

Treatment and prophylaxis guidelines for Vitamin D deficiency in infants, children and adolescents.

SUMMARY

Who is at risk?	Vitamin D deficiency is increasing in incidence in our population. Those at particular risk are listed under section 5A of the document.
Prophylaxis	400 units (10 microgram) a day as part of a multivitamin preparation is suitable for infants, children and adolescents.
Diagnosis	Clinical symptoms that may present are listed in section 5B along with initial investigations to be carried out by the GP If 25-hydroxy vitamin D is less than 25nmol/L treat, if between 25 – 50nmol/L give prophylaxis.
If Calcium is low?	Immediate referral to paediatric hospital secondary care service.
Treatment	Vitamin D – the doses of colecalciferol or ergocalciferol for different ages are: <ul style="list-style-type: none"> • Infant 1 to 6 months: 3000 units daily • Children 6 months to 12 years: 6000 units daily • Over 12 years to adult: 6000 – 10000 units daily
Monitoring	Aim for 25 hydroxy vitamin D > 80nmol/L and ALP within normal limits, check every 3 months. Consider repeat X ray after 6 months to confirm whether radiological features of rickets have resolved. Most children should continue on prophylaxis after deficiency has resolved.
When to refer to secondary care	If the calcium level is low or if there is symptomatic hypocalcaemia (irritability, brisk reflexes, seizures or other neurological abnormalities). Child with deformities or abnormalities related to rickets. Diagnosis is not certain or there appear to be no risk factors. Poor response (NB: this is often due to poor adherence to medication).
Further information and products available	Information about current vitamin D products available, licensing and supply problems is available in section 5D. In general for prophylaxis offer a multi-vitamin preparation eg Abidec® or Dalivit® and for treatment use colecalciferol liquid 3000 units per ml. Remember to check the whole family as there are likely to be co-existing risk factors and deficiencies.

INTRODUCTION

This guidance has been written by Dr Nicola Bridges, Paediatric Endocrine Consultant, based at Chelsea and Westminster Hospital (C&W), also performing joint clinics with Dr Mike Coren, Imperial Healthcare NHS Trust (ICHT). It was written on request of Westminster PCT following requests from GPs partly due to availability problems of various vitamin D products. The guideline is endorsed by the paediatric team at ICHT. The majority of cases of vitamin D deficiency can be treated and prevented in primary care. This document gives an overview of the causes, investigations and treatment of vitamin D deficiency, as well as when to refer to secondary care.

DEFINITIONS

Infant – child between the ages of 1 month and 1 year

Child – Between the ages of 1 to 12 years

Adolescent – Between the age of 12 – 18 years

ALP - alkaline phosphatase enzyme (from liver and bone)

ICHT Imperial College Healthcare NHS Trust

C&W Chelsea and Westminster Healthcare NHS Trust

SCOPE

Paediatric and adolescent patients at ICHT, C&W

PCTs – Westminster, K&C, H&F – *to be confirmed*

A. Prophylaxis of Vitamin D deficiency

➤ ***Which children and adolescents are at risk of vitamin D deficiency or rickets?***

Sunlight on the skin is a source of vitamin D, but the UK is far enough North that it is not possible for anyone to get enough vitamin D from sunlight exposure alone.

Those at most risk of Vitamin D deficiency are infants who have been exclusively breastfed for over 6 months, particularly if their mother is also at risk of vitamin D deficiency or they have not started to take a good range of solid foods. Adolescents who eat a poor diet or have limited sun exposure due to clothing are also at risk.

Other risk factors for vitamin D deficiency are:

- Poor diet
- Clothing which limits sunlight exposure or avoidance of sunlight
- Pigmented skin
- Children and adults with disabilities which limit the time they spend outside
- Mothers who have breastfed previous children without taking supplements
- Phenytoin and carbamazepine treatment

➤ ***Current recommendations for vitamin supplementation in infants and children***

The Department of Health recommends a daily supplementation of vitamins A, C and D for:

- Breastfed infants from six months of age (or from 1 month of age if there is any doubt about the mother's vitamin status during pregnancy)
- Formula-fed infants who are over six months and taking less than 500mL (a pint) of infant formula per day
- All children between 1 and 5 years of age

This recommendation is particularly important for children who are picky or fussy eaters, those of Asian, African, Afro-Caribbean or middle eastern origin and those living in northern areas of the UK.

People who are not exposed to much sun, eg those confined to indoors for long periods and those who cover their skin for cultural reasons should have supplements.

Infants aged 0-6 months should not need supplements as they should get adequate amounts from breast milk or infant formula milk. If there is any doubt about the mother's use of vitamin supplements during pregnancy and/or breastfeeding, breastfed infants will benefit from vitamin D supplements from 1 month of age.

(see www.healthystart.nhs.uk).

In 2005 only 7% of babies over 6 months were receiving supplements.

-See preparations (section 5D) for a suitable supplement.

➤ **Vitamin D prophylaxis dose**

A dose of 400 units daily (as part of a multivitamin preparation eg Abidec or Dalivit) is sufficient to prevent rickets and vitamin D deficiency . This prophylaxis should be given to:

- infants or children previously treated for rickets or vitamin D deficiency
- high risk groups of infants, children and adolescents of all ages:
 - Poor diet
 - Clothing which limits sunlight exposure or avoiding sunlight
 - Pigmented skin
 - Children and adults with disabilities which limit the time they spend outside
 - Mothers who have breastfed previous children without taking vitamin D supplements
 - Phenytoin and carbamazepine treatment
- Breastfed infants from six months (or from 1 month of age if there is any doubt about the mother's vitamin status during pregnancy)
- Formula-fed infants who are over six months and taking less than 500 ml infant formula per day
- Children between 1 and 5 years of age

Vitamin D deficiency in mothers during pregnancy and breastfeeding is the cause of deficiency in their infants, so prophylaxis should be given to pregnant or breastfeeding women.

NICE guidelines on antenatal care 2008 (CG062) *“All women should be informed at the booking appointment about the importance for their own and their baby’s health of maintaining adequate vitamin D stores during pregnancy and whilst breastfeeding. In order to achieve this, women may choose to take 10 micrograms of vitamin D per day, as found in the Healthy Start multivitamin supplement. Particular care should be taken to enquire as to whether women at greatest risk are following advice to take this daily supplement.”*

B. Treatment of Vitamin D Deficiency

➤ ***Diagnosis of rickets and vitamin D deficiency***

Clinical features of vitamin D deficiency:

Infants

Widened epiphyses (thick wrists and ankles)
Bowed legs or wide based gait
Floppiness and irritability

Older children, adolescents and adults

Bone pain
Muscle weakness
Poor growth

Initial investigations if there is clinical suspicion:

U and E (Urea and electrolytes)

Calcium

Phosphate

Liver function tests

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

(25 Hydroxy)Vitamin D level (this can fluctuate according to intake and so it is possible to have a normal value with clinically obvious rickets).

Radiology – An X-ray does not need to be done in all cases. The typical X ray appearances of rickets are characteristic and do not occur in other calcium or bone disorders. Radiological rickets is caused by vitamin D deficiency (intake or absorption), with the only (extremely rare) exception being inborn errors of Vitamin D metabolism. It is possible to be significantly vitamin D deficient without obvious bony abnormality, and older children and teenagers with vitamin D deficiency do not develop the features of rickets.

➤ ***Vitamin D therapy for the treatment of rickets and vitamin D deficiency***

Usual doses:

Infant 1-6 months: 3000 units colecalciferol or ergocalciferol daily

Child 6 months-12 years: 6000 units colecalciferol or ergocalciferol daily

Over 12 years to adult: 6000-10000 units colecalciferol or ergocalciferol daily

It is not practical to give a sufficient dose using combined calcium and vitamin D preparations so this should be given as colecalciferol or ergocalciferol liquid, 3000 units/ml or in older children as ergocalciferol 10,000 units tablets if available, otherwise the liquid must be used.

Who should be treated:

- Anyone with 25-hydroxyvitamin D levels less than 25 nmol/L. (Anyone with levels of 25-50 nmol/L should be given prophylaxis of 400 units daily).
- Any child with radiological features of rickets, even if the 25-hydroxyvitamin D levels are in the normal range
- Infants and children with complex medical disorders eg liver disease, intestinal malabsorption, may require higher, pharmacological, doses of vitamin D which would require intensive monitoring.

➤ ***Target levels for treatment and the risks of vitamin D toxicity***

The laboratory normal range for Vitamin D as 25-hydroxyvitamin D is 25 - 120nmol/L. Data looking at bone density shows reduced bone density even with levels in this range, suggesting that the cut off should be higher than 25, at 80nmol/L. The aim of treatment should be to reach a serum level of over 80nmol/L. Levels of 250nmol/L have been reported following sunlight exposure and therapy without

adverse effects, and toxicity is likely to require serum levels over 500nmol/L. There are few published reports of hypercalcaemia following colecalciferol or ergocalciferol treatment. Studies have confirmed the safety of relatively high doses given to children and adults with or without vitamin D deficiency.

➤ **Calcium supplements for treating hypocalcaemia in children and adolescents**

Any infant or child with low calcium levels or showing symptoms of hypocalcaemia should be immediately referred to secondary care at ICHT St Mary's Hospital or Chelsea and Westminster NHS Trust where appropriate treatment would be initiated.

Calcium supplements should give 30-75mg/kg (equivalent to 0.75 to 2.00mmol/kg/day) in 3 divided doses. For most children and adolescents liquids or effervescent tablets are preferable. Calcium supplements should be continued until the serum calcium is normal (see below).

➤ **Treatment and monitoring**

Treatment doses of colecalciferol or ergocalciferol should be given until alkaline phosphatase (ALP) is within normal limits, 25-hydroxyvitamin D levels over 80nmol/L, and radiological features of rickets have resolved.

- **Biochemical vitamin D deficiency without bony abnormality or hypocalcaemia:**
After 3 months treatment recheck the investigations above. If ALP is within normal limits and 25-hydroxyvitamin D levels over 80nmol/L change to a multivitamin preparation for prophylaxis. If not, continue another 2-3 months and recheck.
- **Biochemical vitamin D deficiency with radiological rickets:**
After 3 months treatment recheck the investigations above. If ALP is within normal limits and 25-hydroxy vitamin D levels over 80nmol/L change to a multivitamin preparation for prophylaxis. Children with severe rickets may require longer treatment. Consider repeating the X-ray after 6 months to confirm radiological resolution of the rickets. Complete resolution may take longer than this and monitoring should continue until it does.
- **Biochemical vitamin D deficiency with hypocalcaemia:**
Children with symptomatic hypocalcaemia (irritability, brisk reflexes, seizures or other neurological abnormalities) **must be referred to hospital urgently**. Calcium supplements (see above) must be started at the same time as vitamin D treatment for any child with serum calcium below the normal range. Continue with calcium supplements until the calcium levels are normal. Calcium, phosphate and liver function tests should be re-checked and checks continued at least monthly until calcium levels are normal. After 3 months treatment re-check the investigations above. Treat with vitamin D for 3 months and if ALP is within normal limits and 25-hydroxyvitamin D levels over 80nmol/L change to a multivitamin preparation for prophylaxis. If not, continue another 2-3 months and recheck. This is the most severely affected group and is most likely to need longer treatment.
- The most likely reason for failure of biochemical resolution or of healing of rickets is poor adherence to treatment.
- Most infants and children will continue to have risk factors for vitamin D deficiency and so should continue on prophylaxis with a multivitamin preparation after treatment.

C. Referral

➤ **Who should be referred to the hospital paediatric services?**

If vitamin D deficiency is confirmed, treatment can be commenced in primary care. The following groups should be referred to hospital paediatric services:

- All infants and children with hypocalcaemia, even if asymptomatic (these children must be referred urgently)
- Any child with deformities or orthopaedic abnormalities related to rickets (refer to general paediatrics rather than orthopaedics).
- If the diagnosis is not certain or there appear to be no risk factors
- Poor response to treatment

Children with more complex issues can be referred to paediatric endocrine clinics:
 St Mary's (Dr Coren, Monthly joint clinics with Dr Bridges or Dr Alexander)
 Chelsea and Westminster Hospital (Dr Bridges, Dr Alexander).

Other members of the family

If a breastfed child is vitamin D deficient, it is likely that his/her mother is as well. Siblings may have similar risk factors. Consider testing and treating other members of the family.

If you have any queries regarding the duration of vitamin D treatment or monitoring requirements please contact the specialist paediatric team (Dr Coren or Dr Bridges) for further information.

Contact details for specialist services:

Contact details of specialist paediatric services

Dr Michael Coren
 Consultant Paediatrician
 St Mary's Hospital, Imperial College Healthcare NHS Trust
 Praed St
 London
 W2 1NY
 020 3312 6710
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D. Preparations and supply issues

➤ Preparations of vitamin D for treating rickets and vitamin D deficiency

Colecalciferol (D3) and ergocalciferol (D2) are used for prophylaxis and treatment of rickets and Vitamin D deficiency. They are of similar efficacy.

10 micrograms of colecalciferol or ergocalciferol is equivalent to 400 units.

The hydroxylation of colecalciferol and ergocalciferol to 1,25 hydroxyvitamin D is controlled by parathyroid hormone, thus reducing the risk of inducing hypercalcaemia at higher doses. For this reason ergocalciferol or colecalciferol are used for managing nutritional rickets and vitamin D deficiency, and alfalcidol and calcitriol are not suitable for this indication. Ergocalciferol is suitable for vegetarians and vegans as this is derived from plants.

Available preparations include:

- Colecalciferol liquid 3000 units/ml (manufactured “special” (see below)) (this is the formulation usually stocked in hospital pharmacies and the most commonly prescribed for deficiency). See GP notes below for prescribing and supply information.
- Ergocalciferol liquid 3000 units/ml (manufactured “special” (see below))
- Ergocalciferol tablets 10,000 units (250 microgram) (licensed)
- There are a range of calcium and vitamin D preparations which contain 400-800 units (10-20 micrograms) of colecalciferol or ergocalciferol
- Abidec, Dalivit and most over the counter multivitamins contain 400 units (10 micrograms) of colecalciferol or ergocalciferol in 0.6 ml which can be used for prophylaxis. This is double the licensed dose for children under 1 year of age however is safe. Abidec maybe preferred as it contains less Vitamin A. Alternatively the “healthy start” vitamins may be used.

➤ Supply issues with Vitamin D preparations

Over the last few years there have been many intermittent supply problems with vitamin D preparations including the licensed tablets which has resulted in the necessity to use manufactured “specials”. These are UK manufactured products made under a “manufacturing license” rather than the product having a full “product license”. It is however preferable to use these products to give colecalciferol or ergocalciferol rather than using the less suitable alfalcidol or calcitriol as stated above.

➤ Information for GPs on prescribing and supply of colecalciferol 3000units/ml liquid

Colecalciferol liquid 3000 units/ml is the most commonly prescribed form of vitamin D for the treatment of rickets and deficiency. This product may not be available on your EMIS or VISION computer system when prescribing. If this is the case, a handwritten prescription would suffice, ensuring you clearly state the strength and dose (in units) on the prescription. If you have any queries, please contact the PCT Medicines Management team for advice.

It is useful to know that this liquid is available as a special from the following manufacturers in case you get any queries from the community pharmacist:

Colecalciferol liquid* Cardinal Health Martindale Products Hubert Rd Brentwood Essex CM14 4LZ 0800 137 627	Ergocalciferol liquid The Specials laboratory Unit 1 Regents Drive Lower Prudhoe Industrial Estate Northumberland NE42 6PX 0800 028 4925
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** Please note that the Martindale formulation is the less expensive of these two specials and has a longer shelf life. You may wish to notify the Community Pharmacist of this (or highlight choice of manufacturer on script), however, be aware that both products may not always be available due to supply issues.*

For further information regarding manufactured specials contact:

Paediatric Pharmacy dept, ICHT, ask to speak to a pharmacist. Penny Fletcher is the Senior lead pharmacist.

Telephone: 020 3312 6046

References

Recent comprehensive review of the subject

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Zeghoud, F. (1994) Vitamin D prophylaxis during infancy: comparison of the long-term effects of three intermittent doses (15, 5, or 2.5 mg) on 25-hydroxyvitamin D concentrations. *The American Journal of Clinical Nutrition*, 60, 393.

Department of health recommendations

www.healthystart.nhs.uk

-Vitamin D and other vitamin supplements for infants and children

NICE guideline CG62 - -supplements for pregnant and breastfeeding mothers

IMPLEMENTATION

Training required for staff	NO
If yes, who will provide training	
When will training be provided?	
Date for implementation of guideline	October 1st 2009

MONITORING / AUDIT

When will this guideline be audited?	2010
Who will be responsible for auditing this guideline?	Dr Mike Coren
Are there any other specific recommendations for audit?	No

REVIEW

Who will review this guideline?	Dr Mike Coren, Consultant paediatrician
Please indicate frequency of review: Drug related guidance should be reviewed every 2 years Therapy related guidance should be reviewed every 5 years Clinical treatment guidance should be reviewed every 3 – 5 years	2 years
Date of next review	October 2011

GUIDELINE DETAIL

Start Date: (date approved by Divisional Q&S Committee)	12.11.09	
Dates approved by:	Paediatric Guidelines Group	24 Sep 09
	CPG5 Quality and Safety Board	13.11.09 (Chair's Action)
Have all relevant stakeholders (Trust sites, CPGs and departments) been included in the development of this guideline?	Via paediatric guidelines committee ICHT MMC local PCTs – to go to Westminster, H&F, K&C	
Who will you be notifying of the existence of this guidance?	Paediatric doctors ICHT, GPs, PCTs – Westminster, H&F, K&C	
Related documents:	Paediatric Endocrine guidelines 2008	
Author/further information:	Dr Nicola Bridges, Dr Mike Coren Consultant Paediatricians St Mary's Hospital 020 7886 6710 Michael.Coren@imperial.nhs.uk	
Document review history:	n/a new guideline	
Next review due	October 2011	
This guideline replaces	n/a new guideline	

INTRANET HOUSEKEEPING

Key words	Vitamin D, Colecalciferol, Cholecalciferol, Ergocalciferol, rickets
Which CPG does this belong to?	5
Which subdivision of the guidelines spine should this belong to?	Paediatrics, general / endocrine
Title for the intranet if different from the document (please note that documents sit alphabetically so should not start with "guideline for...")	Vitamin D deficiency in children and adolescents - Treatment and prophylaxis guidelines.