

VITAMIN D

ADULTS AND POST-PUBERTAL CHILDREN

Frequently Asked Questions and Answer Sheet For GPs and other Health Professionals

1 WHO IS AT RISK OF VITAMIN D DEFICIENCY

There are no population based estimates of incidence of deficiency in the UK and it is thought that many cases do not reach clinical attention. Detailed epidemiology is scarce, but it is thought upwards of 25% of the population is vitamin D insufficient, and therefore at risk of the clinical consequences of vitamin D deficiency.

Diagnoses of rickets and osteomalacia are thought to represent a small proportion of the population that is deficient or insufficient.

There is poor data on the implementation of the current advice on the use of dietary supplements containing vitamin D in at-risk groups. Local intelligence and information from the 2005 Infant Feeding Survey suggests that the majority of women do not take vitamin D supplements during pregnancy.

The following groups are most at risk of vitamin D deficiency:

- Insufficient exposure to the sun
 - Housebound or spend little time outdoors
 - Cover skin for cultural reasons
 - Heavy use of high SPF-containing sunscreen or moisturisers
- Pregnant or breastfeeding women
- Pregnant and breastfeeding women who are obese (BMI>30)
- Age over 65 years
- People with darker skin
- Diet that restricts major sources of vitamin D
- Family history of deficiency/osteomalacia
- Malabsorption syndromes
- Low bone density
- Taking anticonvulsants, cholestyramine, rifampicin, glucocorticoids or anti-retrovirals

2 WHAT ARE THE DEPARTMENT OF HEALTH RECOMMENDATIONS FOR VITAMIN D?

All UK Health Departments recommend:

- All pregnant and breastfeeding women should take a daily supplement containing 10 micrograms of vitamin D, to ensure the mother's requirements for vitamin D are met and to build adequate fetal stores for early infancy.
- All infants and young children aged 6 months to 5 years should take a daily supplement containing vitamin D in the form of vitamin drops, to help them meet the requirement set for this age group of 7-8.5 micrograms (280-340 IU) of vitamin D per day. However, those infants who are fed infant formula will not need vitamin drops until they are receiving less

than 500ml of infant formula a day, as these products are fortified with vitamin D. Breastfed infants may need to receive drops containing vitamin D from one month of age if their mother has not taken vitamin D supplements throughout pregnancy.

- People aged 65 years and over and people who are not exposed to much sun should also take a daily supplement containing 10 micrograms (400 IU) of vitamin D.

The Scottish CMO has published information leaflets for the public and health professionals. The web reference can be found below.

<http://www.scotland.gov.uk/Topics/Health/health/Health/EatingHealth/vitaminD>

3 WHAT ARE THE SYMPTOMS OF VITAMIN D INSUFFICIENCY AND DEFICIENCY?

Vitamin D insufficiency can be asymptomatic or may present with onset of non-specific musculoskeletal aches, pains, and general tiredness. Even vitamin D deficient patients may be asymptomatic; or may have muscle weakness, localised or generalised bone pain, tenderness and even fractures.

Prolonged deficiency leads to osteomalacia. It is also associated with osteoporosis, hip fractures and falls in older people.

There is some evidence that low vitamin D levels are associated with an increased risk of certain cancers and other chronic diseases including multiple sclerosis, heart disease and hypertension, diabetes, and autoimmune disorders.

4 DECIDING WHO SHOULD BE TESTED FOR VITAMIN D DEFICIENCY

Routine testing of vitamin D levels of asymptomatic patients in primary care is *NOT* recommended.

Assessing the patient:

- If the patient has no risk factors for vitamin D deficiency, no action is required.
- If the patient has one or more risk factors and NO symptoms of vitamin D deficiency, then:
 - give advice about safe and unprotected exposure to the sunshine.
 - give advice about a healthy balanced diet, including adequate calcium intake.
 - recommend OTC vitamin D supplementation. Colecalciferol is the treatment of choice as it is the active form of vitamin D. OTC products are readily available at pharmacies, many supermarkets, and over the internet. As a rough guide, a year's supply of OTC supplements usually costs less than £20. For most adults, a daily dose of between 10 and 25 micrograms (400 - 1,000 units) is sufficient but a higher dose may be required for people with darker skin or who do not get much sunshine. For these patients doses of 2000-4000IU (50-100 micrograms/day) may be required. Please check on compliance – the supplementation is meant to be lifelong unless lifestyle/risk factors change.
 - ensure that pregnant or breastfeeding women know about 'Healthy Start' vitamins (www.healthystart.nhs.uk).

- If the patient has one or more risk factors AND widespread bone pain or tenderness or myalgia, or proximal muscle weakness, AND other relevant conditions/medical history, then manage the primary diagnosis or refer as appropriate. ['Other relevant conditions' include:
 - Hypercalcaemia
 - Metastatic calcification
 - Renal stones (caluli)
 - Severe hypercalciuria
 - Stage 4 CKD or eGFR<30ml/minute
 - Primary hyperparathyroidism
 - PMR/myositis (morning stiffness)
 - Any other red flags]

- If the patient has one or more risk factors AND widespread bone pain or tenderness or myalgia, or proximal muscle weakness, with NO relevant conditions/medical history, **then test for vitamin D.**

The following investigations should be carried out:

- Vitamin D
- Serum calcium (to exclude hypercalcaemia and obtain baseline for monitoring)
- Alkaline phosphatase and phosphate
- Liver and renal function
- Full blood count

Only test if both risk factors and symptoms are present, there are no relevant conditions which could account for the symptoms, or if clinically appropriate.

5 WHY ARE WE TESTING FOR VITAMIN D RATHER THAN PARATHYROID HORMONE?

Why measure surrogate markers if you can measure the real thing? In addition, patients can be profoundly vitamin D deficient and still have a normal PTH (usually at the upper end of normal with a calcium reading at the lower end of normal).

6 INTERPRETING VITAMIN D LABORATORY RESULTS

Samples sent to Bradford Teaching Hospitals NHS Foundation Trust:

Samples are tested for both vitamin 25-hydroxy-vitamin D3 (animal form of vitamin D) and 25-hydroxy-vitamin D2 (plant form of vitamin D).

Laboratory test: Tandem Mass Spectrometry (MS/MS), far superior than immunoassays in terms of sensitivity and specificity.

Laboratory reports include a vitamin D2 level, a vitamin D3 level, a total vitamin D level and a comment about whether the total level is sufficient or not. The value of D2 can be helpful in assessing compliance in patients prescribed ergocalciferol.

Vitamin D2 levels would be expected to be low in humans unless patients are supplemented with ergocalciferol.

Patients taking cholecalciferol would have a high reading of vitamin D3, provided they were taking the medication correctly.

Test turn-around time: between two and four weeks.

Interpretation of reports for vitamin D deficiency / insufficiency: consider the total vitamin D level.

Samples sent to Airedale NHS Foundation Trust:

Samples are tested for both 25-hydroxy-vitamin D3 (animal form of vitamin D) and 25-hydroxy-vitamin D2 (plant form of vitamin D).

Laboratory test: Enzyme Immunoassay Test. The test under-estimates 25-hydroxy-vitamin D2 by approximately 20%.

Laboratory reports include a total vitamin D level only. Values for vitamin D3 and vitamin D2 are not provided separately. No comment is currently provided.

The turn-around time for results is maximum two weeks, often sooner.

Interpretation of reports for vitamin D deficiency / insufficiency: consider the total vitamin D level.

High dose vitamin D should be prescribed for patients with vitamin D deficiency (<20nmol/L). Patients with vitamin D insufficiency (20-60nmol/l) should be recommended to purchase OTC supplementation. Higher doses (2000IU – 4000 IU/day) of supplementation may be required if vitamin D levels are at the lower end of the insufficiency spectrum. Repeat vitamin D levels after 4-6 months and adjust recommended dose as required.

The matter of prescribing for adults with diagnosed insufficiency has been considered at great length and discussed at the GP Commissioning Executive, with prescribing leads, and at the Osteoporosis Clinical Advisory Group. The decision has been taken not to prescribe for this group at this time as the epidemiology of insufficiency is not clear, and there is no vitamin D product available at an affordable price in the quantities likely to be required. Prescribing for this group would likely put significant cost pressures in the system. It is recognised that this is an important issue, and the decision will be reviewed in the future.

Please consider the season when interpreting vitamin D levels. Vitamin D levels are typically low in spring and are usually higher in autumn. A level of approximately 40nmol/L in spring is less severe than a similar level in autumn. The latter means the patient is at risk of deficiency over winter and should take some OTC supplements. A level of <20nmol/l is deficient irrespective of season but likely to indicate a higher risk of overt osteomalacia in autumn.

7 HOW ARE VITAMIN D 'DEFICIENCY' AND 'INSUFFICIENCY' DEFINED?

The level of 25-hydroxyvitamin D (25(OH)D) in the blood is the best indicator of vitamin D status. Nationally, there is debate about the cut-off point below which is defined as 'deficient', with general consensus that levels below 20 to 25 nmol/L qualify as 'deficient'. However, there is less agreement nationally on optimal 25(OH)D levels, with levels between 50 and 80

nmol/L being suggested. In addition, different laboratories may use different methods to measure serum or plasma 25(OH)D concentration, resulting in lack of standardisation.

In Bradford and Airedale vitamin D deficiency is defined as <20nmol/L; and insufficiency is defined as 20-60nmol/L.

8 WHICH HIGH DOSE VITAMIN D PRODUCT SHOULD I PRESCRIBE?

High strength vitamin D for treating deficiency: Pro D3 Colecalciferol 20,000IU capsules.

ProD3 is NOT a special and should be prescribed by name rather than Dekristol. ProD3 is a cost-effective vitamin D preparation. The range is marketed as a nutritional supplement. Nutritional supplements are generally subject to food safety labelling legislation. Further information is available from <http://www.prod3.co.uk>

Unlicensed colecalciferol preparations should not be prescribed as they are not cost-effective.

Patients should be prescribed 40,000 IU/week of Pro D3 (colecalciferol) for 8 weeks. Stress the importance of compliance. Adequate calcium intake (1000mg/day) is important whilst giving high dose Vitamin D. If dairy intake is low (i.e. less than 1 pint of milk a day and little or no cheese and yoghurt) also consider prescribing usual Ca and vitamin D to be taken alongside until high dose Vitamin D course complete. More information about calcium requirements is available from: <http://www.bradfordhospitals.nhs.uk/healthcare-professionals/speciality-specific-guidelines/referral-guidelines-rheumatology/guidance-on-specific-conditions/osteoporosis-2/Calcium%20Sheet.pdf>

Review at 12 weeks. If patient is still symptomatic, check compliance, repeat vitamin D, Ca and ALP levels. If the vitamin D level is still less than 20nmol/L, repeat the course of Pro D3 and reinforce compliance. If the vitamin D level is between 20-60nmol/L, recommend maintenance therapy for life with OTC Colecalciferol products of 1000IU daily. Higher doses (2000IU – 4000 IU/day) of supplementation may be required if vitamin D levels are at the lower end of the insufficiency spectrum. Repeat vitamin D levels after 4-6 months and adjust recommended dose as required.

Review at 24 weeks. If patient is still symptomatic, repeat vitamin D, Ca and ALP levels. If patient is still deficient, with suspected underlying undiagnosed pathology, refer to endocrine specialist.

9 WHAT ABOUT ERGOCALCIFEROL INJECTIONS?

Only consider ergocalciferol 300,000IU IM single dose injection for truly non-compliant patients as there is some evidence that it is less effective. This would have to be repeated every 2 months until patient vitamin D replete and then as often as required to maintain vitamin D levels in normal range (i.e. every 3-4 months).

10 ALFACALCIDOL AND CALCITRIOL

Alfacalcidol and calcitriol are not considered appropriate for community use for patients with vitamin D deficiency unless advised by a Renal Specialist due to the risk of hypercalcaemia.

11 WHAT ADVICE SHOULD I GIVE ABOUT SOURCES OF VITAMIN D?

▪ Sunlight

The major source of vitamin D for most humans is exposure to ultraviolet B radiation in sunlight. Approximately 90% of the vitamin D that the body needs is produced in this way. The season, latitude, and time of day, all strongly influence vitamin D production. In addition, personal factors such as avoiding exposure to the sun, heavy use of high SPF-containing sunscreen or moisturisers, skin pigmentation, age (the ability of the skin to manufacture vitamin D decreases with age), and certain medical conditions all make it impossible to recommend a one-size-fits-all level of exposure to the sunshine.

Generally, in the UK, exposing the face and forearms to sunshine most days without sunscreen between 11am and 3pm in the summer months (April-September), for less time than it takes the skin to redden (approx 20 minutes), and taking care not to burn, should be sufficient for most people. People with darker skin pigmentation need more time in the sun to make the same amount of vitamin D than people with lighter skin pigmentation.

▪ Supplements

Taking vitamin D supplements can be a useful way for people to get enough vitamin D. This is especially important for people whose bodies can't make enough vitamin D from sunlight, such as people who spend most of their time indoors, elderly people who have thinner skin, those who cover up, people with restricted diet, those with medical conditions with poor absorption from the gut and those who use high factor sunscreen even in the UK. It is also very important for people who need more vitamin D than usual, such as babies and growing children, and pregnant and breastfeeding women.

▪ Food

Most foods do not contain much vitamin D, and it is not possible to obtain an adequate amount of vitamin D from dietary sources alone (both natural sources and vitamin D-fortified foods). Foods that contain vitamin D include:

- oily fish, such as salmon, mackerel, pilchards and sardines
- eggs
- fortified fat spreads
- fortified breakfast cereals (check nutrition label)
- powdered milk

12 HOW DO MY PATIENTS GET VITAMIN D SUPPLEMENTS?

Vitamin D supplements can be bought from pharmacies, many supermarkets, and over the internet. As a rough guide, a year's supply usually costs less than £20. For most adults, a daily dose of between 10 and 25 micrograms (400 - 1,000 units) is enough - higher dose for people with darker skin or who do not get much sunshine.

Some patients may be eligible for Health Start vitamins. See questions 16 – 18.

13 WHAT ABOUT SUPPLEMENTATION IN OSTEOPOROSIS?

Patients with osteoporosis require an adequate intake of calcium and vitamin D. Vitamin D enhances the intestinal absorption of calcium and low vitamin D levels are associated with impaired calcium absorption and a consequent rise in PTH. This can lead to excessive bone resorption.

Falls and fractures – evidence suggests that supplementation with vitamin D and calcium more effective than vitamin D alone, particularly in those in institutional care.

Evidence and opinion supports vitamin D combined with calcium being the most effective treatment for prevention of fractures in older people, rather than vitamin D alone. However increased calcium intake may also be associated with increased risk of MI, therefore there needs to be a careful balancing of risks and benefits. The National Prescribing Centre and MHRA have recommended that the evidence is insufficient to warrant advising against calcium prescribing currently.

Most patients with osteoporosis require approximately 800 IU of vitamin D and 1200-1500mg elemental calcium daily.

This is especially important if they are on bisphosphonate therapy or other specific treatments for osteoporosis, and steps should be taken to ensure the patient is vitamin D replete before commencing bisphosphonates.

There are a variety of preparations available containing a combination of calcium and vitamin D3 such as Calcichew D3 Forte (now also available as caplet), Adcal D3 (now also available as caplet), Calceos, Cacit D3 and Calfovit D3. It is important that patients are prescribed a combined calcium and vitamin D preparation, rather than a single calcium supplement as it is the vitamin D component which is most important. Although multivitamin preparations are available, most contain only 400 IU vitamin D which is inadequate.

More information about calcium requirements is available from:

<http://www.bradfordhospitals.nhs.uk/healthcare-professionals/speciality-specific-guidelines/referral-guidelines-rheumatology/guidance-on-specific-conditions/osteoporosis-2/Calcium%20Sheet.pdf>

14 WHICH VITAMIN D PREPARATIONS ARE SUITABLE FOR A VEGETARIAN OR VEGAN DIET?

Ergocalciferol is derived from a common plant steroid, whereas colecalciferol is produced from a precursor which is most commonly derived from an animal source such as sheep wool fat. Colecalciferol products derived from wool fat are not acceptable to vegans, and may also be unacceptable to vegetarians if the wool fat is from slaughtered animals. Magnesium stearate (used as an excipient) may be produced from an animal or vegetable source.

Detailed information about the suitability of available vitamin D products in the UK for vegetarian or vegan diets can be found at the National Electronic Library for medicine website:

<http://www.nelm.nhs.uk/en/NeLM-Area/Evidence/Medicines-Q--A/Which-vitamin-D-preparations-are-suitable-for-a-vegetarian-or-vegan-diet/>

15 ARE WOMEN WHO BREASTFEED ADVISED TO TAKE VITAMIN D SUPPLEMENTS?

Yes. UNICEF's Baby Friendly Initiative has produced a statement on vitamin D supplementation for breastfed babies. Vitamin D deficiency is unusual in babies born to term to mothers with adequate vitamin D levels. However, babies are at risk of vitamin D deficiency if the mother has deficient vitamin D levels during pregnancy. Babies born with deficient vitamin D levels will not correct that deficiency with breastmilk alone, due to the low level of vitamin D in breastmilk.

16 WHAT IS THE GOVERNMENT'S HEALTHY START SCHEME?

Healthy Start is a UK-wide government scheme to improve the health of low-income pregnant women and families on benefits and tax credits.

Eligible pregnant women and families with children under 4 years can get free vouchers every week to spend on milk, plain fresh and frozen fruit and vegetables, and infant formula milk. Eligible families can also get free vitamins.

For more information go to www.healthystart.nhs.uk. This website has sections for health professionals and members of the public.

17 WHO IS ELIGIBLE FOR HEALTHY START VITAMINS?

Pregnant women and children under four years old on low income and all pregnant women under 18 in the UK are eligible* for Healthy Start vitamins as part of the government's Healthy Start scheme.

A new policy for Bradford and Airedale PCT has been agreed from April 2012 which goes beyond the government's eligibility criteria for the Healthy Start scheme. Under this policy the following groups are eligible for Healthy Start vitamins:

- All pregnant women will receive four bottles of free Healthy Start pregnancy vitamins at the booking/first midwifery appointment to last throughout pregnancy.
- All infants from birth to six months will receive free Healthy Start infant drops from health visiting services.
- Families fulfilling the government's eligibility criteria for Healthy Start* will be encouraged to apply for vouchers in order to continue supplementation from 6 months to four years. Applications for Healthy Start are available online or from health visitors or local health centres. Forms need to be signed by a health professional (eg health visitor).
- Children not eligible for Healthy Start and assessed as being 'at risk'*** by the health visitor of vitamin D deficiency will continue to receive free vitamins for up to two years from health visiting services.

** Eligibility for Healthy Start is defined as at least 10 weeks pregnant or have a child under four years old **and** the pregnant women or her family is in receipt of:*

- *Income Support, or*
- *Income-based Jobseeker's Allowance, or*
- *Income-related Employment and Support Allowance, or*
- *Child Tax Credit (but not Working Tax Credit unless your family is receiving Working Tax Credit run-on only*) **and** has an annual family income of £16,190 or less (2012/13).*

Pregnant women under 18 years also qualify if you are under 18 and pregnant, even if they don't receive any of the above benefits or tax credits.

Further information can be found on the Healthy Start website at www.healthystart.nhs.uk

*** Assessment for being 'at risk' is at the discretion of the health visitor or clinician and includes:*

- *Children who are from South Asian, African, African-Caribbean or Middle Eastern communities*
- *Exclusively breastfed babies and some formula fed babies*
- *Siblings close in age*
- *Family history of deficiency*
- *Children during periods of rapid growth such as in infancy*
- *Children with chronic conditions (malabsorption, JIA, rheumatic conditions, chronic steroid use, diabetes, disability and reduced mobility)*
- *Medications interfering with Vit D metabolism e.g. phenytoin, carbamazepine, steroids, rifampicin)*
- *Babies and children whose skin is not exposed directly to the sunlight through choice of clothing, use of sun-block or by remaining indoors*

18 WHICH VITAMINS ARE IN THE HEALTHY START VITAMINS?

- Healthy Start women's vitamin tablets
The daily dose is one tablet, which contains:
 - 70 milligrams of vitamin C
 - 10 micrograms of vitamin D
 - 400 micrograms of folic acid.

They are suitable for vegetarians and free from milk, egg, gluten, soya and peanut residues. The shelf life is two years from manufacture.

- Healthy Start infants and children's vitamin drops
The daily dose of five drops contains:
 - 233 micrograms of vitamin A
 - 20 milligrams of vitamin C
 - 7.5 micrograms of vitamin D3.

The vitamins are suitable for vegetarians and free from milk, egg, gluten, soya and peanut residues, and have a shelf life of 10 months from manufacture.

19 HOW IS VITAMIN D MADE BY OUR BODIES IN RESPONSE TO SUNLIGHT?

Vitamin D3 made in the skin and vitamin D2 or vitamin D3 obtained from the diet are biologically inactive, and require hydroxylation in the liver to form 25-hydroxyvitamin D. 25-hydroxyvitamin D is the major circulating form of vitamin D and is measured in laboratory tests to determine vitamin D levels in the blood.

25-hydroxyvitamin D is also inactive and is hydroxylated in the kidneys to form the active 1,25-dihydroxyvitamin D.

Fig.1 Sources and Metabolism of Vitamin D

