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Guidelines for the treatment and prophylaxis of Nutritional Vitamin D deficiency and Rickets in children and adolescents in secondary and primary care

Risk factors for vitamin D deficiency

Sunlight is a source of vitamin D. However, in the UK it is not possible for everyone to get enough vitamin D from sunlight exposure alone. Please see below for details on risk factors in children:

- Infants who are exclusively breastfed, especially if the mother is also at risk of vitamin D deficiency
- Pigmented skin
- Children and adolescents with disabilities which limit the time they spend outside
- Anticonvulsant (phenytoin and carbamazepine, primidone or phenobarbitone) treatment
- Childhood or adolescent obesity

Recommendations for supplementation and prophylaxis

Prophylaxis supplementation is readily available from fortified foods and not always necessary to prescribe.

Daily supplementation of vitamin D is recommended for:

Primary prevention:

- At risk breastfed infants from birth (premature babies and mothers who are vitamin D deficient)
- Formula (containing vitamin D) fed infants who take less than 500 mL of formula/day
- Children 6 months to 5 years of age

On-going supplementation:

- Infants or children previously treated for rickets or vitamin D deficiency
- Children from ethnic minorities who have darker skin. Clinical deficiencies have been most reported among children of African-Caribbean and South Asian origin.
- Children who are not exposed to much sun, for example those who cover their skin for cultural reasons, who are confined indoors for long periods (e.g. living in flats)

Vulnerable children on anticonvulsants:

- Children on phenytoin, carbamazepine, primidone or phenobarbitone prescribed for medical conditions

Dosing: 300iu - 400iu (8mcg - 10mcg) daily are sufficient to prevent rickets and vitamin D deficiency in babies and children. Children may need continued supplementation after the age of 5yrs during growth periods.

For patients in high risk groups supplementation should continue indefinitely.

Healthy Start Programme in primary care

This is part of a national campaign for pregnant women or women with children aged 6 months to four years of age to receive vitamin supplementation and vouchers. This is prophylactic dose, and the prescribing of multivitamin drops in primary care should be avoided as Healthy Start Programme should be accessed or equivalent vitamins purchased.

Rickets

The commonest cause of rickets is simple nutrient deficiency from low sun exposure combined with inadequate dietary intake.

Malabsorption syndromes such as coeliac disease and cystic fibrosis should be considered, especially where there is a poor response to vitamin D treatment. Certain metabolic, renal and liver diseases can also lead to rickets.

Peak incidence of rickets is between 3 and 18 months of age. A deficient state exists for months before there are any signs on physical examination. Children with rickets are often miserable and in pain.

Symptoms and signs of rickets:

- bowing of legs (genu varum)
- knock knees (genu valgum)
- anterior bowing of the femur
- painful wrist swelling (distal radius)
- prominent costochondral joints "rickety rosary"
- softening of the skull with frontal bossing, and delayed fontanelle closure
- spinal curvature
- bone pain
- dental deformities (delayed tooth formation, enamel hypoplasia)

The above is from the CEG guidance on rickets in children and can be accessed:

<http://www.blizard.qmul.ac.uk/ceg-resource-library/clinical-guidance/clinical-guidelines/10-vitamin-d-january-2011/file.html>

Pre-treatment investigations and monitoring of treatment

Note: Vitamin D levels are quoted as total Vitamin D (25-OHD) – (Ergocalciferol Vitamin D₂+ colecalciferol D₃).

For a quick reference guide: see appendix 1 on page 6 for the **VITAMIN D GUIDANCE – PATHWAY SUMMARY FOR CHILDREN**

Vitamin D deficiency = < 30nmol/L

Vitamin D insufficiency = 30 - 50nmol/L

Vitamin D adequate = > 50nmol/L

Vitamin D deficiency – investigations to consider

Pre-treatment	Serum 25 OHD, bone profile, renal & liver profiles to confirm diagnosis; FBC and Ferritin level if necessary to look for associated nutritional deficiencies
Monitoring	If symptoms have resolved following treatment, no further monitoring is required and the patient should be switched to prophylactic doses

Rickets or Vitamin D deficiency with hypocalcaemia – investigations to consider

Pre-treatment	Serum 25 OHD, bone profile, renal & liver profiles; consider Parathormone (PTH) if hypocalcaemic; FBC and Ferritin level often helpful; X-ray bone/wrist when suspecting Rickets	
Monitoring	Bone profile 25 OHD	Regular monitoring (2 – 3 weekly) for calcium (bone profile) until hypocalcaemia is resolved; Vitamin D level at 3 months of treatment to monitor adequacy, guide further treatment and to prevent overtreatment in rickets, vitamin D deficiency with hypocalcaemia and neonates with vitamin D deficiency
	ECG and Cardiac Echo	Do ECG and consider Cardiac Echo – in those presenting with severe hypocalcaemia

Rickets – consider treatment in primary care after discussing with Paediatric Registrar or Paediatric consultant

Vitamin D deficiency with hypocalcaemia - urgent referral to secondary care/ contact Paediatric Registrar or Paediatric consultant and discuss

Dose titration in Rickets or Vitamin D deficiency with hypocalcaemia

Serum 25 OHD after 3 months treatment	Action
< 30nmol/L – deficient vitamin D level	Possibility of non-adherence, consider stoss therapy
30 - 50 nmol/mL – insufficient vitamin D level	Continue with current treatment dose and reassess in 3 months
> 50 nmol/mL – adequate vitamin D level	Prescribe prophylaxis

Re-testing vitamin D level

Responsibility for vitamin D level re-testing should be undertaken by the treating physician which can be either the GP or the hospital physician.

If vitamin D level is needed to be re-tested within a six month window (in rickets or vitamin D deficiency with hypocalcaemia or neonates with vitamin D deficiency), an additional email should be sent at the time of the request to the following members of the pathology team who perform the test to ensure that it is performed:

Andrew Staunton: andrew.staunton@bartshealth.nhs.uk

Molly Zaman: molly.zaman@bartshealth.nhs.uk

Treatment of Vitamin D deficiency and rickets

If the child is hypocalcaemic calcium supplementation should be prescribed. In active rickets, increased milk intake should be encouraged and, if this is poor, additional calcium supplements can also be given.

Oral daily dosing

- 1 month to 6 months: 1500 units daily
- 6 months to 12 years: 3000 units daily (adjusted as necessary for weekly doses)

- 12 to 18 years: 5000 units daily (adjusted as necessary for weekly doses)

Note: It is not practical to give a sufficient dose using combined calcium and vitamin D preparations. So treatment doses should be given as either colecalciferol or ergocalciferol. Colecalciferol is preferable to Ergocalciferol as it is slightly more effective. The above Vitamin D doses are lower than those recommended in the BNF for children. These doses are effective and do not require routine monitoring unless the patient is treated for vitamin D deficiency with rickets or vitamin D deficiency with hypocalcaemia or neonates with vitamin D deficiency.

Duration of treatment: minimum 12 weeks (3 months)

Dosing in vitamin D insufficiency

The daily oral dose in Vitamin D insufficiency is the same as in vitamin D deficiency. The recommended duration of treatment is 6 weeks.

Dosing in intestinal malabsorption or in chronic liver disease

- Child 1 to 12 years: 10000 - 25000 units daily
- Child 12 to 18 years: 10000 – 40000 units daily

The total monthly dose by intramuscular injection can be administered as a single dose as it is an oily formulation with a slow release effect (unlicensed dose).

Stoss therapy (high dose therapy)

Stoss therapy may be considered if there are concerns with regards to adherence. The single IM dose can also be considered for patients with cystic fibrosis (CF) or inflammatory bowel syndrome (IBD) with malabsorption. It involves oral or intramuscular administration of the total treatment dose of vitamin D given in two divided doses twelve hours apart if given orally or as a single dose if given IM. This may need to be repeated (usually every 3 months) if poor compliance persists with maintenance dosing.

Check bone profile (for calcium level) 2-3 weeks post treatment and vitamin D level 2-3 months post treatment.

1 to 12 months: 150000 units in 2 divided doses PO or single dose IM

1 to 12 years: 300000 units in 2 divided doses PO or single dose IM

12 to 18 years: 500000 units in 2 divided doses PO or single dose IM

Note: In chronic conditions such as CF children may be prescribed treatment doses of vitamin D for longer periods, particularly if they have a low Z-score on recommendation by secondary care.

Special note on treatment of vitamin D deficiency for neonates

Deficiency - Vitamin D < 30nmol/L, total daily dose of colecalciferol 1000 units

(Baby maybe on multivitamins already; Dalavit 0.3 mls OD / Abidec 0.3mls will contain 200 units of vitamin D2)

NB: There isn't a dose in children BNF for under < 1 month

The consensus view from a group of clinicians from the children's bone health conference is 1000-1500 units for these babies with Vitamin D deficiency; suggested checking vitamin D level in 3 months.

Contraindications to Vitamin D supplement

- Hypercalcaemia
- Evidence of vitamin D toxicity
- Metastatic calcification

Adverse effects of Vitamin D

If the recommended doses are adhered to side effects are rare. Side effects are generally associated with excessive intake of Vitamin D leading to the development of hypervitaminosis D (vitamin D level >150nmol/L) and hypercalcaemia. The symptoms of hypercalcaemia include anorexia, nausea and vomiting, headache, dry mouth, fatigue and muscle weakness

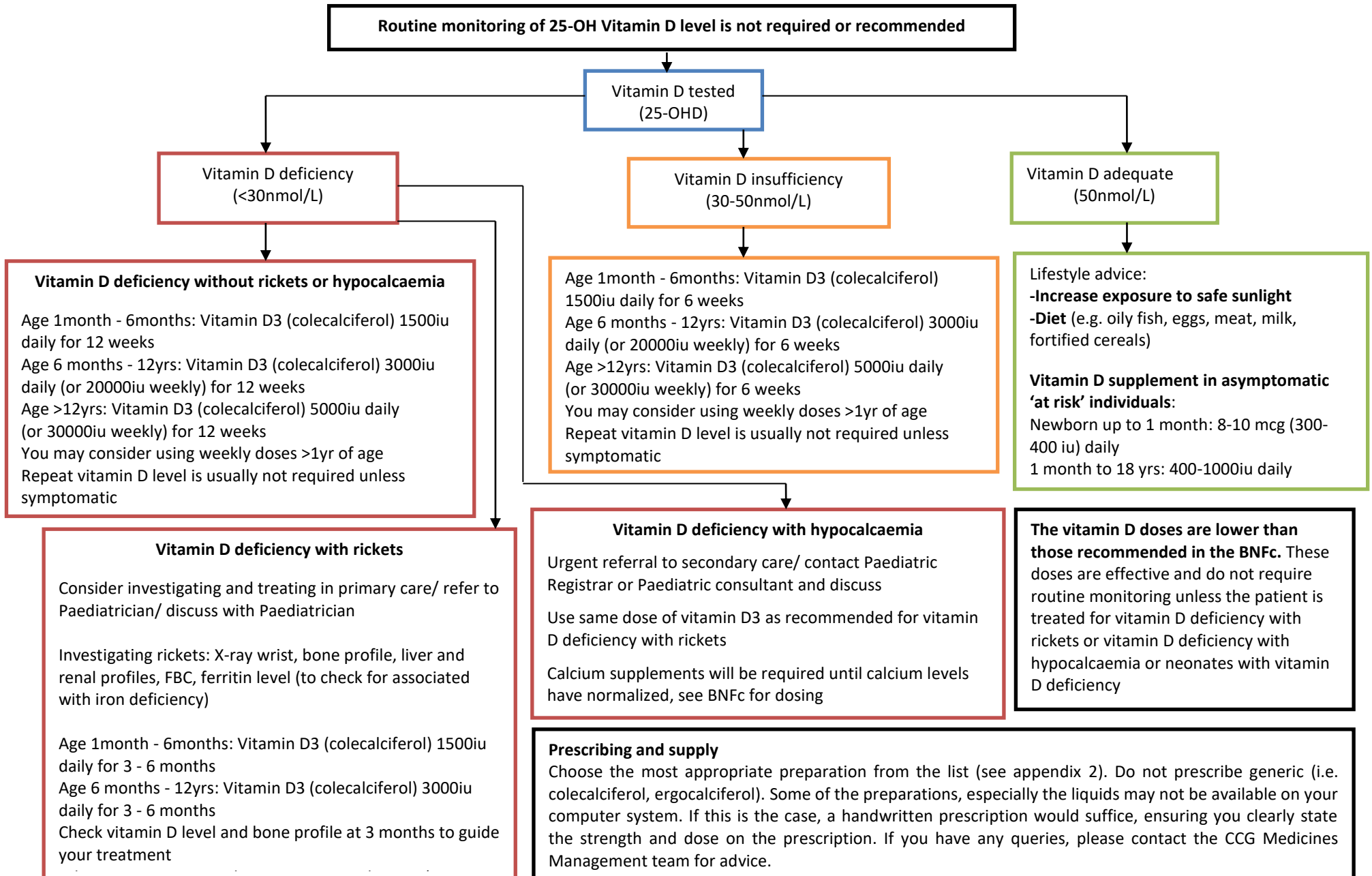
Drug interactions for Vitamin D

- Magnesium-containing antacids: hypermagnesaemia may develop in patients on chronic renal dialysis
- Digitalis glycosides: hypercalcaemia in patients on digitalis may precipitate cardiac arrhythmias
- Anti-convulsants: vitamin D requirements may be increased in patients taking anti-convulsants (e.g. carbamazepine, phenobarbital, phenytoin and primidone)

Information for hospital prescribing at Barts Health NHS Trust

Prescribing for prophylaxis and vitamin D deficiency, please refer patient back to GP.
Active rickets or symptomatic Vitamin D deficiency requiring urgent start of treatment – initiate treatment on hospital outpatient's prescription.

APPENDIX 1
VITAMIN D GUIDANCE – PATHWAY SUMMARY FOR CHILDREN



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APPENDIX 2

Vitamin D Preparations available (licensed and unlicensed – list not exhaustive)

Colecalciferol (Vitamin D3) and Ergocalciferol (Vitamin D2) are used for prophylaxis and treatment. Doses are equivalent; however colecalciferol is slightly more effective.

Alfacalcidol (1-hydroxy Colecalciferol) and Calcitriol (1,25 dihydroxy Colecalciferol) are not suitable for the management of nutritional rickets and vitamin D deficiency as they can cause hypercalcaemia and do not correct the deficiency. Therefore these must not be used for the treatment of Vitamin D deficiency.

Preparation	Manufactured by & licensed status	Pack size & price	Dietary requirements
Fultium-D3 800 IU capsules	Internis Pharmaceuticals Ltd	30 capsules (£2.52) 90 capsules (£8.85)	Contains gelatin which is halal and kosher compliant but not suitable for vegetarians
Fultium-D3 3,200 IU capsules	Licensed product	30 capsules (£13.32) 90 capsules (£39.96)	
Fultium-D3 20,000 IU capsules		15 capsules (£17.04) 30 capsules (£25.52)	
Fultium-D3 Drops 2740 IU/mL	Internis Pharmaceuticals Ltd Licensed product	25 mL (£10.70) Once opened use within 6 months	Suitable for vegetarians - The active ingredient is derived from sheep wool Not Halal or Kosher certified Does not contain soya, nut or gelatine
THORENS 10 000 I.U. /ml oral drops, solution	Galen Limited Licensed product	10mL (£5.85) After first opening the bottle: the product may be stored for a maximum of 6 months	Thorens oral solution contains colecalciferol and refined olive oil The colecalciferol is derived from cholesterol from wool grease (lanolin) and considered to be suitable for vegetarian patients but not vegan patients The colecalciferol in Thorens is halal and kosher-certified. The olive oil excipient has not been certified as halal or kosher
Invita D3 2,400 IU/ml oral drops	Consilient Health Ltd	10mL (£3.60) After first opening the	InVita D3 is gluten-free, alcohol-free, yeast-free and is olive oil based

	Licensed product	bottle: the product may be stored for a maximum of 3 months	It does not use any ingredients from slaughtered animals and does not contain gelatine or porcine sourced materials The vitamin D3 is sourced from lanolin from sheep's wool
Aciferol (Colecalciferol) 3000iu/ml Liquid	Fontus Health Sold as food/nutritional supplement	100ml (Packed as two 50ml bottles) (£19.99) Bottle should be discarded 8 weeks after opening	Free from alcohol, gelatine, gluten, soya, peanut oil Suitable for vegetarians
Valupak® Vitamin D3 1000iu tablet	Valupak Vitamins Ltd Sold as food/nutritional supplement	60 small size tablets (£0.74)	Free from milk, egg, yeast Suitable for vegetarians No nuts used in product but manufacturer cannot guarantee production in nut free environment
SunVit-D3® 20,000iu tablets	Sunvit-D3 Ltd Sold as food/nutritional supplement	28 film coated tablets (£3.87)	The tablets are free from wheat, gluten, soya, nut and gelatin. Suitable for vegetarians and a halal diet
Ergocalciferol intramuscular injection 300000iu/ml (Focus Brand) Can be used for stoss therapy	Recipharm Limited Distributed Focus Pharmaceuticals Licensed Product	10 x 300000 iu/ml (£96.25)	
Dalivit® Drops contains Vitamin D2 400iu (10mcg) and 5000iu of Vitamin A per 0.6ml dropper Also contains vitamins B complex and C	Boston Healthcare Ltd Sold as multivitamin drops for healthy growth and development	25ml (£6.33) and 50ml (£10.82) bottles	Does not contain peanut oil (arachis oil) Suitable for vegetarians and vegans

References

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RCPCH (2003). *Medicines for children (2nd edition)*

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GUIDE FOR VITAMIN D IN CHILDHOOD, October 2013, from the Royal College of Paediatrics and Child Health (RCPCH) website: <http://www.rcpch.ac.uk/system/files/protected/page/vitdguidancedraftspreads%20FINAL%20for%20website.pdf>

<http://www.dalivit.co.uk/>

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<http://www.sunvitd3.co.uk/>

<http://www.blizard.qmul.ac.uk/ceg-resource-library/clinical-guidance/clinical-guidelines/10-vitamin-d-january-2011/file.html>

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