Vitamin D deficiency in adults

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**RED FLAGS?**

**Not present: give vitamin D treatment dose**

**Consider referral to metabolic bone clinic**

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**Vitamin D deficient:**

- 25(OH) vitamin D <25nmol/L

**Vitamin D insufficient:**

- 25(OH) vitamin D 25-50nmol/L

**Vitamin D sufficient:**

- 25(OH) vitamin D >50nmol/L

**RED FLAGS?**

- Present: consider referral to specialist

- Not present: give vitamin D treatment dose

- Consider referral to metabolic bone clinic

- Give lifestyle advice

- Management of excessive vitamin D replacement
1 Background information

Quick info:
The most common cause of vitamin D deficiency in the UK is lack of sunshine exposure, either as a result of dark skin, covering, or inability to go outside.

Groups at risk of vitamin D deficiency:

• people who are not exposed to much sun, for example those who cover their skin for cultural reasons, who are housebound or confined indoors for long periods
• people from ethnic minorities who have darker skin, because their bodies are less able to produce vitamin D. Clinical deficiency has been most reported among children of African-Caribbean and South Asian origin
• all pregnant and breastfeeding women, especially teenagers and young women are particularly at risk of vitamin D deficiency.
• children under 5 years of age
• all people aged 65 years and over
• at-risk people also on long term treatment with enzyme-inducing anticonvulsants (phenytoin, phenobarbital, primidone, sodium valproate or carbamazepine) should be considered for Vitamin D supplementation, especially if dietary intake of calcium is also low

Other risk factors for Vit D deficiency include obesity and malabsorption (such as Crohn’s disease). If suspected, refer for specialist advice.

A number of conditions have been associated with Vitamin D deficiency but the link has not been proven to be causative: examples include Breast, Prostate and Colon cancer, Diabetes, Rheumatoid Arthritis and Multiple Sclerosis. Thus there is currently no good evidence base with which to justify prevention or treatment of these conditions with vitamin D supplementation.

Vitamin D treatment doses are contraindicated in patients with hypercalcaemia or metastatic calcification, or where there may be significant interactions with other medications, seek specialist advice.

In the treatment of osteoporosis, co-prescription of calcium and vitamin D is recommended when bisphosphonates are prescribed. All patients should be given appropriate dietary and lifestyle advice.

References:
Diagnosis and management of vitamin D deficiency BMJ 2010; 340:b5664
IOM Report Brief November 2010: Dietary reference intakes for calcium and vitamin D
Scientific Advisory Committee on Nutrition - Update on vitamin D Feb 2007
Drugs and Therapeutic Bulletin 2006;44:25-29 Primary vitamin d deficiency in adults.
NICE Guidelines on Maternal and child nutrition March 2008
Review article. NEJM 2007;357:266-81 M.F.Horlick.
JCEM March 2011, 96(3):E436-E446 Relationship between Vitamin D, Parathyroid hormone and bone health Sai. Walters, Fang & Gallagher
Clinical Effectiveness Group Barts & the London Vitamin D guidance January 2011.
BNF

2 Patient information

Quick info:
http://www.bda.uk.com/foodfacts/VitaminD.pdf


http://www.patient.co.uk/health/Vitamin-D-Deficiency.htm

3 Key messages for this pathway
Vitamin D deficiency in adults

Quick info:
This pathway has been locally developed for use in South West Hampshire.

Key messages for this pathway:
- screening for vitamin D deficiency in asymptomatic individuals is NOT recommended
- symptomatic Vitamin D deficiency is extremely rare in Caucasians in UK
- low level supplementation with OTC vitamin D or the Healthy Start vitamins (at 400 iu vitamin D daily) will not correct profound deficiency but would safely reduce the risk of symptomatic deficiency in high risk populations (e.g. dark skinned individuals)
- 25(OH)Vitamin D assays should be performed only where there are clinical features suggestive of Vitamin D deficiency (most likely in ethnic minorities), or under specialist guidance
- NB: there is no national reference laboratory for 25(OH) Vitamin D assay, and reference ranges and methods of measurement vary across the UK. This guideline draws on available national and local guidance on testing, treating and monitoring vitamin D disorders and represents the local consensus view in South West Hampshire
- at present there is insufficient evidence to make definitive evidence based statements in some areas of practice. Currently there are a number of trials in progress to clarify the best management of vitamin D deficiency states, and the safety of higher dosing regimes for routine supplementation

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4 Management of vitamin D status

Quick info:
The following interventions are recommended:

- vitamin D severe deficiency:
  - serum 25-OHD <25 nmol/L
  - give treatment dose
- vitamin D insufficiency:
  - serum 25-OHD 25 - 50 nmol/L
  - give supplement dose
- vitamin D sufficiency:
  - serum 25-OHD >50 nmol/L
  - give lifestyle advice
- vitamin D excess:
  - serum 25-OHD >250 nmol/L
  - stop treatment

Simple vitamin D deficiency can be prevented by taking an oral supplement of:

- 10 micrograms (400 units) of ergocalciferol (calciferol, vitamin D2) or colecalciferol (vitamin D3) daily

Standard vitamin D capsules contain gelatine. If an alternative is needed then consider liquid formulations such as

- 10,000iu/ml solution (Zymad brand) x 10ml
- 20,000iu/ml drops (Sterogyl brand) x 20ml
Vitamin D deficiency can occur in people whose exposure to sunlight is limited and in those whose diet is deficient in vitamin D. In these individuals, ergocalciferol or colecalciferol in a dose of 20 micrograms (800 units) daily by mouth may be given to treat vitamin D deficiency; higher doses may be necessary for severe deficiency. Since there is no plain tablet of this strength available, calcium and ergocalciferol tablets can be given (although the calcium is unnecessary). Preparations containing calcium with colecalciferol are available for the management of combined calcium and vitamin D deficiency, or for those at high risk of deficiency (see also Osteoporosis and Calcium Supplements). Vitamin D deficiency caused by intestinal malabsorption or chronic liver disease usually requires vitamin D in pharmacological doses, such as ergocalciferol tablets up to 1 mg (40 000 units) daily; the hypocalcaemia of hypoparathyroidism often requires doses of up to 2.5 mg (100 000 units) daily in order to achieve normocalcaemia. Vitamin D requires hydroxylation by the kidney to its active form, therefore the hydroxylated derivatives alfacalcidol or calcitriol should be prescribed if patients with severe renal impairment require vitamin D therapy. Symptoms of overdosage or toxicity are due to hypercalcaemia.

- anorexia, nausea, vomiting, diarrhoea, constipation, lassitude, vertigo, polyuria, thirst, sweating, headache and weight loss

NB: Patient who are symptomatic and hypercalcaemic should have their management discussed with specialist clinicians without delay.

Please also note local advice: Alfacalcidol or calcitriol should be prescribed under specialist supervision and are NOT recommended for routine supplementation or repletion treatment for vitamin D deficiency in a primary care setting.

5 Healthy Start and other options for vitamin supplements

Quick info:
Information on the national Healthy Start Vitamins scheme can be found at [http://www.healthystart.nhs.uk](http://www.healthystart.nhs.uk)
Healthy Start Vitamins for women (containing ascorbic acid, vitamin D and folic acid) are available free of charge to eligible women during pregnancy and until their baby is one year old, or alternatively may be available direct to the public - further information for health care professionals can also be accessed at [http://tinyurl.com/3yckebe](http://tinyurl.com/3yckebe)

Healthy Start Children's Vitamin Drops (containing vitamin A, vitamin D and ascorbic acid) are also available free of charge to children under 4 in eligible families.

Healthy Start locations in Hampshire PCT:
- families should be directed to their Health Visiting team

Healthy Start locations in Southampton City PCT:
- Bassett Green Clinic at Sure Start Swaythling
- Bitterne Park Family Point
- Family Point at Bitterne United Reform Church Hall
- Family Point at Cutbush Children's Centre
- Lordshill Family Point
- Nicholstown Surgery
- Pickles Coppice
- Shirley Family Point at Victor Street Salvation Army Hall
- Shirley Health Centre
- Stay & Play Eastpoint
- St Mary's Surgery
- Sure Start Byron Road
- Thornhill Clinic Family Point
- Woolston Clinic
- Woolston Family Point

Healthy Start Vitamins are not available on NHS prescription via the usual supply routes.

Vitamin D preparations may also be purchased over the counter (OTC) from pharmacies and health food shops, with 200-400iu daily recommended in pregnancy.
Vitamin D is also contained in many multivitamin preparations and some OTC pregnancy supplements.

6 General advice for asymptomatic but concerned patients

Quick info:
Dietary intake delivers around 2-4mcg (80-160iu) of vitamin D per day:
- oily fish (canned or fresh) is the best source of vitamin D
- small quantities of vitamin D are found naturally in:
  - egg yolk
  - liver
  - meat
  - dairy products
- vitamin D fortification is mandatory in margarine and formula milk
- many breakfast cereals are fortified with vitamin D

90% of daily vitamin D requirement is obtained by the action of UVB sunlight on the skin. For most adults who do not fall within the risk groups, 2-3 exposures of sunlight per week during April to September are enough to achieve healthy vitamin D levels. Length of exposure is dependent on skin type and a common sense approach is needed. Typically up to 20-30 minutes per exposure is sufficient, avoiding high factor sunscreen for short exposures. This is not advice to get a suntan and sunburn should be avoided at all costs.

Vitamin D supplementation is in doses of 400-1000 iu daily, but no more than 400iu daily should be used in pregnancy. Additionally, most OTC multi-vitamin preparations contain adequate doses of 200-400iu daily and supplementation doses are not usually required in patients who are not at risk for other reasons.

Supplements can be purchased over the counter from pharmacies or health food shops. Relatively inexpensive examples include;
- 'Holland and Barrett D3' colecalciferol 400iu capsules or tablets
- 'Holland and Barrett D3 Sunvite' 1000iu caplet
- 'Boots D3', 'Natures Remedy' or 'Biolife' 400iu-1000iu tablets

7 Clinical presentation

Quick info:
There is no level of 25(OH)-vitamin D below which symptoms are always present, and these clinical presentations are very rare in white individuals in UK.

The potential musculoskeletal manifestations of vitamin D deficiency are:
- proximal muscle weakness
- bone pain
- bony deformity
- stress fractures
- soft tissue pain (should only be considered in high risk groups (see Background information box) with chronic soft tissue pain)

Investigations may show:
- low/low-normal serum calcium
- normal/raised alkaline phosphatase
- normal/raised PTH

The histological appearance in the bone is "osteomalacia", where the protein matrix of the bone is normal, but is insufficiently mineralised.

These are non-specific symptoms and are also a feature of other conditions such as polymyalgia rheumatica, inflammatory arthritis, hypothyroidism and myeloma. Consider performing specific investigations for these conditions before considering Vitamin D deficiency.

NB: There is no indication to check vitamin D status, unless the patient presents with signs or symptoms of vitamin in D deficiency.
8 Pregnant women

Quick info:
In the mother Vitamin D deficiency leads to an increased risk of calcium malabsorption, bone density loss, poor weight gain, myopathy, and higher parathyroid hormone levels.
In the infant there is a risk of neonatal hypocalcemia, hypocalcemic seizures, infantile heart failure, enamel defects, large fontanelle, reduced bone mineral density or congenital rickets (or rickets of infancy if breastfed).
For these reasons Vitamin D 400iu daily is recommended for ALL pregnant or breastfeeding women, until the child is 1 year of age.
Those at higher risk of vitamin d deficiency in pregnancy include:
• women who are not exposed to much sun, for example those who cover their skin for cultural reasons, who are housebound or confined indoors for long periods
• women from ethnic minorities who have darker skin, because their bodies are less able to produce vitamin D. Clinical deficiency has been most reported among children of African-Caribbean and South Asian origin
• multiple pregnancies within a short time frame
• women on certain anticonvulsant medication
Any pregnancy vitamin supplement containing vitamin D purchased OTC should be sufficient with a dose of up to 400iu daily. Some women may be eligible for the healthy start vitamins. [http://www.healthystart.nhs.uk](http://www.healthystart.nhs.uk)
Higher doses may be needed but only for mothers who present with symptoms as described above.
Supplements of vitamin D containing vitamin A should not be prescribed in pregnancy as excessive vitamin A doses are associated with foetal CNS malformations.
Currently there is no evidence available regarding the use of routine higher doses of vitamin D in pregnancy, and there may be a link with the use of higher doses and atopy later in children. We do not therefore recommend routine higher doses at present.
Consider referral to a specialist if in doubt.

9 Initial investigations

Quick info:
If clinically symptomatic suspected vitamin D deficiency, carry out initial blood tests to measure:
• 25(OH) vitamin D NB: do not request 1,25 (OH) vitamin D assay, this is a special assay which should only be requested by secondary care in specific circumstances
• bone profile
• renal profile
Consider checking PTH to rule out primary hyperparathyroidism if the calcium level is high, or in the upper quartile of the normal range at any time, pre or post treatment.
If the calcium level is low or low normal, repeat this and check PTH before initiation of treatment to exclude hypoparathyroidism (PTH will be high if vitamin D deficiency is present alone).
NB: PTH levels in blood remain stable for 6-8 hours before degrading, and delay in getting blood to the lab may result in tests not being processed within this window. Consider transit and processing time when advising the patient of the most appropriate place and time for phlebotomy to be performed for PTH assay.

13 RED FLAGS?

Quick info:
Consider specialist referral at diagnosis if any of the following are present:
• renal impairment, eGFR <30mls/min
• renal stones
• hypercalcaemia
• hyperparathyroidism
• sarcoidosis
• active tuberculosis
• malabsorption, e.g. coeliac disease
• chronic liver disease
These conditions are those where calcium level may be adversely affected by treatment or the absorption or conversion of 25(OH) vitamin D to 1,25(OH) Vitamin D is affected and therefore specialist involvement may be required.

14 Give vitamin D supplement

Quick info:
Recommend vitamin D supplementation 400-1000 iu daily.
Supplements can be purchased over the counter from pharmacies or health food shops. Relatively inexpensive examples include;
• ‘Holland and Barrett D3’ colecalciferol 400iu capsules or tablets
• ‘Holland and Barrett D3 Sunvite’ 1000iu caplet
• ‘Boots D3’, ‘Natures Remedy’ or ‘Biolife’ 400iu-1000iu tablets
Alternatively higher doses can be prescribed (usually by exception) as
• Adcal D3 x 2 tablets daily (especially if calcium is also low)
• Colecalciferol 1000iu plain tablet (Prescribe as Vigantoletten brand, x 90 tablets, available from IDIS as a special order unlicensed product)
Standard vitamin D capsules contain gelatine. If an alternative is needed then consider liquid formulations such as
• 10,000iu/ml solution (Zymad brand) x 10ml
• 20,000iu/ml drops (Sterogyl brand) x 20ml
If symptoms are unlikely to be due to vitamin D deficiency, consider other causes such as polymyalgia rheumatica, inflammatory arthritis, hypothyroidism and myeloma.

16 Not present: give vitamin D treatment dose

Quick info:
If the patient is not pregnant, treat with high dose colecalciferol (vitamin D3) in one of the following dosing schedules :
• 60,000 iu given weekly for 8-12 weeks
or
• 60,000 iu given monthly for 3 months with Adcal-D3, two tablets daily. (This option is worth consideration if calcium levels are also low and/or dietary calcium intake is likely to be low).
These doses are most cost-effectively delivered by prescribing 3x 20,000iu capsules of a colecalciferol product called Dekristol (20,000 iu capsules cost ~ £20 for a pack of 50).
Standard vitamin D capsules contain gelatine. If an alternative is needed then consider liquid formulations such as
• 10,000iu/ml solution (Zymad brand) x 10ml
• 20,000iu/ml drops (Sterogyl brand) x 20ml
If patient is pregnant treat with :
• Healthy Start vitamins
or
• vitamin D supplements (10mcg or 400iu)
NB: do not give higher doses of vitamin D in pregnancy.

17 Give lifestyle advice

Quick info:
Lifestyle advice - appropriate sun exposure and diet
Dietary intake delivers around 2-4mcg (80-160iu) of vitamin D per day:
• oily fish (canned or fresh) is the best source of vitamin D
• small quantities of vitamin D are found naturally in:
  • egg yolk
Vitamin D deficiency in adults

- liver
- meat
- dairy products
  - vitamin D fortification is mandatory in margarine and formula milk
  - many breakfast cereals are fortified with vitamin D

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18 Management of excessive vitamin D replacement

Quick info:
Vitamin D excess if serum 25-OHD >250 nmol/L:
  - if asymptomatic and serum calcium <3.5mmol/L, stop the vitamin D supplementation - no need for referral. If serum calcium raised, re-check with vitamin D estimation after 1 month
  - if symptomatic hypercalcaemia or serum calcium >3.5mmol/L this needs acute medical advice/ admission

19 Consider referral to metabolic bone clinic

Quick info:
Check compliance and consider referral if symptoms of vitamin D deficiency are still present following a 3 month treatment course, the 25 (OH) vitamin D level has not significantly improved, or symptoms are still present despite correcting the Vitamin D deficiency. If not already ruled out then consider alternate diagnoses e.g polymyalgia rheumatica, inflammatory arthritis, hypothyroidism and myeloma:
  - muscle weakness
  - bone pain
  - chronic soft tissue pain in high risk groups
  - bony deformity
  - fractures
If vitamin D level is partly corrected at 3 months, consider repeating with a further 3 months of treatment.

20 Follow up investigations

Quick info:
Repeat blood tests after 8-12 weeks of treatment dose to measure:
  - 25(OH) vitamin D
  - bone profile
  - PTH, particularly if the calcium level is high, or at the upper end of normal
Following successful treatment, patients will not require further routine 25(OH) vitamin D testing, unless symptoms recur. If no improvement following adequate treatment for 3 months, check compliance.

21 Give lifestyle advice

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Lifestyle advice - appropriate sun exposure and diet
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22 Maintenance vitamin D therapy

Quick info:
Following treatment, the patient should be maintained on a daily dose of vitamin D of 800-1000iu with either an over the counter vitamin supplement (see below), or Adcal D3 two tablets daily (prescribable) if the dietary calcium intake is also likely to be low, and there are no contraindications to calcium supplementation.

Supplements can be purchased over the counter from pharmacies or health food shops. Relatively inexpensive examples include:
  • 'Holland and Barrett D3' colecalciferol 400iu capsules or tablets
  • 'Holland and Barrett D3 Sunvite' 1000iu caplet
  • 'Boots D3', 'Natures Remedy' or 'Biolife' 400iu-1000iu tablets

Alternatively higher doses of vitamin D alone may be prescribed in an unlicensed way (by exception) as
  • Colecalciferol 1000iu plain tablet (Prescribe as Vigantoletten brand, x 90 tablets, available from IDIS as a special order unlicensed product)

23 Management of excessive vitamin D replacement

Quick info:
Vitamin D excess if serum 25-OHD >250 nmol/L:
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