Vitamin D Deficiency and Nutritional Rickets: Supplementation and Treatment in Infants and Children

(Alder Hey Children’s NHS Foundation Trust)

The attached guideline is authored by Alder Hey Children’s NHS Foundation Trust

It has been reviewed by the Children’s Guideline & Procedure Group and agreed that this guidance will be followed for children treated at ‘Wirral University Teaching Hospital’.

For further information and advice, below is a link to the Royal College of Paediatrics Child Health Vitamin D guideline:

http://www.rcpch.ac.uk/system/files/protected/page/vitdguidancedraftspreads%20FINAL%20for%20website.pdf

April 2015
Vitamin D Deficiency and Nutritional Rickets:
Supplementation and Treatment in Infants and Children

**Background**
Vitamin D deficiency is a risk for

- Rapidly growing children (infants, young children and adolescents) in the UK, particularly in ethnic minority groups
- Children with chronic diseases such as cystic fibrosis, coeliac disease, liver disease, renal disease, cancer
- Children receiving certain drugs, e.g. anti-convulsants

In 2012, the UK Chief Medical Officers\(^1\) issued advice on supplements for at risk children between 1 month and 5 years of age, and breastfeeding babies likely to be born vitamin D deficient (due to lack of maternal supplementation in pregnancy).

Uptake of supplementation programmes has historically been low, and in recent years rickets is being more commonly recognised in infants and children.\(^2\) Over 80% of Liverpool Somali children have been reported to have low vitamin D levels, although most will be asymptomatic.

### Vitamin D supplementation (for children up to 5 years of age and those with insufficiency)*

<table>
<thead>
<tr>
<th>Population Group</th>
<th>Risk Factors</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants &lt; 6 months and breast fed</td>
<td>Risk factors for low maternal vitamin D level, e.g. Asian and African ethnicity</td>
<td>Healthy Start* vitamin supplement, or standard dose of Dalivit* or Abidec*</td>
</tr>
<tr>
<td>Infants &gt; 6 months</td>
<td>Breast fed or taking less than 500 ml infant formula</td>
<td>Healthy Start vitamin supplement, or standard dose of Dalivit* or Abidec*</td>
</tr>
<tr>
<td>All children 1-5 years</td>
<td></td>
<td>Healthy Start* vitamin supplement, or standard dose of Dalivit* or Abidec* Safe sun exposure Dietary vitamin D and calcium advice</td>
</tr>
<tr>
<td>Insufficient vitamin D levels (see Table 1)</td>
<td></td>
<td>Follow vitamin D specific supplementation guidelines above until 5 years of age and possibly throughout childhood Safe sun exposure Dietary vitamin D and calcium advice</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>e.g. cerebral palsy, neuromuscular disorders, taking anti-convulsant therapy, cystic fibrosis, malabsorption</td>
<td>Follow disease specific prescribing guidelines or guidance in Table 1 of these guidelines Safe sun exposure Dietary vitamin D and calcium advice</td>
</tr>
</tbody>
</table>

*Multivitamin supplements containing vitamin A should not be used in patients with chronic renal failure. These children should receive vitamin D alone as a supplement.
**Assessment of vitamin D status**

Supplementation can be initiated without testing and therefore biochemical testing for vitamin D deficiency is unnecessary for the majority of children in the primary care setting, unless they are symptomatic.

Follow agreed disease specific monitoring guidelines for those with underlying chronic conditions such as CF, cancer neuromuscular disease, if these are available.

<table>
<thead>
<tr>
<th>Total 25(OH)Vitamin D (nmol/L)</th>
<th>Vitamin D status</th>
<th>Clinical status</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤25</td>
<td>Deficiency</td>
<td><strong>Infants:</strong> Rickets, bone pain, delayed walking</td>
<td>Treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Children:</strong> Chronic pain and weakness, tiredness</td>
<td></td>
</tr>
<tr>
<td>&gt;25-50</td>
<td>Insufficiency</td>
<td>Likely to be asymptomatic</td>
<td>Supplementation</td>
</tr>
<tr>
<td>&gt;50</td>
<td>Adequate</td>
<td>Generally considered adequate for bone and overall health</td>
<td>Dietary/lifestyle advice</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Remember levels may decrease over autumn/winter</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Note: Vitamin D status is determined on total 25-OH Vitamin D level (25-OH Vitamin D2 + 25-OH Vitamin D3) if 25-OH Vitamin D2 and 25 OH Vitamin D3 are reported separately.*

**Vitamin D deficiency**

**Predisposing factors for vitamin D deficient bone disease (rickets)**

- Occurs mainly in dark skinned infants and teenagers
- Lack of skin exposure to the sun particularly with some types of traditional clothing
- Use of sun block
- Prolonged breast feeding
- Exclusion diets
- Vegetarian diet
- Malabsorptive disease states
- Renal/liver disease
- Immobility
- Anticonvulstant treatment (e.g. sodium valproate, carbamazepine)

**Clinical presentation of vitamin D deficiency**

- Vitamin D deficiency is usually asymptomatic but infants and young children may present with classic features of bow legs, swollen wrists and delayed walking. Severe cases may have bone pain presenting as unexplained crying.
- When present, symptoms are often vague and in teenagers may present as aches and pains in legs. Positive Gower’s sign is an early clue (proximal myopathy).
- Occasionally hypocalcaemia in (breastfeeding) infants may cause convulsions.
- **The presence of low vitamin D levels in isolation does not necessarily indicate this to be the cause of symptoms, as deficiency is commonly found in young children and may only require supplementation.**
Investigations (when symptomatic vitamin D deficiency clinically suspected)

Clinicians should have a low index of suspicion for rickets, but routine supplementation is of more value than investigating large numbers of children without overt symptoms.

Investigation may be of help if adherence is expected to be poor or symptoms develop.

Symptomatic rickets should be investigated as below.

- U&Es, Creatinine
- FBC
- Bone profile (Ca, Mg, phosphate, alkaline phosphatase)
- 25-OH Vitamin D levels (combined vitamin D2 and D3)

Additional tests depending on clinical context

- Ferritin (as asymptomatic iron deficiency often co-exists)
- 1,25 OHVitamin D (if suspecting renal rickets or where vitamin D levels are normal but biochemistry indicates vitamin D bone disease). This investigation should not be done routinely.
- Parathyroid hormone (not routinely done unless biochemistry is atypical for nutritional vitamin D deficiency, or clinical rickets)
- X-ray knee or wrist (only if the patient clinically has rickets or significant symptoms)

<table>
<thead>
<tr>
<th>Table 2: Differential diagnosis</th>
<th>Calcium</th>
<th>Phosphate</th>
<th>Alkaline Phosphatase (AlkP)</th>
<th>Parathyroid hormone (PTH)</th>
<th>Total 25-OH-Vitamin D 2+3</th>
<th>1,25 Vit D (not done routinely)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritional vitamin D deficiency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary lack and malabsorption</td>
<td>low or normal</td>
<td>low or normal</td>
<td>high or normal</td>
<td>high or normal</td>
<td>low</td>
<td></td>
</tr>
<tr>
<td>Renal rickets</td>
<td>low</td>
<td>high</td>
<td>high</td>
<td>high</td>
<td>normal</td>
<td>very low</td>
</tr>
<tr>
<td>Inherited vitamin D deficiency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vit D dependent rickets (Pseudo-vitamin D deficiency)</td>
<td>low</td>
<td>low</td>
<td>high</td>
<td>high</td>
<td>normal</td>
<td>low</td>
</tr>
<tr>
<td>Hereditary vitamin D resistance (receptor mutation)</td>
<td>low</td>
<td>low</td>
<td>high</td>
<td>high</td>
<td>normal</td>
<td>very high</td>
</tr>
<tr>
<td>Hypophosphataemic rickets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophosphataemic rickets</td>
<td>normal</td>
<td>low</td>
<td>high</td>
<td>Normal (can be low/high)</td>
<td>normal*</td>
<td>variable</td>
</tr>
</tbody>
</table>

*inappropriately so
Therapeutic treatment of vitamin D deficiency (< 25 nmol/L)

In patients over 6 months of age, aim for a TOTAL replacement dose of 200,000 units given as daily or weekly replacement doses as below; the prescribed administration schedule should aim to maximise treatment adherence.

<table>
<thead>
<tr>
<th>Age</th>
<th>Less than 1 month</th>
<th>1 month-6 months</th>
<th>Over 6 months-adult*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose of colecalciferol or ergocalciferol</td>
<td>1000 units daily for 1 month</td>
<td>3000 units daily for 1 month</td>
<td>6000 units daily for 1 month</td>
</tr>
</tbody>
</table>

*The following regimen may promote adherence:-
Capsules: colecalciferol 20,000 units daily for one week (7 days), then 20,000 units weekly for 3 weeks (i.e. total of 10 doses of 20,000 units)
Liquid: 25,000 units daily for one week (7 days) then 25,000 units weekly for 1 week (i.e. total of 8 doses of 25,000 units)

Consider whether a licensed formulation can be used (some small flexibility in the prescribed dose may enable this). Alternatively the off-label use of a licensed formulation or the use of an unlicensed formulation may be necessary.

There is little evidence to support the need for calcium supplementation, but calcium intake from food should be assessed and improved if needed. If this is not achievable then consider calcium supplementation.

NB. Vitamin D 200 units = 5 micrograms of colecalciferol (D3) = 5 micrograms of ergocalciferol (D2).

Monitoring treatment response

- Review at the end of the treatment course. Ask the patient to bring all of their vitamin D medicine bottles to the review, to assess adherence. Consider repeating a blood test if symptoms persist and there is evidence of non-compliance.

If results are abnormal (vitamin D levels are deficient)

- Continue treatment for a further 1 month and
- Check, bone profile (+/-PTH) and
- Continue until biochemistry normal

When to refer to the Metabolic Bone Service (MBS) at Alder Hey

- Patients who show a poor response to treatment
- Patients with symptomatic rickets with significant metabolic abnormalities, e.g. PO4 < 0.75mmol/l
- Where a secondary cause is suspected, e.g. liver, malabsorption or renal disease
- Metabolic bone disease, not related to vitamin D deficiency
**Poor adherence to treatment**

If poor adherence to treatment is a contributory cause, the metabolic bone service would consider giving high dose bolus ergocalciferol therapy (called Stoss ‘bolus’ therapy) which can be given orally or by IM injection.

**Stoss therapy**

- Oral ergocalciferol 150,000 units (3 x 50,000 unit capsules) as an observed dose every 3 months until biochemistry returns to normal.
- An alternative regimen of 50,000 units orally once a month for 3 months can be used.
- Ergocalciferol injection (available as 300,000 unit/ml) can be given by intra-muscular injection at a dose of 150,000 units (prepare to repeat after 1 month) or at a dose of 300,000 units (which may last for 3 months).
- Daily supplementation with vitamin D should be continued.
- Calcium supplementation is often given concurrently in infants when hypocalcaemia exists.

Parents must be informed of the symptoms of hypercalcaemia when starting high dose vitamin D (Stoss) therapy (e.g. anorexia, nausea, vomiting, headache, abdominal pain, polyuria) and advised to seek medical attention if their child develops any of these symptoms. **Whenever Stoss therapy is given the bone profile must be checked after 1 month to ensure that hypercalcaemia has not occurred.**

**Education on longer term vitamin D health**

- To prevent recurrence in patients who have completed treatment with therapeutic doses, long term supplementation and safe sun exposure are advised.
- Explain that it can take between 1-2 years for the bones to remodel.
- Explain that body stores take a long time to be replenished and so supplements are needed for a long time.
- Advise that siblings and other family members should also be supplemented.
VITAMIN D PREPARATIONS (stocked at Alder Hey)

Vitamin D alone (for therapeutic treatment)

- **Colecalciferol (Fultium D3™) 3,200 unit capsule [licensed product]**

- **Colecalciferol 20,000 unit capsules (e.g. Biovitamin™ D3 capsules).** Also available in primary care. [Unlicensed product]

- **Ergocalciferol (or colecaciferol) capsules 1.25 mg (50,000 units)** - only for use under supervision at Alder Hey (referrals to Metabolic Bone Service - MBS) [Licensed product]

- **Colecalciferol (InVita D3™) oral solution 25,000 unit/ml; 1 ml ampoule for oral use [Licensed product]**

- **Colecalciferol oral solution 3000 unit/ml (= 15,000 unit/5ml).** This product is an unlicensed medicine. It is available as a manufactured special in both primary and secondary care settings, but is more expensive than other formulations and should be reserved for those patients who cannot swallow solid dose forms or where the dose volume of the licensed product is too small to be measured.

- **Ergocalciferol injection 300,000 units/ml (through MBS) [Licensed product]**

Multivitamin preparations (available for supplementation)

To ensure adequate vitamin D status in healthy children and well children with vitamin D insufficiency, and to prevent recurrence of deficiency after vitamin D treatment.

- **Healthy Start Children's Vitamin Drops** (community clinics only) - 5 drops daily contains 7.5 micrograms (300 IU) vitamin D₃, 233 micrograms vitamin A and 20 mg vitamin C.

Children can get these supplements free without prescription from 1 month to 4 years if parents are in receipt of welfare benefits.

In Liverpool, Healthy Start Vitamins are free for all children up to 2 years of age from the Children’s Centres.

The product is suitable for vegetarians and free from milk, egg, gluten, soya and peanut residues.

[http://www.healthystart.nhs.uk](http://www.healthystart.nhs.uk)

- **Abidec™ or Dalavit™ 0.6 ml daily provides 400 units vitamin D daily.** (Available on prescription or to buy). [Licensed products]

Multivitamin preparations containing vitamin A are not suitable for patients with chronic renal failure. These patients should receive vitamin D supplementation alone.

Vitamin D preparations (available for supplementation)

- **Colecalciferol (Fultium D3™) 800 unit capsule [Licensed product]**
References

1. Chief Medical Officers (UK). Vitamin D - advice on supplements for at risk groups 2012 CEM/CMO/2012/04
   Gateway reference 17193.  

2. Moy R.J et al Successful public health action to reduce the incidence of symptomatic vitamin D deficiency.  
   Archives of disease in childhood 2012;97:952-954

Other relevant guidance

Guide for Vitamin D in childhood. RCPCH October 2013  
http://www.rcpch.ac.uk/system/files/protected/page/vitdguidancedraftspreads%20FINAL%20for%20website.pdf

East and South East England Specialist Pharmacy services. Vitamin D deficiency and insufficiency: Using appropriate
available products January 2013  

Alder Hey Children’s NHS Foundation Trust Vitamin D Guideline Working group

Dr James Bunn (General Paediatrics)  
Dr Poonam Dharmaraj (Endocrinology)  
Anita Aindow (Pharmacy Medicines Information)  
Catrin Barker (Chief Pharmacist)  
Andrea Gill (Pharmacy)  
Emma Whittle (Senior Dietician)  
Ruth Watling (Head of Dietetics)
Vitamin D Deficiency and Nutritional Rickets: Supplementation and Treatment in Infants and Children

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Author(s)</th>
<th>Status</th>
<th>Comment(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Dec 14</td>
<td>Catherine Collingwood (Principal Biochemist)</td>
<td>Current</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Sep 14</td>
<td>Alder Hey Children’s NHS Foundation Trust Vitamin D Guideline Working Group</td>
<td>Archived</td>
<td></td>
</tr>
</tbody>
</table>

Review and Revision(s) Log
Record of revision(s) made to guidelines since Version 1

<table>
<thead>
<tr>
<th>Section Number</th>
<th>Page Number</th>
<th>Revision(s) made</th>
<th>Reason for revision(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Updated to reflect laboratory advise on determination of Vitamin D status</td>
</tr>
</tbody>
</table>