

Vitamin D Deficiency and Nutritional Rickets: Supplementation and Treatment in Infants and Children

Background

Vitamin D deficiency is a risk for;

- Rapidly growing children (infants, young children and adolescents) in the UK, particularly in ethnic minority groups
- Children with chronic diseases such as cystic fibrosis, coeliac disease, liver disease, renal disease, cancer
- Children receiving certain drugs, e.g. anti-convulsants

In 2012, the UK Chief Medical Officers⁽¹⁾ issued advice on supplements for at risk children between 1 month and 5 years of age, and breastfeeding babies likely to be born vitamin D deficient (due to lack of maternal supplementation in pregnancy).

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213703/dh_132508.pdf

Uptake of supplementation programmes has historically been low, and in recent years rickets is being more commonly recognised in infants and children.⁽²⁾

Current UK government recommendations on Vitamin D supplementation to maintain bone and muscle health suggest for:

- **Young people and children aged 5 years and over:** consider taking a daily supplement containing 400units of vitamin D between October and March when there is limited sun exposure. All year round supplements could be considered for those who have very little or limited sun exposure or who have dark skin (because they may not be able to make enough vitamin D from sunlight).
- **Infants and children aged 1-4 years:** give a daily supplement containing 400units vitamin D
- **Babies from birth – 1 year:** give a daily supplement containing 300-400units of vitamin D to babies who are breastfed or if they are taking less than 500ml of infant formula each day.

Table 1

Vitamin D supplementation (for children up to 5 years of age and those with insufficiency)*

The products listed in the table below do not need to be provided on prescription; they can be obtained through the child health clinics for patients up to 5 years of age. Alternatively supplements can be bought over the counter in pharmacies, supermarkets and health food outlets. Appropriate doses for supplementation are described in Table 2.

| Population Group | Risk Factors | Action |
|-----------------------------------|---|--|
| Infants < 6 months and breast fed | Risk factors for low maternal vitamin D level, e.g. Asian and African ethnicity | Healthy Start® vitamin supplement, or standard dose of Dalivit® or Abidec® |
| Infants > 6 months | Breast fed or taking less than 500 ml infant formula | Healthy Start vitamin supplement, or standard dose of Dalivit® or Abidec® |

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| All children 1-5 years | | Healthy Start® vitamin supplement, or standard dose of Dalivit® or Abidec® Safe sun exposure Dietary vitamin D and calcium advice |
| Insufficient vitamin D levels (see Table 3) | | Follow vitamin D specific supplementation guidelines above until 5 years of age and possibly throughout childhood Safe sun exposure Dietary vitamin D and calcium advice |
| Chronic disease | e.g. cerebral palsy, neuromuscular disorders, taking anti-convulsant therapy, cystic fibrosis, malabsorption | Follow disease specific prescribing guidelines or guidance in Table 3 of these guidelines Safe sun exposure Dietary vitamin D and calcium advice |

* Multivitamin supplements containing vitamin A should not be used in patients with chronic renal failure. These children should receive vitamin D alone as a supplement.

Table 2: Standard prevention doses⁴

| Category | Dose and Frequency |
|-----------------------|--|
| Newborn up to 1 month | 300 – 400 units daily |
| 1 month – 18 years | 400 units – 600 units daily Higher doses up to 1000 units daily may be used |

NB. A dose of 10 micrograms of Vitamin D = 400 units

Assessment of vitamin D status

Supplementation can be initiated without testing, and therefore biochemical testing for vitamin D deficiency is unnecessary for the majority of children in the primary care setting, unless they are symptomatic. Follow agreed disease-specific monitoring guidelines for those with underlying chronic conditions such as CF, cancer, neuromuscular disease, where these are available.

| Total 25 (OH) Vitamin D (nmol/L) | Vitamin D status | Clinical status | Management |
|----------------------------------|------------------|---|---------------------------------------|
| ≤25 | Deficiency | Infants: Rickets, bone pain, delayed walking Children: Chronic pain and weakness, tiredness | Treatment |
| >25-50 | Insufficiency | Likely to be asymptomatic | Lifestyle advice* and Supplementation |
| >50 | Adequate | Generally considered adequate for bone and overall health Remember levels may decrease over autumn/winter | Dietary/lifestyle advice* |

* Lifestyle advice: Vitamin D and the Sun Consensus statement 2010, <http://www.bad.org.uk/for-the-public/skin-cancer/vitamin-d/vitamin-d-consensus-2010> accessed 13/2/2023

Note: Vitamin D status is determined on total 25-OH Vitamin D level (25-OH Vitamin D2 + 25-OH Vitamin D3) if 25-OH Vitamin D2 and 25 OH Vitamin D3 are reported separately.

Vitamin D deficiency

Predisposing factors for vitamin D deficient bone disease (rickets)

- Occurs mainly in dark skinned infants and teenagers
- Lack of skin exposure to the sun
 - Particularly with some types of traditional clothing
 - During winter months
 - Spend very little time outdoors (e.g. those who are disabled)
- Use of sun block
- Prolonged breast feeding
- Exclusion diets
- Vegetarian / vegan diet
- Infants over 6 months who have not started to take a good range of solid foods
- Malabsorptive disease states
- Renal/liver disease

- Obesity (BMI > 98th BMI for age centile)
- Immobility
- Anticonvulsant treatment (e.g. sodium valproate, carbamazepine)
- Family history of vitamin D deficiency

Clinical presentation of vitamin D deficiency

- Vitamin D deficiency is usually asymptomatic but infants and young children may present with classic features of bow-legs, swollen wrists and muscular weakness e.g. delayed walking. Severe cases may have bone pain presenting as unexplained crying.
- When present, symptoms are often vague and in teenagers may present as aches and pains in legs. Positive Gower's sign is an early clue (proximal myopathy).
- Occasionally hypocalcaemia in (breastfeeding) infants may cause convulsions.
- Other symptoms or conditions associated with vitamin D deficiency include:
 - Rachitic rosary (swelling of the costochondral junctions)
 - Craniotabes (skull softening with frontal bossing and delayed fontanelle closure)
 - Delayed tooth eruption and enamel hypoplasia
 - Cardiomyopathy (in infants)
- **The presence of low vitamin D levels in isolation does not necessarily indicate this to be the cause of symptoms, as deficiency is commonly found in young children and may only require supplementation.**

Investigations (when symptomatic vitamin D deficiency clinically suspected)

Clinicians should have a low index of suspicion for rickets, but routine supplementation is of more value than investigating large numbers of children without overt symptoms.

Investigation may be of help if adherence is expected to be poor or symptoms develop. Symptomatic rickets should be investigated as below.

- Bone profile (Ca, Mg, phosphate, alkaline phosphatase)
- U&E
- FBC
- 25-OH Vitamin D levels (combined vitamin D2 and D3)

Additional tests depending on clinical context

- Ferritin (as asymptomatic iron deficiency often co-exists)
- 1,25 OH Vitamin D (if suspecting **renal** rickets or where vitamin D levels are normal but biochemistry indicates vitamin D bone disease). This investigation should not be done routinely and should only be requested by specialists.
- Parathyroid hormone (not routinely done unless biochemistry is atypical for nutritional vitamin D deficiency, or clinical rickets)
- X-ray knee or wrist (only if the patient clinically has rickets or significant symptoms)

| Table 2: Differential diagnosis | | | | | | |
|---|---------------|---------------|-----------------------------|---------------------------|---------------------------|---------------------------------|
| | Calcium | Phosphate | Alkaline Phosphatase (AlkP) | Parathyroid hormone (PTH) | Total 25-OH-Vitamin D 2+3 | 1,25 Vit D (not done routinely) |
| Nutritional vitamin D deficiency | | | | | | |
| Dietary lack and malabsorption | low or normal | low or normal | high or normal | high or normal | low | |
| Renal rickets | Low | high | high | high | normal | very low |
| Inherited vitamin D deficiency | | | | | | |
| Vit D dependent rickets (Pseudo-vitamin D deficiency) | Low | low | high | high | normal | low |
| Hereditary vitamin D resistance (receptor mutation) | Low | low | high | high | normal | very high |
| Hypophosphataemic rickets | | | | | | |
| Hypophosphataemic rickets | Normal | low | high | normal (can be low/high) | normal* | variable |

*inappropriately so

Therapeutic treatment of vitamin D deficiency (< 25 nmol/L)

In patients over 6 months of age, **aim for a TOTAL replacement dose of 250,000 units. This can be given as daily or weekly replacement doses as below;** the prescribed administration schedule should aim to maximise treatment adherence.

Table 3:

| Age | Less than 1 month | 1 month – 6 months | Over 6 months – 12 years | Over 12 – 18 years |
|--|---|---------------------------------|--------------------------------|----------------------------------|
| Dose of colecalciferol or ergocalciferol | 1500 units daily for 6 weeks initially then re-check level) | 3000 units daily (for 12 weeks) | 6000 units daily (for 6 weeks) | 10,000 units daily (for 4 weeks) |

Ref: 3,4,5,9,10

**The following regimen may promote adherence:-*

Capsules: colecalciferol 20,000 units **daily for one week (7 days)**, then 20,000 units **weekly for 5 weeks** (i.e. total of 12 doses of 20,000 units)

Liquid: 25,000 units **daily for one week (7 days)** then 25,000 units **weekly for 3 weeks** (i.e. total of 10 doses of 25,000 units)

(The guidance from the National Osteoporosis Society⁽⁶⁾ suggests a total replacement dose of 300,000units. Clinical experience at Alder Hey has shown that a total replacement dose of 250,000units is sufficient to bring the Vitamin D level up adequately.)

Consider whether a licensed formulation can be used (some small flexibility in the prescribed dose may enable this). Alternatively the off-label use of a licensed formulation or the use of an unlicensed formulation may be necessary.

Once the maximum total dose of 250,000units has been reached the initial therapeutic treatment with vitamin D should be reduced to supplemental doses due to the significant risk of hypercalcaemia.³

There is little evidence to support the need for calcium supplementation, but calcium intake from food should be assessed and improved if needed. If this is not achievable then consider calcium supplementation.

NB. Vitamin D 200 units = 5 micrograms of colecalciferol (D3) = 5 micrograms of ergocalciferol (D2).

Monitoring treatment response

- Review at the end of the treatment course. Ask the patient to bring all of their vitamin D medicine bottles to the review, to assess adherence. Consider repeating a blood test if symptoms persist and there is evidence of non-compliance.

If results are abnormal (vitamin D levels are deficient)

- Check compliance with therapy
- Continue treatment for a further 1 month *and*
- Check, bone profile (+/-PTH) *and*
- Continue until biochemistry normal, unless symptoms persist. In which case refer to a specialist.

NICE Clinical Knowledge Summaries follow up recommendations:

- At the end of treatment with high dose vitamin D:
 - Check bone profile (calcium, phosphate, ALP, magnesium). Consider checking calcium levels more regularly (e.g. every 1-2 weeks in the first months of treatment) in children and young people receiving calcium supplements in addition to high dose vitamin D
 - **If hypercalcaemia identified**, assess the person's state of hydration, and consider admission if the person is dehydrated. Discontinue calcium supplement immediately
 - **If calcium levels are normal**, do not recommend long-term calcium supplements. If the person is taking a calcium supplement, advise that it should be stopped
 - **If hypocalcaemia is identified** and the person is symptomatic (irritability, tetany, seizures or other neurological abnormalities), treat accordingly
- After 3–6 months of treatment with high dose vitamin D, check serum 25-hydroxyvitamin D (25[OH]D) levels

- *Please note that 25-OH Vitamin D2 (Ergocalciferol) levels may be underestimated by some Vitamin D methods of analysis. If the patient is receiving Vitamin D2 supplements then measurement of Vitamin D using Mass Spectrometry is recommended (separate 25-OH Vitamin D2 and 25-OH Vitamin D3 reported). For further information contact the Duty Biochemist (0151 252 5486 or Ext 2486 or duty.biochemist@alderhey.nhs.uk).*
 - If 25(OH)D levels are greater than 50nmol/L and bone profile is normal:
 - Advise that the person should take a daily vitamin D supplement throughout the year
 - If 25(OH)D levels are below 50nmol/L, consider other possible causes, including poor compliance with treatment or an underlying disease (e.g. renal or liver disease or malabsorption)
 - If symptoms and signs have not improved despite satisfactory 25(OH)D levels, consider an alternative diagnosis and refer to a specialist for advice

When to refer to the Metabolic Bone Service (MBS) at Alder Hey

- Patients who show a poor response to treatment
- Patients with symptomatic rickets with significant metabolic abnormalities, e.g. persistently low phosphate
- Where a secondary cause is suspected, e.g. liver, malabsorption or renal disease
- Metabolic bone disease, not related to vitamin D deficiency

Poor adherence to treatment

If poor adherence to treatment is a contributory cause, the metabolic bone service would consider giving high dose bolus ergocalciferol therapy (called Stoss 'bolus' therapy) which can be given orally or by IM injection.

Ergocalciferol injection 300,000units/mL is a licensed preparation and for this reason it is the preparation of choice. In circumstances where this injection is unavailable then colecalciferol injection 300,000units/mL can be used as an alternative. The colecalciferol injection is unlicensed in the UK. The pharmacy department can advise on available stock.

In the event that patients do not demonstrate an appropriate response to Stoss therapy with either product, they should be referred to the Metabolic Bone Team for further investigation.

Stoss therapy

- Oral ergocalciferol 150,000 units (3 x 50,000 unit capsules) as an observed dose every 3 months until biochemistry returns to normal.
- An alternative regimen of 50,000 units orally once a month for 3 months can be used.
- Ergocalciferol injection (available as 300,000 unit/ml) can be given by intra-muscular injection at a dose of 150,000 units (prepare to repeat after 1 month) or at a dose of 300,000 units (which may last for 3 months).

- Daily supplementation with vitamin D should be continued.
- Calcium supplementation is often given concurrently in infants when hypocalcaemia exists.

Parents must be informed of the symptoms of hypercalcaemia when starting high dose vitamin D (Stoss) therapy (e.g. anorexia, nausea, vomiting, headache, abdominal pain, polyuria) and advised to seek medical attention if their child develops any of these symptoms. **Whenever Stoss therapy is given the bone profile must be checked after 1 month to ensure that hypercalcaemia has not occurred.**

Education on longer term vitamin D health

- To prevent recurrence in patients who have completed treatment with therapeutic doses, long term supplementation and safe sun exposure are advised.
- Explain that it can take between 1-2 years for the bones to remodel.
- Explain that body stores take a long time to be replenished and so supplements are needed for a long time.
- Advise that siblings and other family members should also be supplemented.

Vitamin D and Covid-19 Infection

There is little evidence for using Vitamin D supplements to prevent or treat Covid-19.

Vitamin D supplements should NOT be offered to adults or children solely to prevent or treat Covid-19 except as part of a clinical trial.

However children and adults should be encouraged to follow UK government advice on taking a Vitamin D supplement to maintain bone and muscle health - see above.

VITAMIN D PREPARATIONS (stocked at Alder Hey)

Vitamin D preparations (for treatment of deficiency)

- **Colecalciferol (Fultium D3™) 3,200 unit capsule** [*licensed product*]
- **Colecalciferol 20,000 unit capsules (Fultium™ D3 capsules).** [*Licensed product*]
- **Ergocalciferol (or colecalciferol) capsules 1.25 mg (50,000 units)** – only for use under supervision at Alder Hey (referrals to Metabolic Bone Service - MBS) [*Licensed product*]
- **Colecalciferol (InVita D3™) oral solution 25,000 unit/ml; 1 ml ampoule for oral use** [*Licensed product*]
- **Colecalciferol (Thorens® Vitamin D3) oral solution 10,000 unit/ml** [*licensed product*] 10 ml bottle
- **Ergocalciferol injection 300,000 units/ml** (through MBS) [*Licensed product*]
- **Colecalciferol injection 300,000units/ml** [*unlicensed product*]

Vitamin D preparations (for supplementation and all doses less than 1000 units)

- Colecalciferol (Fultium D3 Drops) 2740 units/ml (200 units in 3 drops) [*Licensed product*]
- Colecalciferol (Fultium D3™) 800 unit capsule [*Licensed product*]
- Colecalciferol (Invita D3) 400 unit soft capsule [*Licensed product*]

Multivitamin preparations (available for supplementation)

To ensure adequate vitamin D status in healthy children and well children with vitamin D insufficiency, and to prevent recurrence of deficiency after vitamin D treatment.

- **Healthy Start Children's Vitamin Drops** (community clinics only) - 5 drops daily contains 7.5 micrograms (300 units) vitamin D₃, 233 micrograms vitamin A and 20 mg vitamin C.

Children can get these supplements free without prescription from 1 month to 4 years if parents are in receipt of welfare benefits.

In Liverpool, Healthy Start Vitamins are free for all children up to 2 years of age from the Children's Centres.

The product is suitable for vegetarians and free from milk, egg, gluten, soya and peanut residues.

<http://www.healthystart.nhs.uk>

- **Abidec™ or Dalavit™** 0.6 ml daily provides 400 units vitamin D daily. (Available on prescription or to buy). [*Licensed products*]
NB. Abidec™ contains arachis oil – avoid using in patients with peanut allergy.

Multivitamin preparations containing vitamin A are not suitable for patients with chronic renal failure. These patients should receive vitamin D supplementation alone.

References

1. Chief Medical Officers (UK). Vitamin D - advice on supplements for at risk groups 2012 CEM/CMO/2012/04 Gateway reference 17193.
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213703/dh_132508.pdf
2. Moy R.J et al Successful public health action to reduce the incidence of symptomatic vitamin D deficiency. Archives of disease in childhood 2012;97:952-954
3. [NICE Clinical Knowledge Summary – Vitamin D deficiency in children \(Nov 2016\)](#)
4. Royal College of Paediatrics and Child Health - Guide for vitamin D in childhood (Oct 2013)
5. British National Formulary for Children Colecalciferol <https://bnfc.nice.org.uk/drug/colecalciferol.html> accessed 3/7/20 and ergocalciferol accessed 3/7/20 <https://bnfc.nice.org.uk/drug/ergocalciferol.html>
6. National Osteoporosis Society. Vitamin D and Bone Health: A Practical Clinical Guideline for Management in Children and Young People 2015.
7. COVID-19 rapid guideline: Vitamin D. NICE guideline NG187 Published 17 December 2020.
8. www.nice.org.uk/guidance/ng187
9. [Vitamin D deficiency in children. Nottingham University Hospital https://www.nuh.nhs.uk/vitamin-d-deficiency-in-children/](https://www.nuh.nhs.uk/vitamin-d-deficiency-in-children/)
10. Vitamin D deficiency and rickets – Leicester Children's Hospital
<https://secure.library.leicestershospitals.nhs.uk/PAGL/Shared%20Documents/Vitamin%20D%20Deficiency%20and%20Rickets%20UHL%20Childrens%20Medical%20Guideline.pdf>

Other relevant guidance

Guide for Vitamin D in childhood. RCPCH October 2013

<http://www.rcpch.ac.uk/system/files/protected/page/vitdguidancedraftspreads%20FINAL%20for%20website.pdf>

East and South East England Specialist Pharmacy services. Vitamin D deficiency and insufficiency: Using appropriate available products January 2013

http://www.medicinesresources.nhs.uk/upload/documents/Communities/SPS_E_SE_England/Vitamin_D_product_availability_Jan_2013_V1_FINAL.pdf

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| Review and Revision(s) Log | | | |
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| <i>Record of revision(s) made to guidelines since Version 1</i> | | | |
| Section Number | Page Number | Revision(s) made | Reason for revision(s) |
| | Pages 7 and 8 | Updated to include preparation of Vitamin D recommended for doses less than 1000 units | 10 fold medication errors associated with Thorens version of Vitamin D 10,000 units per ml. Now recommending 2740 units per ml preparation for smaller doses |
| Table 3 | 4 | Dose and duration of vitamin D for neonates updated | Some babies seen with rickets following discharge from neonatal unit. Other hospital guidelines support increased doses. References 9 and 10 added |