INTRODUCTION

Vitamin D is essential for skeletal growth and bone health. Dietary sources in the UK are very limited and oily fish is the only significant source. Small amounts are provided by egg yolk, red meat and fortified foods, such as some breakfast cereals and fat spreads (margarine). In addition, infant formula milk has to be fortified with vitamin D (this is voluntary for formula milks for toddlers). Breast milk contains very little vitamin D and is not a significant source. The major natural source is from skin synthesis following exposure to sunlight. In a fair skinned person, 20-30 minutes of sunlight exposure to the face and forearms at midday generates about 2000 units of vitamin D. Two or 3 sunlight exposures per week are sufficient to achieve adequate vitamin D levels in the summer if individuals have adequate levels to begin with. However, those with low vitamin D levels, pigmented skin and the elderly need increased exposure time or frequency to get the same level of vitamin D synthesis. Sun exposure should be avoided if someone has a history of skin cancer, or conditions such as xeroderma pigmentosum or actinic keratosis.

From mid-October to the beginning of April in the UK there is no ambient ultraviolet sunlight of the appropriate wavelength. During this time, the population relies on both body stores from sun exposure in the summer and dietary sources to maintain vitamin D levels.

The recommended oral daily intake of vitamin D for an adult in the UK is around 400IU (10mcg). The average adult daily diet in the UK provides only 3.7mcg of vitamin D for men and 2.8mcg for women. Food sources which contain greater than 5mcg per portion of vitamin D include two teaspoons cod liver oil, 70g sardines, 100g tinned salmon, pilchards or tuna, 110g of cooked mackerel or herring and 130g cooked kipper. Consumption of food sources alone, in the absence of skin synthesis, will not provide optimal vitamin D status. Vitamin D deficiency develops when there is inadequate exposure to sunlight or a lack of vitamin D in the diet and usually takes a long time to develop as there is slow release of the vitamin from body stores to cover times of deficiency.

Factors predisposing to Vitamin D deficiency:

- Inadequate UV light exposure - Northern latitude, Air pollution, Habitual sunscreen use, Dark or pigmented skin, Institutionalised/ housebound/ reduced mobility i.e. wheelchair dependency, Clothing which limits sunlight exposure or avoidance of sunlight
- Poor dietary intake/ malabsorption - Poor diet, Malabsorption including short bowel, cholestatic jaundice, Crohn’s Disease, cystic fibrosis, coeliac disease, Cholestyramine use
- Metabolic risk - Reduced synthesis (eg over 65years old), Pregnant and breastfeeding women particularly teenagers and young women, multiple short interval pregnancies, infants who are exclusively breast fed, Obesity, Increased breakdown eg drugs (rifampicin, anticonvulsants particularly phenytoin or carbamazepine treatment , highly active antiretroviral treatment, glucocorticoids), Reduced stores: liver disease

Definition of Vitamin D Deficiency

Low vitamin D status (sometimes called vitamin D deficiency) is defined by the Department of Health as a plasma concentration of 25 hydroxyvitamin D (the main circulating form of the vitamin) of below 25 nmol/litre (equal to 10 ng/ml). Several risk groups have been identified and the CMO guidance\(^1\) (2012) recommended vitamin D supplementation of 400 units (10mcg) daily to the following groups of the population at risk of vitamin D deficiency:

- All pregnant and breast-feeding women, especially teenagers and young women
- Aged 65 and over.
- People with reduced sun exposure
- People with darker skin, for example of African, African-Caribbean and South Asian origin.

In these groups, supplementation is suggested without measurement of 25-OHD. For these at risk groups described above, advise to take an appropriate over the counter preparation which can be bought at low cost from any pharmacy or health food shop. NB: multi-vitamin preparations are not suitable for the treatment of vitamin D deficiency as this may lead to vitamin A toxicity.

The CMO has also made recommendations for infants and children aged under 5 years.

The National Osteoporosis Society (NOS) have published a practical clinical guideline to support health professionals with an aim to provide a uniform approach in the management of adult patients with vitamin D deficiency. The guideline provides clarity on who should be tested for vitamin D deficiency, how the results should be interpreted and how deficiency should be treated. It is important to highlight that this clinical guideline intends to inform patient management but not to influence public health policy.

**WHEN TO MEASURE VITAMIN D LEVELS**

Consider measuring vitamin D

- In patients presenting with persistent musculoskeletal weakness, myalgia & arthralgia.
- Hypocalcaemia.
- Management of Primary Hyperparathyroidism
- Unexplained osteoporosis/ osteoporosis refractory to treatment
- Malabsorption syndromes

Please note: Requests by GPs for vitamin D testing require a clear indication / rationale for the test. Re-testing after treatment is not currently considered necessary. When measuring vitamin D levels, concurrent illness and seasonal factors should be considered. Recent illness or operations may cause a falsely low reading.

**Interpretation of vitamin D levels**

A lack of national standards on whom to provide with additional vitamin D, when to test and how to treat led to variations in guidance across the country. Recent advice from NOS provides more consistency and makes recommendations on when testing is justified. In agreement with the Institute of Medicine (IOM), they propose that the following vitamin D thresholds are adopted by UK practitioners in respect to bone health;

<table>
<thead>
<tr>
<th>Level</th>
<th>Interpretation</th>
</tr>
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<tbody>
<tr>
<td>&gt;50 nmol/L of 25-OHD</td>
<td>unlikely to require intervention</td>
</tr>
<tr>
<td>30–50 nmol/L of 25-OHD</td>
<td>may be inadequate in some people</td>
</tr>
<tr>
<td>&lt; 30 nmol/L of 25-OHD</td>
<td>deficiency requiring treatment in adult patients</td>
</tr>
</tbody>
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MANAGEMENT - Vitamin D Inadequacy (25-OHD 30-50nmol/l)

Treatment is advised in patients with the following:
- fragility fracture, documented osteoporosis or high fracture risk
- treatment with antiresorptive medication for bone disease
- symptoms suggestive of vitamin D deficiency
- increased risk of developing vitamin D deficiency in the future because of reduced exposure to sunlight, religious/cultural dress code, dark skin, etc.
- raised PTH
- medication with antiepileptic drugs or oral glucocorticoids
- conditions associated with malabsorption.

Where vitamin D alone is required, there is no need for the high dose regime and 800-1,600 units of colecalciferol daily is adequate. It may take up to 3 months to replenish stores. Routine monitoring is not required for vitamin D doses ≤2000 units daily.

<table>
<thead>
<tr>
<th>Product</th>
<th>Dose</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fultium D3 capsule</td>
<td>20mcg vitamin D₃ (800 units colecalciferol)</td>
<td>Contains glycerol and gelatin. The gelatin used in the capsule shell is certified to Halal standards</td>
</tr>
<tr>
<td>Desunin tablet</td>
<td>20mcg vitamin D₃ (800 units colecalciferol)</td>
<td>Licensed UK product Does not contain gelatin, peanut oil or soya. Colecalciferol is derived from healthy live sheep’s wool fat – may be acceptable to vegetarians</td>
</tr>
<tr>
<td>Fultium D3 capsule</td>
<td>80mcg vitamin D₃ (3200 units colecalciferol)</td>
<td>Licensed UK product Contains glycerol and gelatin. The gelatin used in the capsule shell is certified to Halal standards</td>
</tr>
</tbody>
</table>

For bone health, calcium and vitamin D₃ 800 units/day is appropriate. Locally agreed products are as below, though RCHT may not stock the complete range listed.

<table>
<thead>
<tr>
<th>Product</th>
<th>Dose</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calceos chewable tablet</td>
<td>calcium 500mg and 10 mcg vitamin D₃ (400 units)</td>
<td>Licensed UK product One tablet twice a day</td>
</tr>
<tr>
<td>Calfovit D3 powder in sachet</td>
<td>Calcium 1.2g and 20 mcg vitamin D₃ (800 units)</td>
<td>Licensed UK product One sachet daily</td>
</tr>
<tr>
<td>Adcal D3 chewable tablet</td>
<td>calcium 600mg and 10 mcg vitamin D₃ (400 units)</td>
<td>Licensed UK product One tablet twice a day</td>
</tr>
<tr>
<td>Adcal D3 caplet</td>
<td>calcium 300mg and 5 mcg vitamin D₃ (200 units)</td>
<td>Licensed UK product Two tablets twice a day</td>
</tr>
</tbody>
</table>
MANAGEMENT - Vitamin D deficiency (25-OHD <30nmol/L)
For patients with symptoms of deficiency prescribe coleccalciferol 20,000 to 25,000 units orally weekly for 6 weeks followed by coleccalciferol 800-1,600 units daily thereafter. Most patients require only one course of high dose oral therapy and can then be managed on long term maintenance coleccalciferol. Locally agreed products are as follows:

<table>
<thead>
<tr>
<th>Product</th>
<th>LICENSED UK product</th>
<th>Contains glycerol and gelatin. The gelatin used in the capsule shell is certified to Halal standards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fultium D3 capsule</td>
<td>500 mcg vitamin D₃ (20,000 units coleccalciferol)</td>
<td></td>
</tr>
<tr>
<td>InVita D3 oral solution</td>
<td>625 mcg vitamin D₃ (25,000 units coleccalciferol) per 1ml unit amp oral solution</td>
<td>Colecalciferol is derived from healthy live sheep's wool fat – may be acceptable to vegetarians</td>
</tr>
</tbody>
</table>

Maintenance therapy can begin immediately after the completion of the high dose phase. It is recommended to check calcium 4 weeks following the initiation of the high dose phase in case primary hyperparathyroidism has been unmasked.

Routine repeat of vitamin D levels is not needed if symptoms of vitamin D deficiency resolve. If symptoms do not resolve despite adequate vitamin D repletion then the symptoms are not due to vitamin D deficiency.

Patients with high or high-normal calcium levels and vitamin D deficiency may have coexistent primary hyperparathyroidism. Consider referral to a specialist clinic with an interest in calcium eg Endocrine.

Patients with significant hypomagnesaemia (Mg²⁺ <0.5mmol/l) from any cause may develop significant hypocalcaemia due to ineffective release of PTH. PTH measurement is not recommended in patients with severe hypomagnesaemia as it may be uninterpretable. Replacement with combination magnesium and activated vitamin D may be necessary - seek specialist help.

**Alfacalcidol or calcitriol should NOT be used for routine treatment of vitamin D deficiency as they carry a higher risk of toxicity and require close monitoring.**

**Malabsorption syndromes**
Oral therapy is more effective than IM injections except in cases of significant malabsorption.
Options include:
- High dose oral therapy e.g. 20,000 units -25,000 units oral coleccalciferol weekly
- IM injection of ergocalciferol. Initially 300,000 units IM injections 3 months apart followed by maintenance treatment of 300,000 units IM 6 monthly (a licensed product).

**Renal disease**
Patients on haemodialysis at RCH have their vitamin D levels reviewed and replaced as necessary as part of their dialysis care, and therefore will be excluded from this guideline.

**Drug induced vitamin D deficiency**
If the patient is taking drugs that accelerate Vitamin D metabolism or if there are concerns regarding absorption, then, higher doses may be required. The Medicines and Healthcare Regulatory Agency have advised that patients on long-term anticonvulsant therapy require vitamin D supplementation 400 units daily as a prophylaxis.

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