Guidance on the treatment of vitamin D deficiency in adult inpatient units

The role of vitamin D in bone health has been well documented. It plays an important part in regulating calcium and phosphorus metabolism and is linked to rickets, osteomalacia and bone mineral density changes. However, there has also been a growing interest over recent years into its role in neuropsychological functioning, muscle health, cardiovascular disease and falls reduction. A higher incidence of vitamin D deficiency compared to the general population has been noted in depression, anxiety and psychosis with studies in this field ongoing to determine the nature of the associations identified.

Diagnosing vitamin D deficiencies

Serum levels 25-hydroxyvitaminD - 25(OH)D are used to determine likely deficiency. Serum threshold levels vary depending on location, country guidelines and the lab techniques employed and are subject to international debate. In the UK, the following thresholds are generally adopted:

<table>
<thead>
<tr>
<th>Serum 23(OH)D</th>
<th>Vitamin D Rating</th>
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<tbody>
<tr>
<td>&lt;30 nmol/L</td>
<td>Deficiency</td>
</tr>
<tr>
<td>30-50 nmol/L</td>
<td>Insufficiency</td>
</tr>
<tr>
<td>&gt;50 nmol/L</td>
<td>Sufficiency</td>
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</table>

Nice recommends that routine testing is unnecessary for the general population unless:
- They are considered to be at high risk
- There are clinical reasons (e.g. metabolic factors)
- They are showing clinical features of deficiency

Who to test:

- Showing symptoms of osteomalacia:
  - Bone discomfort or pain (often throbbing) in lower back, pelvis or lower extremities Impaired physical function
  - Muscle aches and weakness - usually most noticeable in the quadriceps and glutei, and can result in difficulty in rising from a seated position, or a waddling gait
  - Symmetric lower back pain
- Chronic widespread pain
- Prior to specific treatment where Vitamin D correction is appropriate (e.g. starting antiresorptives)
- People with bone disease not on a Vitamin D containing supplement
- People who are at higher risk and have had a fall
- People who have features of hypocalcaemia (muscle cramps, carpopedal spasm, numbness, paraesthesias, tetany or seizures).

Risk factors:

<table>
<thead>
<tr>
<th>Metabolic Factors</th>
<th>UVB exposure risk factors</th>
<th>Dietary intake and absorption risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>People &gt;65 yo</td>
<td>Pigmented skin: Darker pigments require longer UVB exposure*</td>
<td>Vegitarian/Vegan incorporating a fish-free diet</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>Lack of sunlight exposure – geographical or lifestyle</td>
<td>Short Bowel</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>People who conceal large proportion of skin (eg for cultural or religious reasons)</td>
<td>Malabsorption from disease: Crohn’s, coeliac disease etc</td>
</tr>
<tr>
<td>Drug Interactions: eg anticonvulsants, rifampicin, cholestyramine, glucocorticoids, HAART</td>
<td>Housebound or institutionalised people</td>
<td>Cholestatic liver disease</td>
</tr>
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*Vitamin D synthesis is highly dependent on the concentration of melanin in the skin. Darker skinned people will experience slower vitamin D synthesis than lighter skinned people.
Treating vitamin D deficiencies

The treatment guide below is for correction of vitamin D in patients who are deemed to be either insufficient or deficient based on serum levels and lifestyle. Treatment doses for other vitamin D related conditions such as rickets, hypocalcaemia due to hypoparathyroidism, chronic liver disease malabsorption etc. may require different vitamin D precursors and in varying doses. Treatment for these conditions should only be initiated following guidance from the appropriate specialist.

**Oral correction with vitamin D3 (colecalciferol) should be utilised.** Correction may take the form of a loading regime followed by maintenance, or maintenance regimes alone. The choice of which to use depends partly on serum 23 (OH)D levels and concurrent medication, but largely on presence of deficiency symptoms.

**Loading Regime:** Patients may require loading if their serum levels are particularly low (deficient), and are showing signs of vitamin D deficiency (eg complaining of aches/tenderness which could point to osteomalacia) or are about to start treatment with a potent antiresorptive such as zolendronate or denosumab.

**Maintenance Regime:** Where correction is less urgent and no symptoms are present, no loading dose is needed and maintenance treatment can be initiated immediately.

<table>
<thead>
<tr>
<th>Regime Type</th>
<th>Dose (colecalciferol)</th>
<th>Duration of treatment</th>
<th>Preparation available via WSHT pharmacy services</th>
<th>Cost indication per course (Drug Tariff prices – Jan ’18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loading (Preferred)</td>
<td>40,000 units ONCE WEEKLY</td>
<td>7 weeks</td>
<td>Fultium-D3 20,000 IU capsules</td>
<td>£13.53</td>
</tr>
<tr>
<td>Loading (Alternative)</td>
<td>3,200 units DAILY</td>
<td>12 weeks</td>
<td>Fultium-D3 3,200 IU capsules</td>
<td>£37.29</td>
</tr>
<tr>
<td>Maintenance</td>
<td>800 units DAILY</td>
<td>Ongoing (switch to OTC supply where appropriate)**</td>
<td>Fultium-D3 800 IU capsules</td>
<td>£3.60 (per 30 days)</td>
</tr>
</tbody>
</table>

*Doses should be taken with food where possible to increase absorption.*

Fultium-D3 capsules® have been reformulated and no longer contain arachis oil. The new formulation is safe for peanut allergy sufferers but care should be taken to confirm which stock is on the ward as some of the older arachis oil containing product may still remain in circulation.

The colecalciferol in Fultium-D3® is derived from live sheep’s wool fat and has been certified as suitable for vegetarians by the manufacturers although may not be acceptable to strict vegans. Ergocalciferol (vitamin D2) is plant derived but should not be offered routinely due to cost and difficulties in obtaining supplies.

**Maintenance doses can vary between 800 IU to 2,000 IU daily. Vitamin D3 supplements within this range are widely available in pharmacies, supermarkets and health food shops and patients should be encouraged to purchase these OTC for their ongoing maintenance where appropriate.**

**Monitoring**

Treatment may unmask previously undiagnosed primary hyperparathyroidism. It is recommended that adjusted serum calcium levels be checked within 1 month of completing the loading regime or 1 month after starting maintenance (if no loading was required).

Consider checking serum calcium levels more regularly (for example every 1-2 weeks in the first months of treatment) in people receiving calcium supplements in addition to high-dose vitamin D treatment and whenever nausea or vomiting occur.
Cautions and contraindications to treatment

Cautions:
- Pregnancy & Breastfeeding - seek further advice from pharmacy team (400 IU/day recommended as maintenance, loading not recommended)
- Renal Impairment - Increased risk of soft tissue calcification (Monitor calcium and phosphate levels). In severe renal impairment, colecalciferol is not metabolized normally and alternative forms of vitamin D should be used (seek advice)
- Patients on cardiac glycosides - see drug interactions below
- Sarcoidosis - increased metabolism of vitamin D to its active form. Monitor calcium content in serum and urine.
- Patients on treatment to prevent hypercalcaemia
- Concomitant treatment with other vitamin D containing products - Take into account when calculating dosing requirements

Contraindications:
- Hypersensitivity to vitamin D or product excipients
- Hypervitaminosis D
- Nephrolithiasis
- Conditions resulting in hypercalcaemia or hypercalciuria
- Severe renal impairment

Specific Drug Interactions and Vitamin D supplementation:
- Phenytoin & barbiturates - May reduce effect of vitamin D
- Glucocorticoids - May reduce effect of vitamin D
- Cardiac glycosides - Effect of digitalis and other cardiac glycosides may be accentuated with the oral administration of calcium and D3 combined supplements. ECG and calcium monitoring may be required.
- Ion-exchange resins - cholestyramine may reduce gastrointestinal absorption of VitaminD
- Imidazole antifungals - Interfere with Vitamin D activity
- Dactinomycin - Interferes with vitamin D activity
- Carbamazepine - Predicted to decrease the effects of colecalciferol
- Thiazides and related diuretics - Increased risk of hypercalcaemia

Please refer to the specific manufacturer's SPC for further information on each product.

Discharge planning and prescribing

If treatment has been initiated during the patient's stay, please ensure a supply is made on discharge (quantity as for other discharge medicines) and include in the summary for GP:
- Remaining treatment time for loading dose (if applicable) and maintenance dose to be considered thereafter (usually 800 IU/day)
- Indication of when next adjusted serum calcium should be performed

For patients who do not meet the threshold for treatment, but remain at risk (due to lifestyle factors or immobility for example), the BNF currently recommends a preventive dose of 400 IU/daily. This should not routinely be started in secondary care but patients may be encouraged to purchase a supplement OTC or consult their GP for review and prescribed if appropriate.
Reference Sources Used

- National Osteoporosis Society - Vitamin D and Bone Health: A practical Clinical Guideline for Patient Management. Apr 2013
- Scientific Advisory Committee on Nutrition - Vitamin D and Health. 2016
- IOM report Brief - Dietary reference intakes for calcium and vitamin D. Nov 2010

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