

South Australian Paediatric Practice Guidelines

vitamin d deficiency

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Note

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

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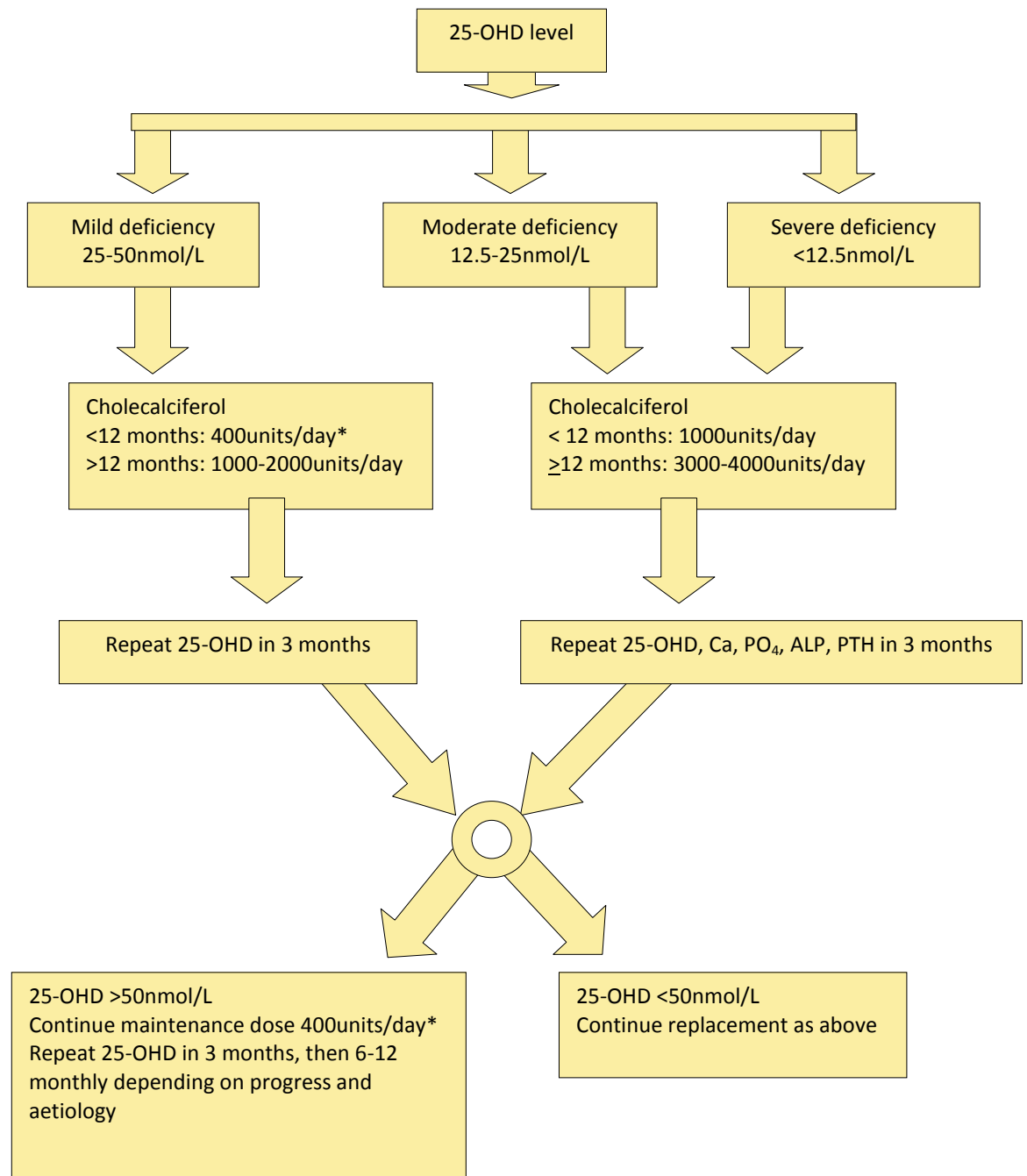
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Management summary and flowchart for vitamin D deficiency



**For convenience, consider using 500units e.g. ½ x OsteVit-D tablet once daily*

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Important points

- > Children in 'at risk' populations should be screened for vitamin D deficiency
- > Ongoing monitoring is required and care should be taken when giving high doses of vitamin D
- > Stoss therapy (high dose vitamin D) can be considered but caution must be taken in those with elevated PTH levels due to the increased risk of hypervitaminosis D leading to hypercalcaemia

Introduction

- > Vitamin D deficiency and nutritional rickets are re-emerging as common paediatric health issues
- > Sunlight is the main source of vitamin D - cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2)
- > Reduced sun exposure (e.g. use of sunscreen, wearing a veil for cultural reasons, more time spent indoors) results in decreased exposure to vitamin D from sunlight. This is particularly evident in dark skinned individuals with increased skin pigment who may require up to 6 times more sun exposure than light skinned individuals
- > Other 'at-risk' populations include infants of vitamin D deficient mothers, dietary deficiency (e.g. prolonged breast feeding), small bowel disorders (e.g. coeliac disease), pancreatic insufficiency (e.g. cystic fibrosis), chronic liver/renal disease, and medications (e.g. anticonvulsants)
- > Although vitamin D deficiency has been associated with conditions such as type 1 diabetes, respiratory illness, cardiovascular disease, altered immunity, and cancer (to name a few), there is limited outcome data to show vitamin D to be causally related in children
- > Numerous preparations of vitamin D are available over the counter and high doses are easily obtained through compounding pharmacists. The aim of this guideline is to ensure that children and adolescents with vitamin D deficiency are adequately replaced and are not given excessive doses of vitamin D

Definitions and abbreviations

VITAMIN D

- > Refers to levels of serum 25 hydroxyvitamin D (25-OHD) which reflects total body stores. Cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2) from sunlight are converted to 25-hydroxyvitamin D (25-OHD) in the liver.
- > To convert ng/ml to nmol/L multiply by 2.496

1,25 DIHYDROXYVITAMIN D

- > In the kidney, 25-OHD is hydroxylated to produce the biologically active form of vitamin D, 1,25-dihydroxyvitamin D (1,25-[OH]₂D, or calcitriol). This step requires the activity of parathyroid hormone (PTH)
- > The actions of 1,25-[OH]₂D are to: (i) enhance absorption of calcium and phosphate from the small intestine; (ii) modify serum calcium concentration both directly and through parathyroid hormone; and (iii) promote skeletal mineralisation
- > Even in severe vitamin D deficiency, levels of 1,25-[OH]₂D can be normal due to compensatory elevation of PTH. Therefore it is of no value in making the diagnosis of nutritional vitamin D deficiency but may be helpful in other less common causes of rickets

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PARATHYROID HORMONE

- > Parathyroid hormone (PTH) is produced in the parathyroid glands and is required to convert the inactive form of vitamin D (25-OHD) to the active form, 1,25-[OH]₂D
- > Elevated levels of PTH often occur in severe or chronic vitamin D deficiency, or when dietary calcium is inadequate

VITAMIN D DEFICIENCY

- > Reference ranges for children differ to those in adults. The optimal level for general health is unknown due to lack of outcome data
- > Recommended guidelines for defining vitamin D deficiency in children and adolescents:

Vitamin D status	25-OHD (nmol/L) level
Normal	≥50
Mild deficiency	26-49
Moderate deficiency	12.5-25
Severe deficiency	<12.5

PO₄ = PHOSPHATE

ALP = ALKALINE PHOSPHATASE

- > ALP is produced by bone and is elevated in conditions of increased bone turnover. This is often associated with calcium deficiency, vitamin D deficiency, and elevated PTH.

Assessment

Risk factors for vitamin D deficiency

- > Infant of vitamin D deficient mother
- > Dietary deficiency e.g. prolonged breastfeeding. Minimal vitamin D is available in the diet (breast milk 25 units/L, milk formula 400 units/L, oily fish, eggs, butter, margarine 50-100 units/d)
- > Dark skin colour – Individuals with increased skin pigment may require up to 6 times more sun exposure than light skinned individuals
- > Reduced sun exposure (e.g. use of sunscreen, extent of clothing covering body)
- > Small bowel disorders (e.g. coeliac disease, inflammatory bowel disease)
- > Pancreatic insufficiency (e.g. cystic fibrosis)
- > Chronic liver/renal disease
- > Medications (e.g. anticonvulsants, rifampicin, isoniazid, chronic glucocorticoids)
- > Obesity (reduces bioavailability of vitamin D)
- > Disabled children (often have poor sun exposure and increased anticonvulsant use)

Common presentations of vitamin D deficiency

- > Hypocalcaemic seizures or tetany, often in the neonatal period
- > Incidental finding on screening investigations
- > Vitamin D deficient rickets - swelling of wrists and ankles, rachitic rosary, genu varum/valgum, frontal bossing, limb pain and fracture, craniotables
- > Other less common presentations - myopathy, delayed fontanelle closure, delayed tooth eruption, enamel hypoplasia, raised ICP, brown tumour (osteoclastoma) secondary to hyperparathyroidism

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Investigations after confirmation of vitamin D deficiency

- > **Mild deficiency** (25OHD 25-50nmol/L): no further investigations are required unless symptomatic
- > **Moderate/Severe deficiency** (25OHD<25nmol/L): the following blood investigations should be considered.
 - > Blood: calcium, phosphate, ALP. Check PTH if has clinical rickets or history suggests low calcium intake
 - > If patient is <1 month old, maternal blood should also be taken
 - > Calcium and phosphate may be normal or low, ALP may be elevated, PTH may be normal or high
 - > Prolonged deficiency may result in high phosphate due to PTH resistance
 - > Infants of vitamin D deficient mothers may have high phosphate due to inadequate PTH release or inadequate renal responsiveness to PTH
- > Radiology: If there is a clinical suspicion of vitamin D deficient rickets, xrays of the wrists or knees should be requested (cupping, splaying, fraying, coarse trabecular pattern of metaphysis, osteopaenia, fractures)
- > If the results do not suggest nutritional vitamin D deficiency, refer to the following table for a differential diagnosis. If a cause other than vitamin D deficiency is suspected then appropriate investigation and management for that condition should be instituted

Differential diagnosis for rickets and hypocalcaemia: laboratory

Causes	Ca	PO ₄	ALP	PTH	25OHD	1,25OHD
Vitamin D deficiency	↓ / N	↓ / N	↑	N / ↑	↓	↓ / N
Hypoparathyroidism	↓	↑	↓ / N	↓ / N	N	↓
Pseudohypoparathyroidism	↓	↑	N / ↑	↑	N	↓
Vitamin D Resistant Rickets	↓	↓	↑	↑	N	↑
Familial Hypophosphataemic Rickets	N	↓	↑	N	N	↓ / N
Vitamin D Dependent Rickets	↓	↓	↑	↑	N	↓

results

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Management

RECOMMENDED VITAMIN D REPLACEMENT

Management summary

Link to summary at beginning of guideline

Stoss therapy (high dose vitamin D therapy)

- > High dose vitamin D therapy (Stoss therapy) can be considered in patients with poor compliance, recalcitrant vitamin D deficiency or vitamin D deficient rickets
- > There are many stoss regimens with doses ranging from 100,000–600,000 units given as single or divided doses. There is currently no consensus on the most effective and safest regimen and until this is studied further, a conservative approach is recommended
- > Vitamin D toxicity (25-OHD > 220nmol/L) may result in hypercalcaemia.. The main symptoms of vitamin D overdose are those of hypercalcaemia: anorexia, nausea and vomiting can occur, followed by polyuria, polydipsia, weakness, nervousness, pruritus, renal stones and renal failure
- > **Stoss therapy should not be given if the PTH is elevated due to the increased risk of vitamin D toxicity. Elevated PTH is more likely to be seen if 25-OHD <25nmol/L and/or dietary calcium is inadequate**
- > A concentrated preparation of vitamin D (40,000 units/mL) is available from the Women's and Children's Hospital pharmacy
- > Other preparations are available through compounding pharmacists but doses greater than 1000 units (25mcg) require a prescription as specified by the National Poisons Standard for 2010 (Therapeutic Goods and Administration, Schedule 4 prescription medication)
- > To replenish vitamin D stores using stoss therapy in **mild deficiency** (25OHD 25-50nmol/L):
 - > <12 months – 40,000units (1mL) orally as a single dose
 - > >12 months – 160,000units (4mL) orally as a single dose
- > To replenish vitamin D stores using stoss therapy in **moderate to severe deficiency** (25OHD less than 25nmol/L):
 - > <12 months – 80,000units (2mL) orally as a single dose
 - > >12 months – 160,000units (4mL) orally as a single dose and consider repeat dosing in 6 weeks
- > Repeat doses can be given 3-12 monthly depending on the clinical situation.
- > Calcium, phosphate and ALP should be checked in 2 months, and 25-OHD should be re-measured in 3 months
- > Care in dosing and monitoring is essential
- > Simultaneous calcium supplementation should be considered if dietary intake is inadequate due to the risk of hypocalcaemia from remineralisation of bone

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Calcium supplementation

- > Low dietary calcium intake contributes to rickets and low bone density and may also be a cause for raised PTH levels.
- > If dietary intake is poor, calcium supplementation is recommended
- > **For calcium preparations, see [APPENDIX 1](#)**

Recommended daily calcium intake

Age	Calcium (mg/day)
0-6 months	200
6-12 months	260
1-3 years	500-700
4-8 years	800-1000
9-18 years	1100-1300

Exposure to sunlight

- > A balance needs to be struck between sufficient sun exposure and minimising the risk of skin cancer. No paediatric data is available but in adults the recommended daily sun exposure time in Australia ranges from 5 min in summer to 40 min in winter. Literature from the US suggests 5-30 min between the hours of 10am-3pm, 2 times a week

Breastfed infants

- > Breastfed infants of veiled/dark-skinned/vitamin D deficient mothers should be given 400 units vitamin D (Pentavite infant drops 0.45mL) daily until at least 12 months of age

Individual cases

- > Individual cases may require modification of above guidelines
- > Mild vitamin D deficiency associated with underlying medical conditions such as malabsorption, low bone density, or elevated PTH, may require higher doses of vitamin D

Follow-up

- > Follow-up should be with the General Practitioner in mild cases with an obvious cause, or General Paediatrician if other concerns
- > If vitamin D deficiency or rickets does not resolve after adequate treatment or in severe or unexplained cases, the child should be investigated for a malabsorptive disorder or a genetic rachitic disorder. Referral to a paediatric gastroenterologist or endocrinologist should be considered

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Appendix 1 vitamin & calcium preparations

Cholecalciferol single ingredient preparations

Strength	Formulation	Brand Name
1000units	Capsules	Blackmores Vitamin D3
1000units	Capsules	BioCeuticals D3 Capsules
1000units	Capsules (liquid)	Ostelin Vitamin D
1000units	Capsules (liquid)	Vita-D Gel Caps
1000units	Capsules	Swisse Vitamin D
1000units	Tablets	*OsteVit-D
1000units	Tablets	YourHealth D3-1000
333.3units/0.038mL	Oral Drops	BioCeuticals D3 Oral Drops
1000units/0.04mL	Oral Drops	BioCeuticals D3 Oral Drops Forte
1000units/0.2mL	Oral Liquid	OsteVit-D Liquid
400units/0.5mL	Oral Liquid	*Manufactured by WCH pharmacy
80,000units/2mL	Oral Liquid	*"Stoss" Therapy manufactured by WCH pharmacy
400units/0.45mL	Oral Drops	*Pentavite Infant Drops (maintenance only)
440units	Capsules	*VitABDECK (maintenance only)

*stocked at WCH pharmacy

Calcium single ingredient preparations

Strength	Formulation	Brand Name
250mg calcium (as citrate)	Tablet	Citracal
500mg calcium (as carbonate)	Chewable tablet (dispersed in water)	*Cal-Sup Chewable Spearmint
600mg calcium (as carbonate)	Tablet	CAL-600
600mg calcium (as carbonate)	Tablet	Calci-Tab 600
600mg calcium (as carbonate)	Tablet	*Caltrate
650mg calcium (carbonate)	Chewable tablet	Cal-Sup Chewable Calcium Chocolate
1000mg calcium (as lactate gluconate, carbonate)	Tablet (dissolved in water)	Sandocal

*stocked at WCH pharmacy

Calcium and cholecalciferol preparations

Cholecalciferol	Calcium	Formulation	Brand Name
100units	350mg calcium (as phosphate)	Chewable tablet	Blackmores Bio Calcium Chewable
100units	350mg calcium (as phosphate)	Tablet	Blackmores Bio Calcium

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100units	600mg calcium (as carbonate)	Tablet	Nature's Way Total Calcium Plus
400units	600mg calcium (as carbonate)	Tablet	Caltrate with Vitamin D
500units	315mg calcium (as citrate)	Tablet	Citracal + D
500units	600mg calcium (as carbonate)	Tablet	Ostelin Vitamin D & Calcium
500units	600mg calcium (as carbonate)	Tablet	Ostevit-D & Calcium Caplets
500units	600mg calcium (as carbonate)	Chewable tablet	Ostevit-D & Calcium Chewable Tablets
500units	650mg calcium (as carbonate)	Chewable tablet	Cal-Sup Calcium + Vitamin D Chewable
880units	1000mg calcium (as carbonate)	Effervescent granules	CALVID Effervescent granules
1000units	600mg calcium (as carbonate)	Chewable tablet	Ostevit-D & Calcium One-A-Day Chewable Tablet

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A literature search was performed on www.pubmed.com using the terms “vitamin D deficiency” “child” “adolescent” “pediatric” “stoss” “management” “treatment”.

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Several guideline sites were consulted for existing guidelines regarding “vitamin D deficiency” and “children”, including:

- > National Guideline Clearing House <http://www.guideline.gov/>
- > National Institute for Health and Clinical Excellence (NICE) <http://guidance.nice.org.uk/CG/published>
- > New Zealand Guidelines Group <http://www.nzgg.org.nz/>
- > Scottish Intercollegiate Guidelines network <http://www.sign.ac.uk/guidelines/published/>
- > British Medical Journal <http://bmj.bmjournals.com/cgi/collection/guidelines>
- > National Institute of Clinical Studies <http://www.nhmrc.gov.au/nics/index.htm>
- > National Health and Medical Research Council <http://www.nhmrc.gov.au/publications/index.htm>
- > Royal College of Nursing Guidelines <http://www.rcna.org.au/Default.aspx?SiteSearchID=360&ID=/results>
- > Royal Australian College of Physicians <http://www.racp.edu.au/page/search>
- > NHS National Library of Guidelines <http://www.library.nhs.uk/guidelinesfinder/>
- > Starship Children's Hospital http://www.starship.org.nz/index.php/pi_pageid/1065
- > John Hunter Hospital intensive Care Guidelines <http://www.philippelefevre.com/JHH-ICU-guidelines/index.php>
- > Royal Children's Hospital – Melbourne Clinical Practice Guidelines <http://www.rch.org.au/clinicalguide/>
- > Princess Margaret Hospital Clinical Practice Guidelines http://www.pmh.health.wa.gov.au/development/manuals/clinical_practice_guidelines/

The following guideline was found to be suitable

- > RCH guidelines http://www.rch.org.au/immigranthealth/resources.cfm?doc_id=10782

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Parenting and Child Health. Women's and Children's Health Network. Available at URL:

<http://www.cyh.com/HealthTopics/HealthTopicDetails.aspx?p=114&np=304&id=18>

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