

LRI Children's Hospital

Vitamin D deficiency and Rickets

Staff relevant to:	Clinical and Nursing staff working within UHL Children's Hospital
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1. Introduction and Who Guideline applies to:

Vitamin D deficiency is highly prevalent in UK. Children and young people in certain groups are at high risk of vitamin D deficiency. These include dark skin (South Asian, African and African-Caribbean), limited sun exposure (veiled, photosensitivity), poor diet including low dietary calcium intake, drug treatment such as anticonvulsants and children with limited mobility who may spend little time outdoors. Rickets is defective mineralisation of osteoid in growing bones due to inadequate body stores of Vitamin D or abnormalities in its metabolism.

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2. Vitamin D:

2.1 Source:

In most parts of the world, the recommended intake of Vitamin D is 400 units/day
Reference nutrient intake (RNI) in children:

0-6 months	8.5 mcg/day = 340 units/day
7-12 months	7 mcg/day = 280 units/day
1-3 years	7 mcg/day = 280 units/day

PS: 10µg (micrograms) vitamin D = 400 units vitamin D

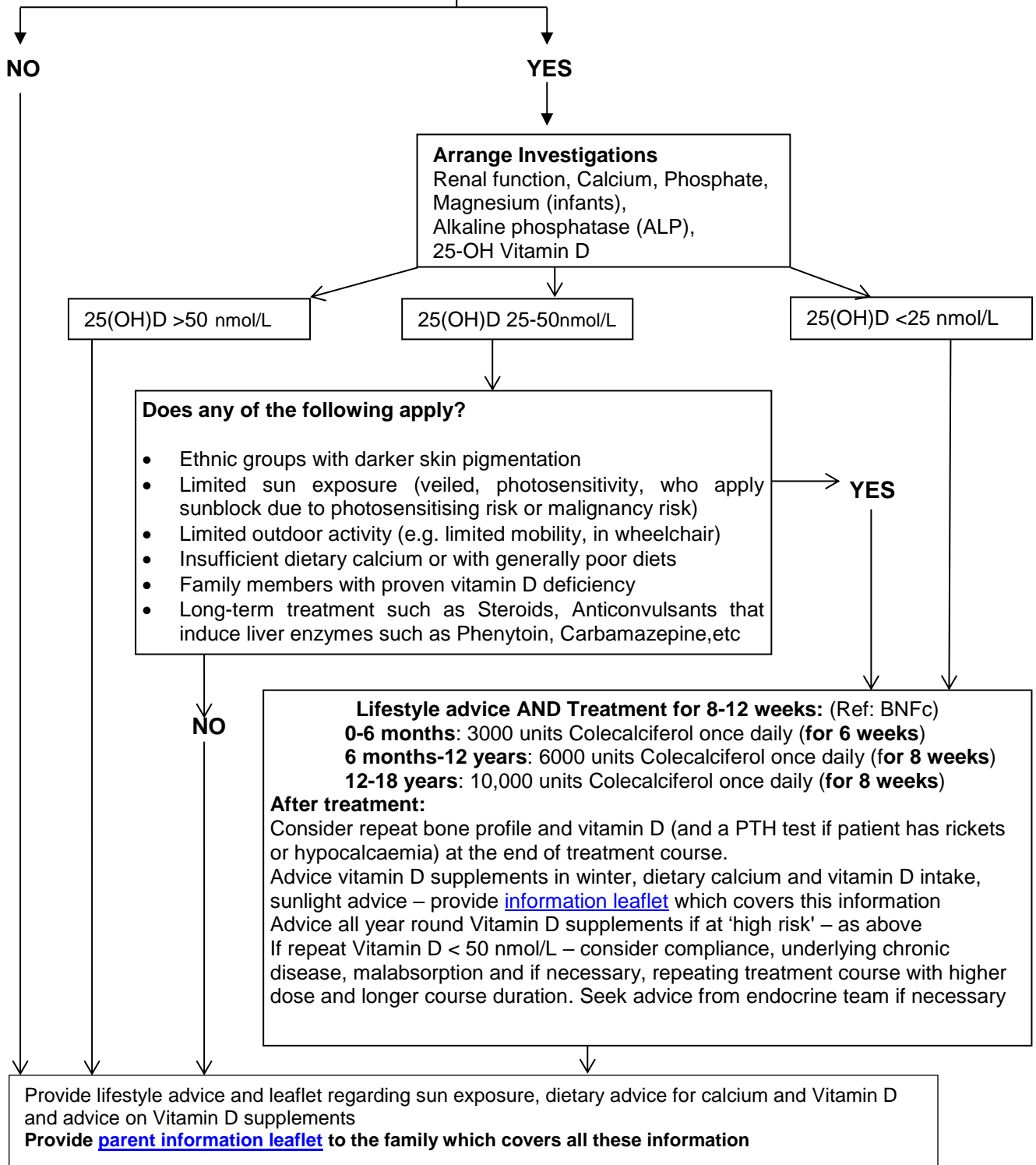
80-90% of Vitamin D is derived from sunlight (UVB). In UK, UVB is best available from early April to end of September between 11 am to 3 pm. Cloud, skin pigmentation, dark traditional clothes, limited sun exposure, application on sunscreen are some of the factors that can affect the Vitamin D synthesis.

Diet is a poor source. Fortified food (breakfast cereals), egg, oily fish are some of these. Human breast milk is a poor source of Vitamin D (**40-80 units per litre of breast milk**) and is a reflection of maternal vitamin D status. Children who have more than 500ml of infant formula a day do not need any additional vitamin D as formula is already fortified.

Flowchart for Children with suspected Vitamin D Deficiency

Indications for testing Vitamin D status met? (*Page 3 for details)

- Symptoms and signs of Rickets
- Symptoms associated such as muscle weakness, tetany, seizures, longstanding unexplained bone pain
- Abnormal investigations – low plasma calcium, high ALP, radiograph -osteopenia/rickets
- Chronic conditions – liver, renal, IBD, CF, immobility, wheelchair-bound
- Drug treatment – Bisphosphonates, steroids, anticonvulsants



Routine screening of vitamin D is not necessary.

2.2 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)
 - craniotables (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 (> three 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 plasma calcium
 - seizures due to low plasma calcium (usually in infancy)
 - infantile cardiomyopathy.
3. Abnormal investigations:
 - low plasma 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).
 - Children with limited mobility (e.g. wheelchair bound) who sustain repeated fractures with/without radiological evidence of osteopenia
5. Treatment with bone-targeted drugs that require vitamin D sufficiency such as bisphosphonates (used in conditions affecting bones such as osteoporosis due to steroids, immobility or inflammatory disorders).
6. Certain group of children and young people are at 'high risk of vitamin D deficiency' so consider a lower threshold for testing in the presence of symptoms in this group:
 - Diets insufficient in calcium (e.g. vegan or low dairy intake) or with generally poor diets
 - Limited sun exposure (e.g. veiled and photosensitive patients and patients who are advised to apply high factor sun block due to photosensitive medications or malignancy risk e.g. cancer survivors)
 - Those who spend very little time outdoors (e.g. those with limited mobility)
 - Those with dark skin, for example people of African, African-Caribbean or South Asian origin, as they may not get enough vitamin D from sunlight.
 - Those who take anticonvulsants that induce liver enzymes such as phenytoin, carbamazepine, primidone or phenobarbitone
 - Family members with proven vitamin D deficiency.

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

2.3 Investigations:

Blood:

Calcium, Phosphate, Magnesium (infants) – see table 1

Alkaline Phosphatase – can be normal or high

25 Hydroxy Vitamin D level – see table 1 and table 2

Parathyroid Hormone – is not essential to make a diagnosis

Table 1: Vitamin D levels

	25 (OH) Vitamin D
Deficiency	< 25 nmol/L
May be inadequate in some people	25 to 50 nmol/l
Adequate Vitamin D status	> 50 nmol/l

Table 2: Stages of Vitamin D Deficiency

	25OHD Levels	Ca Levels	PO ₄ Levels	PTH Levels
Stage 1	↓	↓	--	--
Stage 2	↓	--	↓	↑
Stage 3	↓	↓	↓	↑

Table 1: In the first stage, 25OHD and Ca levels decrease but PO₄ and PTH remain unchanged. In the second stage, 25OHD decrease further but PTH acts to raise Ca levels. PO₄ levels decrease. In the most severe third stage, 25OHD levels continue to decrease but even the raised levels of PTH are not able to keep Ca levels normal so they begin to decrease along with PO₄. (‘↑’ = Increase, ‘↓’ = Decrease, ‘--’ = Unchanged). Adapted from Wagner and Greer, 2008.

Other blood investigations: Consider

Hb, MCV, Ferritin (as often associated with iron deficiency anaemia)

X-ray: Knee or wrist (not essential to make a diagnosis)

2.4 Treatment: (Refer to flowchart on page 2 for summary)

Who will benefit from treatment?

- 25(OH)D > 50 nmol/L – treatment not recommended
- 25(OH)D < 25 nmol/L – treatment recommended
- 25 (OH) D 25-50 nmol/L – treatment recommended if child at ‘high risk of vitamin D deficiency’. If not in the high risk category, treatment not recommended. However, it would be helpful to take into consideration the likely decline in vitamin D status in autumn or winter.

High risk group for vitamin D deficiency are children and young people with:

- Diet insufficient in calcium (e.g. vegan or low dairy intake) or with generally poor diets
- Limited sun exposure (e.g. veiled and photosensitive patients and patients who are advised to apply high factor sun block due to malignancy risk e.g. cancer survivors)
- Those who spend very little time outdoors (e.g. those with limited mobility)
- Those with dark skin, for example people of African, African-Caribbean or South Asian origin, as they may not get enough vitamin D from sunlight.
- Those who take anticonvulsants that induce liver enzymes such as phenytoin, carbamazepine, primidone or phenobarbitone
- Family members with proven vitamin D deficiency.

Colecalciferol Preparations:

Available as oral solution, tablets/capsules or injection. Vitamin D3 (Colecalciferol) preparation is suitable for oral prescription. Some preparations have nut oil so please seek advice from pharmacy when prescribing in children with nut allergy as there are suitable alternative preparations. Ergocalciferol vitamin D2 IM injection 3,00,000 units/ml is available for exceptional cases.

Children with malabsorption, those on medications that impact vitamin D metabolism, and obese children with vitamin D deficiency may require higher replacement doses (two to three times higher than in children without these conditions), followed by higher maintenance dosing. Dose titration may be necessary in view of the variable degrees of malabsorption and supplemental requirements.

Oral Colecalciferol once daily dose:

0 - 6 months age **3000 units** once daily
6 months to 12 years **6000 units** once daily
12-18 years **10000 units** once daily

Course of treatment:

British National Formulary for Children (BNFC) recommends 8-12 weeks of treatment.

Provided treatment adherence is not an issue, a course of at least 6 weeks in total for children under 6 months age, and 8 weeks for children over 6 months age may be adequate.

Oral Colecalciferol once weekly dose:

Note: 7 times the daily dose given as once weekly dose for the same duration of length can be advised if compliance is an issue with once daily dose regime. Vitamin D3 preparation would be more suitable in this regime. ⁸

Alternate options of treatment in Secondary Care only:

1. In older children, especially if compliance is a concern, a single dose can be used (multiply daily dose by 30). It is essential to check the child has a sufficient dietary calcium intake, and that a maintenance Vitamin D dose follows the treatment dose. Vitamin D3 preparation is advisable in this regime. ⁶

2. Vitamin D Stoss Therapy:

"Stoss therapy" consists of a high dose of vitamin D given on a single day. The Global Consensus prefers daily therapy rather than stoss therapy, but recognizes that stoss therapy is sometimes more practical (when malabsorption, compliance with treatment and/or follow-up is an issue), and provides the following dosing recommendations, using oral vitamin D3 (colecalciferol) and not vitamin D2. ⁷

- Infants <3 months of age – Stoss therapy not recommended
- Infants 3 to 12 months of age – A single dose of 50,000 international units (1250 mcg)
- Children 1 to 12 years – A single dose of 150,000 international units (3750 mcg)
- Children ≥ 12 years – A single dose of 300,000 international units (7500 mcg)

This amount of vitamin D should be sufficient to induce healing of the growth plate within three months. Adequate calcium intake should also be assured when using stoss therapy (as with daily therapy).

At the end of the course of treatment:

- a) Stop the treatment
- b) Consider repeat bone profile, 25(OH)D (and PTH if patient has rickets or hypocalcaemia) after completion of the course of treatment.

If 25(OH)D > 50 nmol/L – provide lifestyle/dietary advice

If 25(OH)D < 50 nmol/L – consider compliance, chronic disease, malabsorption, drug interaction – a longer course or higher dose may be required as referred above.

- c) All children who receive treatment should be provided parent information leaflet which provides advice on preventive measures (lifestyle/dietary measures/vitamin D supplements) to prevent further vitamin D deficiency which is inevitable if not adhered to.

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

Other treatment:

1) Calcium: 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 improving dietary calcium intake. A daily intake of 500 mg elemental oral calcium (either dietary or supplemental) with vitamin D treatment, irrespective of age or weight is recommended during treatment of Vitamin D deficiency. In addition, oral calcium is advisable if there is associated hypocalcaemia and clinical evidence of rickets with raised PTH.⁶ If oral calcium commenced, bone profile for serum calcium needs to be monitored closely and oral calcium supplements stopped when serum calcium normalised.

2) Neonatal hypocalcaemic seizures due to vitamin D deficiency can be resistant to treatment. Intravenous calcium infusion is preferred over bolus of calcium gluconate – refer to the Calcium Disorders UHL Childrens Hospital Guideline. Ensure maternal vitamin D status is checked and appropriate treatment commenced immediately through the GP.

Note: Preparations such as One alpha calcidol (1,2 5 Vitamin D preparation) is not appropriate in this condition. Preparation of Vitamin D with calcium (like Adcal, Calcichew, etc.) have only 400-800 units of Vitamin D which is inadequate treatment dose. There is no evidence to suggest benefit of giving calcium with Vitamin D in treatment.

2.5 Primary preventive measures:

Primary preventive measures should be advised to all children and young people but particularly so in the 'high risk' group as listed above. It is also important that all children who receive treatment for vitamin D deficiency are also provided this advice to prevent further deficiency from evolving.

Advice on all the preventive measures are covered in the Parent Information leaflet- please provide a copy to the family

Leaflet can be found on [YourHealth](#)

When to consider referral/seek advice from Paediatric Endocrine Team:

- Atypical biochemistry (persistent low calcium or phosphate despite correction of Vitamin D levels)
- Failure to reduce/normalize alkaline phosphatase levels within 3 months of starting treatment
- Poor response to treatment despite good adherence (defined as a level of 25(OH)D < 50 nmol/L after 8-12 weeks of adherent therapy)
- Family history (parent, siblings) with severe rickets

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Prescribing practice	Audit	Dr Shenoy	5 years	Audit meeting

5. Supporting References

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6. Key Words

Vitamin D deficiency, Rickets, Stoss therapy

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs. As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Savitha Shenoy – Consultant Paediatrician	Executive Lead Chief Nurse
Details of Changes made during review: Signpost to YourHealth website for patient information leaflet added Added – <ul style="list-style-type: none"> • Colecalciferol Preparations • Stoss therapy • Oral calcium dosing 	