National Osteoporosis Society

# Vitamin D and Bone Health:

## A Practical Clinical Guideline for Management in Children and Young People

# Vitamin D and bone health: a practical clinical guideline for management in children and young people

There is currently considerable clinical and academic interest in vitamin D in children and young people. This partly relates to recognition of a resurgence of symptomatic vitamin D deficiency with reports of children presenting with rickets or hypocalcaemic symptoms. An additional development has been the recognition that vitamin D may have a physiological extraskeletal role beyond its traditional function as a key regulator of calcium and bone metabolism. There has been a large increase in requests for measurement of vitamin D with evidence that many individuals have suboptimal vitamin D status, often without symptoms. These guidelines have therefore been produced to guide clinicians in the appropriate investigation and management of vitamin D deficiency in children and young people.

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# Contents

# Glossary and abbreviations

| | |
|---|---|
| $C_3$ epimer | 3-epi-25(OH)D |
| 25(OH)D<br>calcidiol<br>calcifediol | 25-hydroxy vitamin D<br>(calcidiol, calcifediol) |
| HPLC | high-performance liquid chromatography (linked to either fluorescence or MS (tandem MS)) |
| MS | mass spectrometry |
| PTH | parathyroid hormone |
| VDBP | vitamin D binding protein |
| vitamin D | calciferol (either $D_2$ or $D_3$) |
| vitamin $D_2$ | ergocalciferol |
| vitamin $D_3$ | cholecalciferol |

**Conversion factors**

10µg (micrograms) vitamin D = 400IU vitamin D

2.5 nmol/L serum 25OHD = 1 ng/mL serum25OHD

# Key recommendations

- Measurement of serum 25(OH)D is the best way to estimate vitamin D status.
- Routine testing of serum 25(OH)D levels is not recommended and should be restricted to children and young people with a clear indication for measurement.
- Primary prevention via safe sunlight exposure, advice regarding dietary sources of vitamin D and multivitamin supplements are recommended for high-risk groups.
- Treatment should consist of oral preparations of vitamin $D_2$ or $D_3$ given daily for 8 to 12 weeks.
- Many children with vitamin D deficiency have a poor dietary calcium intake and therefore may also require higher dietary calcium intake or calcium supplementation.

## The role of vitamin D in paediatric bone health

Nutritional vitamin D deficiency can lead to health problems in children including rickets, impaired growth, muscle weakness and seizures due to hypocalcaemia.

There is no universal consensus on the biochemical definition of vitamin D deficiency. It is current paediatric practice to use a threshold of serum 25 hydroxyvitamin D (25(OH)D) of less than 25 nmol/L to define vitamin D deficiency. This is based on the fact that symptomatic vitamin D deficiency in children (e.g. rickets, hypocalcaemia) will usually only occur with a serum 25(OH)D level below 25 nmol/L. It is also consistent with current UK and European guidelines.

- Serum 25(OH)D below 25 nmol/L is deficient
- Serum 25(OH)D of 25–50 nmol/L may be inadequate in some people.
- Serum 25(OH)D greater than 50 nmol/L is sufficient for almost the whole population.

## How should we assess vitamin D status?

Measurement of serum 25(OH)D is the best way to assess vitamin D status. The assay used should have the ability to recognise all forms of 25(OH)D ($D_2$ or $D_3$) equally. In practice this means that it should use either HPLC or, more likely, tandem MS. Tandem MS assays can be subject to interference from metabolites such as the C3 epimer, which is synthesised by babies and young children but has also been detected in adult populations. The role of vitamin D binding protein and the impact on free 25(OH)D concentrations currently remains unclear.

## Who should be tested for vitamin D deficiency?

Low levels of vitamin D are common in the UK. It is therefore important to consider whether the child's symptoms or signs could be related to vitamin D deficiency before requesting a vitamin D level.

**Routine screening is not recommended.**

### Indications for testing vitamin D status

1) Symptoms and signs of rickets:
   - progressive bowing of legs (bowing of legs can be a normal finding in toddlers)
   - progressive knock knees
   - wrist swelling
   - rachitic rosary (swelling of the costochondral junctions)
   - craniotabes (skull softening with frontal bossing and delayed fontanelle closure)
   - delayed tooth eruption and enamel hypoplasia.
2) Other symptoms or conditions associated with vitamin D deficiency:
   - long-standing (> 3 months), unexplained bone pain
   - muscular weakness (e.g. difficulty climbing stairs, waddling gait, difficulty rising from a chair or delayed walking)
   - tetany due to low serum calcium
   - seizures due to low serum calcium (usually in infancy)
   - infantile cardiomyopathy.
3) Abnormal investigations:
   - low serum calcium or phosphate, high alkaline phosphatase (greater than the local age-appropriate reference range)
   - radiographs – showing osteopenia, rickets or pathological fractures revealed by radiographs.

4) Chronic disease that may increase risk of vitamin D deficiency:
   - chronic renal disease, chronic liver disease
   - malabsorption syndromes (e.g. coeliac disease, Crohn's disease, cystic fibrosis).
5) Bone diseases in children where correcting vitamin D deficiency prior to specific treatment would be indicated:
   - osteogenesis imperfecta
   - idiopathic juvenile osteoporosis
   - osteoporosis secondary to glucocorticoids, inflammatory disorders, immobility and other metabolic bone conditions.

**In the absence of the above indicators, measurement of vitamin D is not indicated.**

## Primary prevention

Primary preventative measures (at minimum) should be undertaken in patients at high risk. These include advice about safe sunlight exposure, dietary intake of vitamin D and multivitamin supplements.

## Indications for vitamin D supplements

The Department of Health recommends daily vitamin D supplements to the following:

- all children between 6 months and 5 years (unless they are receiving over 500ml of formula milk per day)
- breast-fed infants from the age of 1 month if the mother has not taken vitamin D supplements during her pregnancy

In these cases vitamin D supplements would be delivered through the Healthy Start programme

Other indications for vitamin D supplements:

- Children and young people previously shown to be vitamin D deficient or with a serum 25(OH)D of 25–50 nmol/L should take a supplement containing vitamin D. This should be continued unless there is a significant lifestyle change to improve vitamin D status.
- Vitamin D supplements should be considered in other high-risk groups (see below) for vitamin D deficiency, especially if lifestyle advice is not adhered to.

## Groups at high risk of vitamin D deficiency

Children and young people in the following groups are at high risk of vitamin D deficiency. Primary prevention is therefore particularly important for them.

- children and young people with diets insufficient in calcium (see Appendix 1) or with generally poor diets
- exclusively breast-fed babies from the age of 6 months, especially if the mother is also at risk of vitamin D deficiency or the infant has not started to take a good range of solid foods
- exclusively breast-fed babies from 1 month if the mother has not taken vitamin D supplements in pregnancy, or if she is known to be vitamin D deficient or insufficient
- children and young people with limited sun exposure (e.g. veiled and photosensitive patients)
- disabled children and young people who spend very little time outdoors
- children and young people who have darker skin, for example people of African, African-Caribbean or South Asian origin, because their bodies are not able to make as much vitamin D
- children and young people taking anticonvulsants that induce liver enzymes such as phenytoin, carbamazepine, primidone or phenobarbitone
- children and young people with family members with proven vitamin D deficiency.

## Season

There is a seasonal variation in vitamin D status in the UK, with lower circulating concentrations seen in the population in winter and late spring, compared to summer and autumn. It may be helpful to take into consideration the likely decline in vitamin D status when determining what to do with a child with a low 25(OH)D concentration in autumn or winter.

Having a low 25(OH)D concentration in late summer may reflect a lifestyle that places the individual at risk of vitamin D deficiency. It is important to state that the physiological significance of a given 25(OH)D concentration at a given moment is the same whatever the time of year.

### Dietary vitamin D

Consumption of vitamin-D-rich foods can contribute to improving vitamin D status. Foods rich in vitamin D include:

- oily fish such as sardines, pilchards and mackerel
- eggs, meat and milk (in small and varying amounts)
- margarine, some breakfast cereal, some yoghurt and infant formula, which are fortified with vitamin D.

## Who should be treated?

In those patients where 25(OH)D is tested (see the previous section: the results should be acted upon as follows:

- serum 25(OH)D < 25 nmol/L: treatment recommended.
- serum 25(OH)D 25–50 nmol/L:
  - Give advice on safe sun exposure and diet.
  - Advise oral preparations containing vitamin D 400–600 IU/day for patients aged 1 month to 18 years. This should be continued unless there is a significant lifestyle change to improve vitamin D status.
  - Ensure dietary calcium intake is adequate.
  - Retesting is not normally required if the individual is asymptomatic and compliant with multivitamin supplements.
- Serum 25(OH)D > 50 nmol/L: provide reassurance and give advice on maintaining adequate vitamin D status through safe sunlight exposure and diet.

### Indications for referral to secondary care

The following circumstances indicate referral to secondary care is warranted:

- repeated low serum calcium concentration with or without symptoms (irritability, brisk reflexes, tetany, seizures or other neurological abnormalities)
  - symptomatic: requires immediate referral to A&E if outpatient
  - asymptomatic: discuss treatment with paediatrician
- underlying complex medical disorders (e.g. liver disease, intestinal malabsorption)
- in children, deformities or abnormalities probably related to rickets
- poor response to treatment despite good adherence (defined as a level of 25(OH)D < 50 nmol/L after 8 to 12 weeks of adherent therapy)
- persisting low serum phosphate or low/high alkaline phosphatase.

# How should vitamin D deficiency be treated?

### Either Vitamin $D_3$ or Vitamin $D_2$

Although there are data to show that vitamin $D_3$ is more bioavailable than vitamin $D_2$, both forms have been shown to cure rickets and we would not recommend any difference in the doses used. The doses below are based on what are currently recommended in the *British National Formulary for Children* (BNFC)[3]. However, these may need to be changed dependent on the availability of other vitamin D preparations and evidence of alternative dosing regimens.

- 1–6 months: 3,000 IU orally daily for 8–12 weeks
- 6 months to 12 years: 6,000 IU orally daily for 8–12 weeks
- 12–18 years: 10,000 IU orally daily for 8–12 weeks; a single or divided oral dose totalling 300,000 units can be considered if there is concern about compliance.

### Calcium supplements

Many children with vitamin D deficiency rickets have a poor dietary calcium intake. As their bones are growing, there is a greater risk of negative calcium balance. Therefore, in children consideration should always be given to the need for calcium supplementation. Many children with vitamin D deficiency will have a depleted calcium status and/or a poor calcium intake and may therefore benefit from advice about dietary calcium intake. In some cases calcium supplementation may be worthwhile over the period of vitamin D treatment (see Appendix 1). The recommendations below are from the BNFC:

- birth to 4 years: 0.25 mmol/kg calcium q.d.s
- 5–12 years: 0.2 mmol/kg calcium q.d.s
- 12–18 years: 5–10 mmol calcium q.d.s

Dosing also needs to take into account dietary intake and the size of the child.

**There is no place for the use of 1α-hydroxylated preparations (e.g. alfacalcidol or calcitriol) in the routine management of vitamin D deficiency. Their use is limited to treating significant hypocalcaemia, disorders of malabsorption and renal disease.**

# Monitoring

Bone profile and vitamin D tests (and a PTH test if the patient has rickets or hypocalcaemia) should be repeated at the end of the course of treatment.

If the 25(OH)D level is greater than 50nmol/L and the bone profile is normal:

- Give advice on safe sun exposure and diet.
- Advise multivitamin containing vitamin D 400–600 IU/day. This should be continued unless there is a significant lifestyle change to improve vitamin D status.

If 25(OH)D is below 50 nmol/L:

- Consider poor compliance, drug interactions and underlying disease such as renal disease, liver disease and malabsorption.
- If poor compliance is suspected, a high-dose treatment may be considered if the patient is aged 12–18 years (e.g. 300,000 IU as a single or divided dose).

**Note: If a child's symptoms/signs have not improved despite a satisfactory 25(OH)D concentration, they are unlikely to be related to vitamin D deficiency.**

## Vitamin D toxicity

Serum 25(OH)D concentrations of above 375nmol/L have been associated with hypercalcaemia and hyperphosphataemia but there is no agreement on the threshold concentration or amount of vitamin D that results in toxicity. This is, in part, a reflection of the paucity of studies that address the safety of vitamin D supplementation. In adults, prolonged daily intake of vitamin D up to 10,000 IU or serum concentrations of 25(OH)D of up to 240 nmol/L appear to be safe. Although described, acute vitamin D intoxication is rare and usually results from vitamin D doses much higher than 10,000 IU per day. However, the long-term effects of supplementation with high doses of vitamin D are not known. Risks such as nephrolithiasis cannot be excluded. Caution is required in any child or young person with a granulomatous disease (e.g. tuberculosis or sarcoidosis).

# Appendix 1: Guideline on assessing dietary calcium intake

## Dietary reference values for calcium

| Age | Reference nutrient intake for calcium mg/day (mmol/day) |
|---|---|
| 0–12 months | 525 (13.1) |
| 1–3 years | 350 (8.8) |
| 4–6 years | 450 (11.3) |
| 7–10 years | 550 (13.8) |
| 11–14 years, male | 1000 (25.0) |
| 11–14 years , female | 800 (20.0) |
| 15–18 years, male | 1000 (25.0) |
| 15–18 years, female | 800 (20.0) |

*Note: 1 mmol calcium = 40 mg calcium.*

Reference: Department of Health, *Dietary Reference Values for Food, Energy and Nutrients for United Kingdom* (Report 41), London: TSO, 1991.

## Appendix 1: Guideline on assessing dietary calcium intake

# Calcium-rich foods

Find calcium-rich foods from this list for a bone-healthy diet..[a] Serving sizes are based on average portions.[b] The details below provide a general guide – precise calcium content can vary depending on source of food stuffs.

| Food | Serving size (average) | Calcium (mg) |
|---|---|---|
| **Milk** | | |
| Milk, semi-skimmed | glass, 200 ml | 240 |
| Milk skimmed | glass, 200 ml | 244 |
| Milk whole | glass, 200 ml | 236 |
| Milkshake | takeaway, 300 ml | 387 |
| Soy drink, calcium enriched | glass, 200 ml | 178 |
| **Yoghurt and cream** | | |
| Yoghurt, low-fat, fruit | pot, 150 g | 210 |
| Yoghurt, low-fat, plain | pot, 150 g | 243 |
| Cream, double, whipped | portion, 45 g | 26 |
| Cream single | tablespoon, 15 g | 13 |
| **Cheeses** | | |
| Danish blue | portion, 40 g | 195 |
| Edam | portion, 40 g | 318 |
| Feta | portion, 40 g | 144 |
| Camembert | portion, 40 g | 94 |
| Cheddar | medium chunk, 40 g | 296 |
| Cheese spread | portion, 30 g | 149 |
| Cottage | small pot, 112 g | 142 |
| Mozzarella, fresh | portion, 56 g | 203 |
| Parmesan, fresh | portion, 30 g | 308 |
| **Vegetables** | | |
| Broccoli, boiled | serving, 85 g | 34 |
| Watercress, raw | small bunch, 20 g | 34 |
| Curly kale | serving, 95 g | 143 |
| Okra, stir fried | 8 medium, 40 g | 88 |
| Red kidney beans, canned | 3 tablespoons, 105 g | 75 |
| Chick peas, boiled | 3 tablespoons, 90 g | 41 |
| Green/French beans | serving, 90 g | 50 |
| Baked beans | serving, 135 g | 72 |
| **Nuts** | | |
| Almonds | 12 whole, 26 g | 62 |
| Brazil nuts | 6 whole, 20 g | 34 |
| Hazelnuts | 20 whole, 20 g | 28 |
| Sesame seeds | 1 tablespoon, 12 g | 80 |
| Walnuts | 12 halves, 40 g | 38 |
| Tahini paste | 1 heaped teaspoon, 19 g | 129 |

| Food | Serving size (average) | Calcium (mg) |
|---|---|---|
| **Desserts** | | |
| Cheesecake, fruit | slice, 120 g | 94 |
| Custard made with milk | portion, 120 g | 166 |
| Rice pudding, canned | portion, 200 g | 176 |
| Ice cream, dairy, vanilla | serving, 75 g | 75 |
| Fromage frais, fruit | small pot, 60 g | 52 |
| **Fish** | | |
| Sardines in oil, tinned | portion, 100 g | 500 |
| Whitebait, fried | portion, 80 g | 688 |
| Salmon, tinned | portion, 100 g | 91 |
| Fish paste | small jar, 35 g | 98 |
| **Breads and grains** | | |
| Pasta, plain, cooked | portion, 230 g | 85 |
| Rice, white, boiled | portion, 180 g | 32 |
| White bread | slice, 30 g | 53 |
| Wholemeal bread | slice, 30 g | 32 |
| Muesli, Swiss style | portion, 50 g | 55 |
| **Fruits** | | |
| Apricots, raw, no stone | 4 fruit, 160 g | 117 |
| Figs, ready to eat | 4 fruit, 220 g | 506 |
| Currants | 2 tablespoons, 50 g | 47 |
| Orange | peeled, 160 g | 75 |
| **Other foods** | | |
| Tofu, soy bean, steamed | 100 g | 510 |
| Omelette, cheese | 2 eggs, 120 g | 344 |
| Quiche, cheese and egg | slice, 140 g | 367 |
| Macaroni cheese | portion, 220 g | 374 |
| Pizza, cheese and tomato | 9"–10" pizza, 410 g | 873 |
| Lasagne | portion, 420 g | 420 |

**References**

[a] Food Standards Agency. *McCance and Widdowson's The Composition of Foods*, Sixth Summary Edition. Cambridge: Royal Society of Chemistry, 2002

[b] Food Standards Agency. *Food Portion Sizes* 2002.

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# References


1. Braegger C, Campoy C, Colomb V et al. Vitamin D in the healthy European paediatric population. JPGN 2013;56:692–701.
2. Scientific Advisory Committee on Nutrition. *Update on Vitamin D*. London: TSO, 2007.
3. *British National Formulary for Children 2013–2014*. London: BMJ Group, 2014. Section 9.6.4 Vitamin D.
4. Shaw NJ, Mughal MZ. Vitamin D and child health part 1 (skeletal aspects). Arch Dis Child 2013;98:363–367.
5. Shaw NJ, Mughal MZ. Vitamin D and child health part 2 (Extraskeletal and other aspects). Arch Dis Child 2013;98:368–372.
6. Aggarwal V, Seth A, Aneja S, Sharma B, Sonkar P, Singh S, Marwaha RK. Role of calcium deficiency in development of nutritional rickets in Indian children: a case control study. J Clin Endocrinol Metab 2012;97(10): 3461–3466.
7. Ladhani S, Srinivasan L, Buchanan C, Allgrove J. Presentation of vitamin D deficiency. Arch Dis Child 2004;89(8):781–784.
8. Arundel P, Ahmed SF, Allgrove J, Bishop NJ, Burren CP, Jacobs B, Mughal MZ, Offiah AC, Shaw NJ. British Paediatric and Adolescent Bone Group's position statement on vitamin D deficiency. BMJ 2012; 345:e8182.

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