Vitamin D Deficiency: Evaluation and Treatment

NATIONWIDE CHILDREN’S
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**Pediatric Vitamin D Deficiency**

Vitamin D is crucial for bone health – it plays a role in calcium absorption, increased bone mineral density, and in preventing rickets, osteomalacia and fractures. Vitamin D deficiency has received significant media attention in recent years for its association with bone disorders, and for its possible association with other adverse health outcomes, including cancer, autoimmune diseases, infections, diabetes mellitus and cardiovascular conditions.

**When To Test for Vitamin D Deficiency**

In pediatric practice, measuring serum 25-OH vitamin D levels should be considered for patients at risk for deficiency or those with signs and symptoms relating to the effects of vitamin D deficiency on the skeleton or muscle function. Patients at risk include those with dark skin pigmentation or a body mass index > 95th percentile. Other indications for testing are:

### Indications for Measurements of Serum 25-OH Vitamin D

- **Symptoms and signs of rickets/osteomalacia**
  - Progressive bowing deformity of legs
  - Waddling gait
  - Abnormal knock knee deformity (intermalleolar distance > 5 cm)
  - Swelling of wrists and costochondral junctions (rachitic rosary)
  - Prolonged bone pain (> 3 months duration)

- **Symptoms and signs of muscle weakness**
  - Delayed walking
  - Difficulty climbing stairs
  - Cardiomyopathy in an infant

- **Abnormal bone profile or X-rays**
  - Low serum calcium or phosphorus
  - Elevated serum alkaline phosphatase
  - Osteopenia or signs of rickets on bone X-ray
  - Pathologic fractures

- **Disorders impacting on vitamin D metabolism**
  - Chronic kidney disease
  - Chronic liver disease
  - Malabsorption disorders (cystic fibrosis, Crohn’s disease, celiac disease, bariatric surgery)
  - Medications (anticonvulsants [phenobarb, phenytoin, carbamazepine], glucocorticoids, AIDS medications, antifungals [ketoconazole], cholestyramine)
  - Parathyroid disorders
  - Granuloma-forming disorders (sarcoidosis, tuberculosis, histoplasmosis, coccidiomycosis)

- **Bone diseases (when correcting vitamin D deficiency prior to bone-strengthening therapy would be indicated)**
  - Osteogenesis imperfecta
  - Other causes of primary osteoporosis, such as idiopathic juvenile osteoporosis
  - Secondary osteoporosis (secondary to chronic glucocorticoids, inflammatory disorders, immobility)
**What Levels Are Considered Deficient?**

Definitions of vitamin D deficiency and insufficiency vary among expert groups. The Institute of Medicine (IOM) has defined a serum 25-OH vitamin D level of > 20 ng/mL as sufficient, based on integrated measures of calcium absorption, bone mineral density, osteomalacia and rickets, whereas the Endocrine Society has defined > 30 ng/mL as sufficient. The Pediatric Endocrine Society (PES) guidelines published in 2008 defined deficiency as level < 15 ng/mL and > 20 ng/mL as optimal.

The debate is based primarily on data from the adult literature. Only a limited number of studies have evaluated the effect of vitamin D on bone mass at doses that raise serum 25-OH vitamin D concentrations above 30 ng/mL in pediatric patients. The results are so far inconsistent. Therefore, the higher vitamin D cutoffs of 30 ng/mL have not been the official recommendation of the American Academy of Pediatrics, PES, or their European counterparts.

In our practice in the Pediatric Metabolic Bone Clinic at Nationwide Children’s, the target vitamin D level is > 30 ng/mL for optimal bone health in the patients with osteopenia or osteoporosis. This cutoff is based on several studies that found higher serum 25-OH vitamin D levels (>30 ng/mL) were associated with increased bone mineral density.

**Definitions of Vitamin D Levels*:**

<table>
<thead>
<tr>
<th>Vitamin D Status</th>
<th>IOM</th>
<th>Endocrine Society Classification</th>
<th>Pediatric Endocrine Society Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe deficiency</td>
<td>&lt;5</td>
<td>---</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Deficiency</td>
<td>&lt;15</td>
<td>&lt;20</td>
<td>&lt;15</td>
</tr>
<tr>
<td>Sufficiency</td>
<td>&lt;20</td>
<td>&gt;30</td>
<td>20-100</td>
</tr>
<tr>
<td>Insufficiency</td>
<td>---</td>
<td>21-29</td>
<td>15-20</td>
</tr>
<tr>
<td>Risk of toxicity</td>
<td>&gt;50</td>
<td>---</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Toxicity</td>
<td>---</td>
<td>&gt;150</td>
<td>&gt;150</td>
</tr>
</tbody>
</table>

* measurements in ng/mL
**Treatment**

For children and adolescents with low vitamin D levels but without clinical signs of rickets, vitamin D₃ (cholecalciferol) should be given at the following doses:

- 400-800 IU orally per day if the 25-OH vitamin D level is 20-30 ng/mL.
- 1000 IU orally per day if the 25-OH vitamin D level is <20 ng/mL.
- 2000 IU orally per day for prepubertal children if the 25-OH vitamin D level is <10 ng/mL.
- 4000 IU orally per day for adolescents (or adults) if the 25-OH vitamin D level is <10 ng/mL.

The dose may need to be increased (or doubled) for those with malabsorption, chronic glucocorticoids use, dark skin pigmentation or obesity. Serum 25-OH vitamin D level testing should be repeated in 3 months after giving pharmacologic doses of vitamin D. When the level is optimal, vitamin D should be reduced to a supplementation dose of 400-800 IU/day.

Treatment for vitamin D-deficiency rickets requires therapeutic doses of calciferol (ergocalciferol or cholecalciferol) until biochemistries are normalized. Joint X-ray should be repeated after 3 months to ensure healing of rickets. Usually, treatment is for 2-3 months and may also require calcium supplementation in those with inadequate dietary calcium intake or low serum calcium levels.

Some advocate use of a single-day mega dose of vitamin D, or “Stoss therapy.” However, such regimens can result in hypercalcemia and nephrocalcinosis. There have been reports on propylene glycol toxicity with Stoss therapy when oral vitamin D preparations containing propylene glycol such as Drisdol are used. In teenagers and adults, 50,000 IU of vitamin D₃ (cholecalciferol) can be given orally once per week for 8 weeks.

Otherwise follow these recommendations:

<table>
<thead>
<tr>
<th>Age</th>
<th>Calciferol</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 month</td>
<td>1000 IU by mouth daily</td>
</tr>
<tr>
<td>1-6 months</td>
<td>3000 IU by mouth daily x 8 weeks</td>
</tr>
<tr>
<td>6 months – 12 years</td>
<td>5000 IU by mouth daily x 8 weeks</td>
</tr>
<tr>
<td>&gt;12 years</td>
<td>9000 IU by mouth daily x 8 weeks</td>
</tr>
</tbody>
</table>

Repeat serum 25-OH vitamin D level testing after completion of 8-12 weeks of treatment. If within acceptable parameters, children should receive a supplementation dose (400-600 IU/day) until completion of linear growth. Babies receiving 500 mL or more of formula milk per day do not require supplementation after treatment.