

## County Durham and Darlington

June 2014

### Guidance for the treatment of Vitamin D insufficiency and deficiency

Vitamin D is essential for musculoskeletal health. Vitamin D insufficiency may cause secondary hyperparathyroidism, bone loss, muscle weakness, falls and fragility fractures in the elderly. Vitamin D deficiency can lead to osteomalacia in adults and rickets in children. It has also been suggested that inadequate vitamin D has involvement in disorders of the immune system, cancer and metabolic disorders

#### Sources of vitamin D:

1. Sunlight – this is the major natural source of vitamin D. White populations require 20-30 mins of midday summer sunlight exposure to the face and forearms 2-3 times a week. Individuals with pigmented skin require 2-10 times the exposure of someone with fair skin.

The UK does not have enough suitable UVB during October to March to generate vitamin D.

2. Diet – There are few foods that are rich in vitamin D, sources include oily fish (200-400 IU/100g) and some breakfast cereals (120-320 IU/100g). Dietary intake of vitamin D is thought to be low (80-160 IU/day) on average.

#### Who to test:

1. Patients with bone diseases i.e. osteomalacia or osteoporosis or Paget's disease.

It is recommended that vitamin D deficiency is corrected prior to commencing osteoporosis treatment with a potent antiresorptive agent (zoledronate or denosumab), to avoid the development of hypocalcaemia. Routine 25OHD testing may not be required in an osteoporosis patient where the decision has already been made to co-prescribe vitamin D with an antiresorptive agent.

2. Patients with musculoskeletal symptoms – if patients are suspected of having symptoms caused by osteomalacia or have chronic widespread pain, measurement of 25OHD are reasonable.

**N.B. Routine 25OHD monitoring is unnecessary** but may be appropriate in patients with symptomatic vitamin D deficiency or malabsorption, or where poor compliance with medication is suspected.

#### Assessment of vitamin D status

Vitamin D status is currently best assessed by measurement of serum 25OHD (25-Hydroxy vitamin D) The National Osteoporosis Society has proposed that the following vitamin D thresholds are adopted:

Serum 25OHD: <30 nmol/L= deficient  
30-50nmol/L= adequate in some  
>50nmol/L = sufficient for almost the whole population

The main methods for estimating 25OHD are immunoassay or HPLC attached to fluorescence or mass spectrometry (MS) detection (tandem MS).



If re-testing of Vitamin D levels is needed (e.g. if compliance issues or if no improvement in symptoms) the minimum testing interval is 3-6 monthly. Please also note that some laboratories have requesting strategies in place to ensure appropriate requesting therefore clinical details must have relevant information to the vitamin D request.

### Who and How to treat:

Key aims for treating vitamin D deficiency in patients with bone disease:

The NOS recommends vitamin D<sub>3</sub> as the vitamin D preparation of choice for the treatment of vitamin D deficiency, an oral preparation should be used where possible

Treatment should be based on fixed-loading doses and maintenance therapy

Adequate doses of Vitamin D should be used to ensure correction of deficiency (ideally >50nmol/L)

The clinical consequences of Vitamin D deficiency should be reversed in a timely manner

Toxicity should be avoided

Where rapid correction of vitamin D deficiency is required e.g. in patients with symptomatic disease or those commencing therapy with a potent antiresorptive agent (zoledronate or denosumab) use fixed loading doses followed by a regular maintenance therapy

In less urgent correction of vitamin D deficiency and when co-prescribing vitamin D supplements with an oral antiresorptive agent, maintenance therapy may be started without the need for loading doses

Treatment with vitamin D in those patients with suspected malabsorption disorder, renal or hepatic disease or any condition where there may be an increased risk of toxicity should be discussed with secondary care

Promote the relevance of adequate dietary calcium intake and encourage the use by patients and practitioners of calcium calculators e.g. Calcium Calculator

Osteoporosis patients who are unable to reliably or regularly consume 700mg of calcium daily should receive supplementation with calcium-only or combined calcium and vitamin D supplements.

Combined calcium and vitamin D preparations should not be used as sources of vitamin D for loading doses due to the resulting high dosing of calcium

Supplements should be taken with food to aid absorption



Vitamin D status	Treatment required	Suggested treatment regime	Monitoring recommendations
Serum 25OHD <30nmol/L (deficiency of vitamin D)	Treatment recommended	<p>A loading regime to provide a total of approximately 300,000 IU vitamin D given as a weekly or daily dose over 6 to 12 weeks.</p> <p>Suggested regimes: 20,000IU capsules Pro D3®, (<b>unlicensed product</b>) Cost £9.99 <i>Or</i> Hux D3, (<b>unlicensed product</b>) Cost £2.44 two capsules weekly for seven weeks (280,000 IU) <b>Or</b> 3200IU Fultium D3® capsule, one daily for 12 weeks (<b>licensed</b>) Cost £37.30 Followed by a maintenance regime</p>	<p>Routine monitoring of serum 25OHD is unnecessary but may be appropriate in patients with symptomatic vitamin D deficiency or malabsorption and where poor compliance with medication is suspected.</p> <p>Adjusted serum calcium should be checked 1 month after completing the loading regimen or after starting vitamin D supplementation in case primary hyperparathyroidism has been unmasked.</p> <p>During long-term treatment serum calcium levels should be followed and renal function should be monitored via serum creatinine. Monitoring is particularly important in the elderly who are on concomitant cardiac glycosides or diuretics and in those with a high tendency to calculus formation. Decrease or discontinue treatment when hypercalciuria occurs.</p>
Serum 25OHD 30-50 nmol/L (insufficiency of vitamin D)	<p>Treatment advised when:</p> <ul style="list-style-type: none"> <li>-Fragility fracture, documented osteoporosis or high fracture risk</li> <li>-treatment with antiresorptive agent for bone disease</li> <li>-symptoms suggestive of vit D deficiency</li> <li>-increased risk of developing vit D deficiency e.g. reduced exposure to sun, religious/cultural dress code, dark skin</li> </ul>	<p>Where correction of Vitamin D deficiency is less urgent maintenance therapy may be started without the use of loading doses; a daily maintenance dose of between 800-2000 IU/day (given daily or intermittently at higher doses) is advised. Fultium D3 or Desunin, 1 or 2 daily</p>	



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	<p>-raised PTH Medication with antiepileptic drugs or oral glucocorticoids Conditions associated with malabsorption</p>		<p>Colecalciferol should be used with caution in those with impaired renal function (calcium and phosphate levels should be monitored). Colecalciferol should not be used in those with severe renal insufficiency; alternative vitamin D forms should be used.</p>
<p>Serum 250HD &gt;50 nmol/L</p>	<p>No</p>	<p>Provide reassurance and give advice on maintaining adequate vitamin D levels through safe sunlight exposure and diet</p>	
<p>Adult groups at risk of vitamin D deficiency:</p> <ul style="list-style-type: none"><li>• All pregnant and breastfeeding women, especially teenagers and young women</li><li>• Older people 65 years+</li><li>• People with low or no sun exposure e.g. house-bound or who cover their skin for cultural/religious reasons</li><li>• Those with darker skin e.g. African, South Asian origin as their bodies are unable to make as much vitamin D</li></ul>		<p>Take a daily supplement containing 10µg (400 IU) of vitamin D. Vitamin D supplements can be purchased from Community pharmacies</p>	
<p>All infants/toddlers from 6 months-5 years (unless drinking 500mL or more of infant formula)</p>		<p>Take a daily supplement containing 280 IU/day</p>	
<p>Breastfed babies 1 month – 6 months if mother is vitamin D insufficient/deficient</p>		<p>Take a daily supplement containing 340 IU/day</p>	



There are currently two licensed preparations of vitamin D<sub>3</sub> (colecalciferol 20 micrograms, 800 IU) available, both of which are in the Co. Durham & Darlington APC formulary

**Desunin®** (tablets) - an 800 units tablet also licensed for the prevention and treatment of vitamin D deficiency. It does not contain any gelatine, peanut oil or soybean oil. The tablets contain colecalciferol that has been extracted from the wool of live, healthy sheep – this may be acceptable to vegetarians.

**Fultium D3®** - is a product licensed for the prevention and treatment of vitamin D deficiency. It is available in 800 or 3200 unit strength. Excipients include gelatine, glycerol and peanut oil. The gelatine is halal and kosher compliant.

**ProD3** products all contain colecalciferol (Vitamin D3) which has been extracted from sheep's wool. The liquid is free of alcohol and polyethylene glycol. The capsules do not contain gelatine. The manufacturer states that the products are halal approved for Muslim patients, and are suitable for vegetarians. The ProD3 range can be ordered by pharmacies from the usual distributors (AAH, Phoenix,) or can be supplied directly to the pharmacy.

**HuxD3** is a colecalciferol product. The capsule shell is made of modified corn starch, glycerol (from a vegetarian source) and carragean. The manufacturer states that the capsule contents are certified halal and kosher. The capsule can be squeezed open or chewed for those that cannot swallow. The product is formulated in sunflower oil. It is available from all mainline wholesalers.

In view of the lack of evidence to classify monitoring requirements, clinicians should endeavour to:

1. Detect those who remain deficient after loading
2. Detect those who become deficient during maintenance
3. Detect those patients in whom vitamin D therapy uncovers sub-clinical primary hyperparathyroidism N.B. vitamin D treatment can unmask previously undiagnosed primary hyperparathyroidism, individuals thought to be at risk should be monitored by measurement of adjusted serum calcium levels.

### **Vitamin D toxicity**

When the vitamin D dose is very high (usually as a result of inappropriate high-dose treatment or accidental overdosing) vitamin D toxicity may present as chronic hypocalcaemia. There is some evidence that vitamin D below 10,000IU/day is not usually associated with toxicity, but doses equal to or above 50,000 IU/day for several weeks or months are frequently associated with toxicity. The European Food

Safety Authority has recently concluded that an upper limit of 4000IU (100µg) a day is safe for those over 11 years of age.

Specialist advice should be sought before vitamin D therapy is commenced in patients with tuberculosis and active sarcoidosis, and care should be taken in those with active nephrolithiasis.

Vitamin D deficiency			
Pro D3 Capsules 20,000iu	Two capsules weekly for 7 weeks (14 caps)	£9.99	Unlicensed Halal and suitable for vegetarians
Hux D3 Capsules 20,000iu	As above	£2.44	Unlicensed Halal and kosher, suitable for vegetarians
Desunin tablets 800iu	Four or five tablets daily for 10 weeks (350 tablets)	£42.00	Licensed May be suitable for vegetarians
Fultium D3 Capsules 32000iu	One capsule daily for 12 weeks	£37.30	Licensed Halal and kosher

#### References

(Adapted from a piece of work originally completed by the RDTG)

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