

Diagnosis and Management of Vitamin D Deficiency

Ashford and St Peters Hospitals

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Introduction

Vitamin D deficiency is increasing in incidence in our population according to the recent National Diet and Nutrition Survey 2011. Vitamin D is essential for the absorption of dietary calcium and phosphate and maintenance of bone metabolism.

Vitamin D has other important physiological actions including the regulation of cell growth, immune regulation and Insulin excretion. Based on these actions it is increasingly being recognised as having a protective role in non-musculoskeletal conditions including Cardiovascular Disease, Diabetes, Infections and Autoimmune disorders.

Nomenclature and Reference Ranges

Vitamin D includes D2 (Ergocalciferol) and D3 (Cholecalciferol) collectively known as Calciferol. 1mcg of D2 or D3 is equivalent to 40units.

Reference ranges for vitamin D (25 OHD) RCPCH October 2013

<input type="checkbox"/>	<25	nmol/l	deficient
<input type="checkbox"/>	25-50	nmol/l	insufficient
<input type="checkbox"/>	>50	nmol/l	normal

Sources of Vitamin D

Sunlight

The major natural source of vitamin D is ultraviolet B sun exposure. During summer 20 to 30 minutes of sun exposure to the face and forearms 2 to 3 times a week will provide approximately 2000 IU Vitamin D to the fair skinned population. Those with pigmented skins require 2 to 10 times more exposure. In the United Kingdom there is insufficient UVB of the necessary wavelength between October and March to generate vitamin D. Sun exposure for vitamin D production has to be balanced against the risk of skin cancer. Sunscreens with a sun protection factor of 15 or more block 99% of dermal vitamin D synthesis.

Dietary sources

There are few foods rich in vitamin D. In the UK margarine, infant formula milk and some cereals are modestly fortified with vitamin D.

- Oily fish eg. trout, tuna, salmon, herring, mackerel, sardines, fresh tuna 200-400IU/ 100g
- Cod liver oil 1360 IU per tablespoon
- Margarine 280IU / 100g
- Some breakfast cereals 120-320IU / 100g
- Red Meat 40IU / 100g
- Egg yolk 20 IU per egg yolk
- Infant formula ($\geq 500\text{ml}$)

Recommended Daily Intake of Vitamin D

In the UK a recommended dietary intake has not been set for healthy individuals eating a balanced diet and with exposure to summer sun. The Department of Health has published recommendations (2012) for supplements for certain high risk groups:

Newborn to 1 month	300 to 400 units/day
1 month to 18 years	400 to 1000 units/day

Presentation of Vitamin D deficiency in young children

Severe vitamin D deficiency may cause hypocalcaemic seizures or tetany, particularly in the neonatal period and again during the phase of rapid growth in adolescence (see hypocalcaemic seizure guideline for management)

Rickets

The most common cause is inadequate sun exposure and poor dietary intake. The peak age of presentation is 3 to 18 months.

Symptoms and signs of rickets

- Generalised muscular hypotonia
- bowing of legs (genu varum) or knock knees (genu valgum)
- anterior bowing of the femur
- painful wrist swelling (distal radius)
- prominent costochondral joints “rickety rosary” due to laying down of uncalcified osteoid
- softening of the skull (craniotabes) with frontal bossing, and delayed fontanelle closure (>18-24/12)
- kyphoscoliosis (>2yrs of age due to vertebral softening)
- bone pain
- dental deformities (delayed tooth formation, enamel hypoplasia)
- fractures

Presentation of Vitamin D deficiency in Older Children/Adolescents

Bone pain (hips, pelvis, thigh, foot), proximal muscle weakness and diffuse muscular aches.

Who should be investigated?

- Maternal vitamin D deficiency
- Failure to thrive
- Lack of sunlight exposure
- Decreased Dietary intake eg exclusively breast fed/ delayed weaning/selective eaters/ multiple food allergies
- Malabsorption eg Cystic Fibrosis, Coeliac Disease, Inflammatory Bowel Disease
- Renal and liver diseases
- Increased catabolism (medications e.g. anticonvulsants, glucocorticoids)
- Pigmented skin (with any of the above)
- Unexplained fractures
- Chronic fatigue

Investigations

Blood tests

- Calcium, Phosphate, Alkaline Phosphatase
- 25 Hydroxy Vitamin D level (25 OHD)
- Urea and electrolytes
- Liver function tests
- Hb and Ferritin

Consider

- Parathyroid hormone - rises in Vitamin D deficiency and useful for distinguishing from other rare causes of rickets eg Phosphate deficiency

Radiology

An X-ray does not need to be done in all cases. Radiological rickets is caused by vitamin D deficiency (intake or absorption), with the only (extremely rare) exception being inborn errors of Vitamin D metabolism.

The X- ray appearances of rickets are characteristic:

- Cupping, splaying and fraying of the metaphysis of the ulna, radius and costochondral junction
- Coarse trabecular pattern of metaphysis
- Osteopenia
- ? Fractures

It is possible to be significantly vitamin D deficient without obvious bony abnormality in older children and teenagers with vitamin D deficiency. The plain X- rays may show osteopenia.

Management of Vitamin D deficiency (<25 nmol/l)

Any infant or child with hypocalcaemic seizures should be treated as an emergency and appropriate treatment would be initiated as per the Hypocalcaemia guideline. Calcium supplements should be continued until the serum calcium is normal

Colecalciferol (vitamin D3) is considered the preferred form of vitamin D for treatment. It has been reported that Colecalciferol raises vitamin D levels more effectively than Ergocalciferol (vitamin D2) and has a longer duration of action.

Contraindications:

Hypersensitivity to vitamin D or any of the excipients in the product used
Hypervitaminosis D
Nephrolithiasis
Diseases or conditions resulting in hypercalcaemia and/or hypercalciuria
Severe renal impairment

Pseudohypoparathyroidism as the vitamin D requirement may be reduced due to phases of normal vitamin D sensitivity, involving the risk of prolonged overdose. (Invita D3).

For cautions and side effects see Summary of Product Characteristics

Doses (BNF)

Child 0-6 months	3,000 units oral daily
Child 6/12 – 12yrs	6,000 units oral daily
Child 12-18yrs	10,000 units oral daily

These doses should be given for 8 weeks only. The child should then be started on maintenance doses.

In circumstances of poor compliance, treatment with an intramuscular dose of Ergocalciferol can be given following Consultant decision as this is an unlicensed product.

- Child 6/12-12yrs 150,000 units
- Child >12yrs 300,000 units

The Vitamin D level should be checked 2 months after the course/ injection and if still suboptimal (<50 nmol/l) then another dose can be given.

Daily maintenance supplements for children

Neonate	300-400 units/day
Child 1 month-12 yrs	400-800 units/ day.
12-18 yrs	800-1000 units/day

Management of Vitamin D insufficiency (25-50 nmol/l)

These children should receive daily maintenance supplements at the above doses as well as advice on dietary advice and safe sun exposure.

Reference ranges for vitamin D (25 OH D) RCPCH October 2013

<input type="checkbox"/>	<25 nmol/l	deficient
<input type="checkbox"/>	25-50 nmol/l	insufficient
<input type="checkbox"/>	>50 nmol/l	normal

Vitamin D Products (maintenance and insufficiency)

Product	Strength	Dose	Suitability
Fultium D3 drops	400 units in 6 drops (2740 units/ml)	0 to 1 month: 6 drops (400 units) od 1 month to 12 yrs: 6 to 12 drops (400 to 800 units) od 12 to 18 yrs: 12 to 15 drops (800 to 1000 units) od	In Coconut oil and palm kernel oil
Fultium D3 capsules	800 units	1 capsule (800 units) od	12 to 18 years only
Abidec	400 units in 0.6mls	0.6 mls (400 units) od	Not suitable for peanut or soya allergy Not to exceed 0.6mls
InVita D3 oral solution	25,000 units/ml	1 ml (25,000 units) once every 6 weeks	1 to 18 years

Vitamin D Products (deficiency)

Product	Strength	Dose	Suitability
Fultium D3 drops	400 units in 6 drops (2740 units/ml)	0 to 6 months : 1 ml (2740 units) daily 6 months to 12 years: 2 mls (5480 units) daily 12 to 18 years: 3 mls (8220 units) daily	In Coconut oil and palm kernel oil
Fultium D3 capsules	20,000 units	20,000 units every 2 weeks for 6 weeks	12 to 18 years only Not suitable for peanut or soya allergy

Monitoring

After 2 months Vitamin D, serum calcium, phosphate and ALP should be rechecked in all children prescribed Vitamin D. The aim of treatment should be to reach a total Vitamin D level of >50 nmol/l with a normal ALP for age and resolution of radiological changes.

If the vitamin D level is not >50 nmol/l continue treatment for a further 2 months and recheck.

Once the total vitamin D level is within the normal range treatment should be changed to maintenance supplements as this group of children are likely to have on going risk factors for vitamin D deficiency.

The family and siblings of children with rickets are highly likely to be vitamin deficient. It is good practice to review family members and provide supplementation for those at high risk.

In vitamin D insufficiency treatment is not needed once levels are normal if underlying cause has been resolved.

In patients with renal failure, serum calcium should be checked regularly for a few weeks after starting treatment

References:

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2. Pearce S, Cheeetham T, Diagnosis and management of vitamin D deficiency. BMJ, 2010; 340:142-7
3. Barts and the London NHS trust, Vitamin D guidance. January 2011.
4. NHS Surrey PCT Guidelines for the Treatment of Vitamin D Deficiency and Insufficiency in Adults (June 2011)
5. Michael F. Holick, Neil C. Binkley et al. Evaluation, Prevention and Treatment of Vitamin D deficiency, An Endocrine Society Clinical Practice Guideline; Journal of Clinical Endocrinology & Metabolism, July 2011, 96(7): 1911–1930.
6. Imperial College Healthcare NHS Trust, Treatment and prophylaxis guidelines for Vitamin D deficiency in infants, children and adolescents. 2009.
7. Summary of Product Characteristics for Fultium D3 drops June 2016
8. Summary of Product Characteristics for Fultium D capsules 800units and 20,000 units. June 2016
- 9 Summary of Product Characteristics for Invita D3 oral solution 25,000units/ml, June 2016
- 10 RCPCH Guide for Vitamin D in Childhood October 2013
- 11 Scientific Advisory Committee on Nutrition 2016

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