 years</th>
<th>18 years and older</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficiency</td>
<td>&lt;20 ng/mL</td>
<td>&lt;20 ng/mL</td>
</tr>
<tr>
<td>Insufficiency</td>
<td>--</td>
<td>20-29 ng/mL</td>
</tr>
<tr>
<td>Optimum level</td>
<td>≥20 ng/mL*</td>
<td>30-80 ng/mL</td>
</tr>
<tr>
<td>Possible toxicity</td>
<td>--</td>
<td>&gt;150 ng/mL</td>
</tr>
</tbody>
</table>


Vitamin D 1, 25-Dihydroxy

- Normal – 19.9-79.3 pg/mL
  - Normal result does not rule out deficiency