Vitamin D and Iron treatment

Definitions of vitamin D status	
Severe deficiency	< 12.5 nmol/L – test for calcium and liver function
Moderate deficiency	12.5 – 29 nmol/L– test for calcium and liver function
Mild deficiency	30 – 49 nmol/L
Sufficient	>= 50 nmol/L
Elevated	> 250 nmol/L

Age	Level	Treatment (oral doses D3)
< 3 months (term) ***Discuss with Paediatrician prior to Treatment***	**Mild deficiency** 30 – 49 nmol/L	Vitadol C 10 drops per day for 3 months
	Repeat bloods after 6 months	
	Moderate or severe deficiency < 30 nmol/L	Vitadol C 10 drops per day for 3 months
	Repeat bloods after 3 or 6 months	
3 – 12 months	**Mild deficiency** 30 – 49 nmol/L	Vitadol C 10 drops per day for 3 months
	Repeat bloods after 6 months	
	Moderate or severe deficiency < 30 nmol/L	50,000 IU and review after 3 months, consider repeating dose
	Repeat bloods after 3 or 6 months	
1 – 18 years	**Mild deficiency** 30 – 49 nmol/L	150,000 IU stat
	Repeat bloods after 6 months	
	Moderate or severe deficiency < 30 nmol/L	150,000 IU stat and repeat at 6 weeks
	Repeat bloods after 3 or 6 months	

Iron Deficiency Investigations and Diagnosis: Infants age<3 years

Iron deficiency exists when **Serum Ferritin is <10 mcg/l.**

- It is strongly indicated by low MCV <72fl + High RDW >14.0%.
- Give dietary advice on iron rich foods and the avoidance of tea and whole unmodified cows milk before the age of 12 months. Iron medication is optional.
- Repeat bloods at **6** months

Iron deficiency anaemia exists if in addition **Haemoglobin is <110 g**/l.

- Ferrous sulphate syrup 3 mg/kg/day of elemental iron as a single daily dose for three months.
- Repeat bloods at **3** months

Prevention and treatment of infant and childhood vitamin D deficiency in Australia and New Zealand: a consensus statement

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ABSTRACT

- Vitamin D deficiency has re-emerged as a significant paediatric health issue, with complications including hypocalcaemic seizures, rickets, limb pain and fracture.
- A major risk factor for infants is maternal vitamin D deficiency. For older infants and children, risk factors include dark skin colour, cultural practices, prolonged breastfeeding, restricted sun exposure and certain medical conditions.
- To prevent vitamin D deficiency in infants, pregnant women, especially those who are dark-skinned or veiled, should be screened and treated for vitamin D deficiency, and breastfed infants of dark-skinned or veiled women should be supplemented with vitamin D for the first 12 months of life.
- Regular sunlight exposure can prevent vitamin D deficiency, but the safe exposure time for children is unknown.
- To prevent vitamin D deficiency, at-risk children should receive 400 IU vitamin D daily; if compliance is poor, an annual dose of 150 000 IU may be considered.
- Treatment of vitamin D deficiency involves giving ergocalciferol or cholecalciferol for 3 months (1000 IU/day if < 1 month of age; 3000 IU/day if 1–12 months of age; 5000 IU/day if > 12 months of age).
- High-dose bolus therapy (300 000–500 000 IU) should be considered for children over 12 months of age if compliance or absorption issues are suspected.

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Vitamin D deficiency and nutritional rickets are again emerging as major paediatric health issues in Australia and New Zealand.[1-5] The major cause is reduced synthesis of vitamin D_3, with dark-skinned individuals or those who remain covered when outdoors for cultural reasons being most at risk. In this consensus statement, we review vitamin D metabolism and the risk factors for, and features of, vitamin D deficiency in infants, children and adolescents, and provide recommendations for treatment and subsequent prophylaxis.

Vitamin D and metabolites

"Vitamin D" (calciferol) refers to both cholecalciferol (vitamin D_3) and ergocalciferol (vitamin D_2). Cholecalciferol is produced by the action of ultraviolet B light (UVB; wavelength, 290–320 nm) on 7-dehydrocholesterol in the skin of humans, and is the form of vitamin D found in oily fish. Ergocalciferol is formed when ultraviolet (UV) light irradiates the fungal steroid, ergosterol. Very little ergocalciferol is available naturally in food, but it is the most readily available supplemental vitamin D. Once made in the skin or ingested, vitamin D is transported to the liver where it is hydroxylated into 25-hydroxyvitamin D (25-OHD, or calcidiol), the major circulating form of vitamin D. The concentration of 25-OHD in the serum reflects total body stores of vitamin D, and is used to assess vitamin D status. In the kidney, 25-OHD is hydroxylated to produce the biologically active form of vitamin D, 1,25-dihydroxyvitamin D (1,25-$[OH]_2$D, or calcitriol). The actions of 1,25-$(OH)_2$D 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.[6]

Vitamin D sources in Australia and New Zealand

Sunlight

The major source of vitamin D (more than 80%) in Australia and New Zealand is skin exposure to sunlight (UVB radiation).[7] Sun exposure also causes 99% of non-melanoma skin cancers and 95% of melanoma in Australia.[8] Thus, a balance needs to be struck between sufficient sun exposure to maintain adequate vitamin D_3 production and minimising the risk of skin cancer. No Australian or New Zealand paediatric data are available on the duration of UVB radiation exposure required to maintain adequate levels of vitamin D. Despite this, a recent Australian position statement on the risks and benefits of sun exposure advised that babies would receive enough UVB to maintain healthy vitamin D concentrations, even using sun protection, if small amounts of skin were exposed to sunlight for very brief periods before 10:00 and after 16:00 hours.[9] Adult data on the duration of sun exposure to hands, arms and face and vitamin D_3 production have recently been published.[10] Given the different body proportions of children and the reduced capacity to synthesise vitamin D with ageing,[11] children would likely require less sun exposure to produce an equivalent amount of vitamin D_3 to that of adults. Further, those at greatest risk of vitamin D deficiency in our community — individuals with increased skin pigment — may require up to six times the sun exposure to achieve the same increase in vitamin D concentrations as individuals with light-coloured skin.[12] Glass and sunscreen absorb UVB radiation, which decreases vitamin D_3 production,[13] and may increase the likelihood of vitamin D deficiency,[14] especially in individuals with pigmented skin.

Diet

An infant's vitamin D concentration reflects that of the mother.[15] If a mother is vitamin D replete, her infant has an 8–12 week store of vitamin D.[15] Human milk from vitamin D replete women has a vitamin D concentration of only 25 IU (< 1 μg) per litre.[16,17] Most commercial baby formulas in Australia and New Zealand contain 400 IU (10 μg) of vitamin D_3 per litre. An intake of 500 mL of baby formula per day therefore provides 200 IU (5 μg) of vitamin D, which is the amount recommended by the American Academy of Pediatrics as an adequate intake for healthy infants and children.[18] Milk supplemented with vitamin D_3 (up to 200 IU per 250 mL) has

recently become available. However, the average daily intake of vitamin D by Australian adults from sources such as oily fish, eggs, and butter or margarine remains at only 50–100 IU (1.2–2.6 μg).[7] So, without adequate sun exposure, consumption of vitamin D-fortified milk or vitamin D supplementation, it is difficult for pregnant and lactating mothers, breastfed babies, or children to obtain an adequate daily vitamin D intake from diet alone.

Definitions of vitamin D deficiency

Serum 25-OHD concentration provides the best indicator of vitamin D status, and should be used when testing for deficiency states (normal concentration, > 50 nmol/L).[10] The concentration of 1,25-$(OH)_2$D must not be used, as it may be elevated even in severe vitamin D deficiency. Different 25-OHD assays give different results, with some not determining 25-OHD_2 (ergocalciferol) as well as they do 25-OHD_3 (cholecalciferol).[19] This may result in spuriously reduced 25-OHD results in children supplemented with ergocalciferol.

Mild vitamin D deficiency: Serum 25-OHD concentration of 25–50 nmol/L. Serum levels over 50 nmol/L prevent secondary hyperparathyroidism[14,20] and elevated alkaline phosphatase levels.[21,22]

Moderate vitamin D deficiency: Serum 25-OHD concentration of 12.5–25 nmol/L. The incidence of hypocalcaemia and rickets increases with moderate deficiency.[3]

Severe vitamin D deficiency: Serum 25-OHD concentration less than 12.5 nmol/L. Vitamin D concentrations less than 12.5 nmol/L are seen in over 70% of children with rickets and over 90% of children with hypocalcaemia.[3]

Vitamin D is a potent steroid hormone that may have important physiological actions outside mineral homeostasis, including the regulation of cell differentiation and proliferation and immune function.[23,24] Therefore, defining vitamin D sufficiency on the basis of calcium homeostasis and bone turnover alone may not reflect all its potential actions.

Infants and children at risk of vitamin D deficiency

Current Australian and New Zealand Paediatric Surveillance Unit (APSU and NZPSU) surveys examining the incidence of and risk factors for vitamin D-deficiency rickets will improve our understanding of paediatric vitamin D deficiency. From the current data, risk factors associated with vitamin D deficiency in infants and children can be broken down into three broad areas (Box 1).[1-3,5,10,21,25,26] It is likely that multiple factors apply in a single affected individual. For example, recent migrants with a refugee background from Africa and the Middle East are at risk of vitamin D deficiency because of their dark skin, poor nutrition, reduced sunlight exposure and the prolonged breastfeeding of infants.

Features of vitamin D deficiency

Vitamin D deficiency has both osseous and non-osseous sequelae (Box 2). The most recognised are the osseous complications of rickets and osteomalacia. Rickets results from poor osteoid mineralisation adjacent to the growth plate, and osteomalacia from inadequate osteoid mineralisation at sites of bone modelling and remodelling.[27] While rickets is only seen during growth, with a peak incidence during the periods of rapid growth in early infancy and early puberty,[27] osteomalacia is common to both children and adults.

1 Causes of vitamin D deficiency in children and adolescents

- Reduced intake or synthesis of vitamin D_3
  - ➢ Being born to a vitamin D-deficient mother; most commonly veiled or dark-skinned women, or women of Asian background who actively avoid exposure to sunlight
  - ➢ Prolonged breastfeeding
  - ➢ Dark skin colour
  - ➢ Reduced sun exposure — veiled or modest clothing, chronic illness or hospitalisation, intellectual disability, and excessive use of sunscreen
  - ➢ Low intake of foods containing vitamin D
- Abnormal gut function or malabsorption
  - ➢ Small-bowel disorders (eg, coeliac disease)
  - ➢ Pancreatic insufficiency (eg, cystic fibrosis)
  - ➢ Biliary obstruction (eg, biliary atresia)
- Reduced synthesis or increased degradation of 25-OHD or 1,25-$(OH)_2$D
  - ➢ Chronic liver or renal disease
  - ➢ Drugs: rifampicin, isoniazid and anticonvulsants

25-OHD = 25-hydroxyvitamin D or calcidiol.
1,25-$(OH)_2$D = 1,25-dihydroxyvitamin D or calcitriol. ◆

2 Osseous signs of vitamin D deficiency (common to less common)

- Swelling of wrists and ankles
- Rachitic rosary (enlarged costochondral joints felt lateral to the nipple line)
- Genu varum, genu valgum or windswept deformities of the knee
- Frontal bossing
- Limb pain and fracture
- Craniotabes (softening of skull bones, usually evident on palpation of cranial sutures in the first 3 months)
- Hypocalcaemia — seizures, carpopedal spasm
- Myopathy, delayed motor development
- Delayed fontanelle closure
- Delayed tooth eruption
- Enamel hypoplasia
- Raised intracranial pressure
- Brown tumour secondary hyperparathyroidism

Radiological features

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

Non-osseous features of vitamin D deficiency include dilated cardiomegaly[28] and marrow fibrosis with pancytopenia or microcytic hypochromic anaemia. Note the co-existence of vitamin D deficiency and iron deficiency.[3] Other possible associations include disregulation of immune function and cellular differentiation and proliferation, and type 1 diabetes.[23,24,29]

Biochemical features of vitamin D deficiency

Vitamin D deficiency results in hypocalcaemia, secondary hyperparathyroidism, hypophosphataemia and elevated alkaline phosphatase titres.[3] Many variations on this pattern may be observed,

3 Management of vitamin D deficiency

Age	Hypocalcaemia*		Vitamin D deficiency†		Monitoring
	Seizure	No seizure	Acute	Maintenance	
< 1 month 1–12 months > 12 months	10% calcium gluconate: 0.5 mL/kg (max 20 mL) intravenously over 30–60 minutes.	Calcium: 40–80 mg/kg/day (1–2 mmol/kg/day) orally in 4–6 doses, and Calcitriol: 50–100 ng/kg/day orally in 2–3 doses until serum calcium level is > 2.1 mmol/L.	Vitamin D: 1000 IU (25 μg) daily for 3 months. Vitamin D: 3000 IU (75 μg) daily for 3 months, or 300 000 IU (7500 μg) over 1–7 days. Vitamin D: 5000 IU (125 μg) daily for 3 months, or 500 000 IU (15 000 μg) over 1–7 days.	Vitamin D: 400 IU (10 μg) daily or 150 000 IU (3750 μg) at the start of autumn.‡	**1 month:** Serum calcium and alkaline phosphatase. **3 months:** Serum calcium, magnesium, phosphate, alkaline phosphatase, calcidiol, parathyroid hormone. Wrist x-ray to assess healing of rickets. **Annual:** Calcidiol.

* Aim of therapy is to stop seizure activity, not to normalise serum calcium.[27] If seizures persist, a repeat bolus should be given and a calcium infusion of up to 4 mmol/kg/day may be required to maintain normocalcaemia. Calcium may be used intravenously to treat hypocalcaemia in the absence of seizures, but the risk of calcium burns and scarring must be considered. 1α-hydroxyvitamin D_3 is an alternative to calcitriol at 60–120 ng/kg/day. † Ergocalciferol (vitamin D_2) or cholecalciferol (vitamin D_3). ‡ This is high-dose vitamin D therapy (stoss therapy), and hypercalcaemia and nephrocalcinosis have been reported with such therapy in well nourished children.[31]
Calcitriol = 1,25-dihydroxyvitamin D. Calcidiol = 25-hydroxyvitamin D. ◆

4 Recommended daily intake of calcium for healthy children[33]

Age	Adequate intake of calcium (mg/day)
0–6 months	210
6–12 months	270
1–3 years	500
4–8 years	800
9–18 years	1300

with elevated alkaline phosphatase titres being seen most commonly. Not infrequently, infants with profound hypocalcaemia and secondary hyperparathyroidism have normal or elevated serum phosphate levels, which may represent parathyroid hormone resistance at both the bone and renal level from prolonged vitamin D deficiency.[3,30] This can lead to confusion with hypoparathyroidism or pseudohypoparathyroidism, as serum calcium and phosphate concentration results are frequently available before those for vitamin D and parathyroid hormone (PTH).[3] Concentrations of calcitriol (1,25-$[OH]_2$D) may be low, normal or high at the time of diagnosis, and are of no value in making the diagnosis.

Recommendations for treating moderate to severe vitamin D deficiency

Both ergocalciferol (25-OHD_2) and cholecalciferol (25-OHD_3) are effective therapy for vitamin D deficiency, with ergocalciferol being the most widely available preparation (Box 3). Replenishment of vitamin D stores requires a total vitamin D dose of 100 000–500 000 IU, depending on age (Box 3).[32] Treatment with calcitriol (1,25-$[OH]_2$D) is only indicated for hypocalcaemia (see below). Calcium supplementation is recommended if dietary intake is poor (Box 4). It should be noted that dietary calcium deficiency is a major risk factor for the development of rickets in Africa, and should be considered in the migrant population.[31] If vitamin D deficiency or rickets does not resolve after adequate treatment, the child should be investigated for a malabsorption disorder (eg, coeliac disease) or a genetic rachitic disorder (eg, X-linked hypophosphataemic rickets).

The most serious consequence of vitamin D deficiency is hypocalcaemic seizure. While most common in infants aged less than 6 months, seizures can occur at any age. Bolus intravenous calcium is indicated to treat seizures and carpopedal spasm. A calcium infusion may be required if control is not achieved with 1 to 2 bolus doses (Box 3). Care must be taken when administering calcium intravenously, as extravasation results in severe chemical burns to the skin and subcutaneous tissues. Although it may be argued that 1,25-$(OH)_2$D production after administration of 25-OHD would be sufficient to reverse hypocalcaemia, it is our opinion that either calcitriol or 1α-hydroxyvitamin D_3 be coadministered until the serum calcium concentration is within normal limits. Children should be kept under close observation until the serum calcium concentration is over 1.8 mmol/L.

While vitamin D deficiency is the most common cause of hypocalcaemia after the first 4 days of life, other causes include dietary phosphate load, hypomagnesaemia, transient hypoparathyroidism, transient PTH resistance and congenital hypoparathyroidism.[34] Levels of PTH and magnesium should therefore be assessed during the initial investigation of paediatric hypocalcaemia.

Stoss therapy

High-dose vitamin D therapy (stoss therapy) is an effective method for treating established or recalcitrant vitamin D deficiency.[31,35] It involves oral or intramuscular administration of the total treatment dose of vitamin D (cholecalciferol or ergocalciferol), 300 000 IU (7500 μg) to 500 000 IU (12 500 μg), as a single dose, or two to four divided doses.[36] The interval between doses can vary from days to several weeks

Consensus process

This consensus statement was developed by a working group which included members of the Australasian Paediatric Endocrine Group, Paediatric Bone Australasia, migrant health paediatricians, obstetricians, public health specialists and a member of the working group responsible for the adult guidelines on vitamin D and bone health. All authors had an active role in the development of the statement and agree to its recommendations. Treatment guidelines were arrived at through a combination of published best practice and local experience. ◆

depending on the protocol followed. There are many stoss therapy regimens, and further study is required to finalise the most effective regimen and ensure safety. After stoss therapy, the biochemical follow-up recommended is similar to that for daily dosing.

In Australia, concentrated vitamin D is not commercially available, limiting stoss therapy. In New Zealand, Calciferol Strong (50 000 IU cholecalciferol; PSM Healthcare, Auckland, NZ) — an oral preparation — is available.[10] High-dose vitamin D for intramuscular injection effectively treats vitamin D deficiency secondary to malabsorption,[35] but is not available in Australia or New Zealand. To facilitate the use of stoss therapy, a wider variety of vitamin D preparations are required in Australia and New Zealand.

Prevention of vitamin D deficiency

Infants (< 12 months)

The most important factor for the development of vitamin D deficiency in infants is maternal vitamin D status.[26,27] All pregnant women, especially those who are veiled or dark-skinned, should have their serum 25-OHD concentration evaluated during the first trimester of pregnancy. If they are moderately to severely vitamin D deficient, pregnant women should be treated with 3000–5000 IU daily until the serum 25-OHD concentration is over 50 nmol/L.[10] These preparations should not contain vitamin A, which may lead to fetal toxicity. After this serum concentration is achieved, they should receive 400 IU daily, as should women with a mild deficiency.[10,37] Routine vitamin D supplementation of all pregnant women is a controversial subject,[37,38] and until local data are available on the incidence of vitamin D deficiency, this cannot be recommended.

We endorse breastfeeding for all infants. However, breast milk is a poor source of vitamin D.[16,17] The American Academy of Pediatrics recommends supplementing all breastfed infants with vitamin D until they are weaned to 500 mL per day of vitamin D-fortified formula.[18] While similar recommendations cannot be made in Australia and New Zealand until data are available on the vitamin D status of "low-risk" infants,[26] breastfed infants of veiled or dark-skinned mothers should be supplemented with 400 IU vitamin D daily (eg, 0.45 mL Pentavite; Roche Consumer Health, Sydney, NSW) until at least 12 months of age.[31] Other vitamin D preparations may be available at hospital pharmacies.

Toddlers and adolescents

While most healthy children in Australia and New Zealand receive enough sunlight exposure to maintain adequate vitamin D levels, a significant number living in the more temperate zones develop mild vitamin D deficiency during winter.[21] In Tasmania, 8% of 8-year-old and 68% of 16-year-old children have serum 25-OHD concentrations less than 50 nmol/L.[21,22] New Zealand data are comparable, with 50% of all children in all age groups with serum 25-OHD concentrations less than 50 nmol/L. If children can be encouraged to participate in regular outdoor activities, blanket vitamin D supplementation for children and adolescents is not warranted.

Children who are dark-skinned, veiled, exposed to reduced sunlight or who have an underlying medical condition, should receive 400 IU vitamin D daily (eg, be given a multivitamin) to prevent vitamin D deficiency.[18] Siblings of a child diagnosed with vitamin D deficiency should be screened.[3] The help of local community and cultural groups will be of major importance in ensuring the dissemination of these prevention strategies.

Competing interests

None identified.

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Low Vitamin D

There are two published Australian position statements on Vitamin D in adults and in infants/children[1, 2]. 'Vitamin D' refers to both D3, cholecalciferol (produced in the skin) and D2, ergocalciferol (the form in food). New American Academy of Pediatrics guidelines on Vitamin D intake were published in October 2008 recommending an *increased* intake of 400 IU daily for all infants, children and adolescents.

Guidelines for high dose prescribing in primary care in Victoria are available.
Most Vitamin D is made in the skin from the action of sunlight. People with darker coloured skins may need to spend up to 6 times as long in the sun (as someone with light coloured skin) to make an adequate quantity of Vitamin D[3], which may be up to 5 hours a day in winter (with arms and face exposed)[4]. The amount of sunlight required for adequate Vitamin D in children is unclear[2]. Most Australians only get 10 - 25% of their Vitamin D from diet. Vitamin D is not found in many foods; some types of fish and liver contain reasonable amounts, there is a small quantity in eggs. Some dairy products are fortified with Vitamin D (e.g. milk, all forms of margarine).

Risk factors for low Vitamin D include:

- Dark skin colour
- Reduced sun exposure (covering clothing, time inside)
- Duration of time since migration
- Breast feeding with other risk factors present (skin colour, maternal vitamin D levels low, time inside)

Medications that induce liver enzymes (e.g. anticonvulsants, isoniazid) can increase breakdown of vitamin D; reducing serum levels.

Up to 90% of the African population in Melbourne will have low Vitamin D. The normal level for Vitamin D in children is 50 - 160 nmol/L; deficiency is defined as levels < 25 nmol/L, insufficiency as levels 25 - 50 nmol/L. In adults a higher cutoff for normal levels is used; optimal levels are > 75 nmol/L. Biochemical rickets is defined as a raised alkaline phosphatase (ALP) +/- raised parathyroid hormone (PTH). Typically low Vitamin D is associated with high ALP, low Ca, secondary hyperparathyroidism, low phosphate, but this may vary.

Note: Vitamin D 1 mcg = 40 IU. To convert ng/ml to nmol/L multiply by 2.5

Assessment

History

- Low-grade bony and muscular pain and fatigue with exercise.
- Dairy intake and symptoms of low calcium (muscle cramps).
- Hypocalcaemic seizures or stridor may be a problem in infants < 6 months old, they are rare beyond this age
- Sunscreen use and time spent outside

Exam

- ***Rickets*** - deformity in *growing* bones due to failure of mineralisation of osteoid.
    - Peaks of incidence in infancy and at puberty.
    - Deformity reflects the age/growth of the child when the onset of low Vitamin D occurred, it can be in any direction.Consider other causes if asymmetrical.
    - Look for bony deformity, splaying of wrists and ankles, bossing, delayed fontanel closure (normally closed by 18 months, 100% by 23 - 26 months), rosary (rare).
    - Deformity usually corrects after correction of low Vitamin D.
- ***Other osseus effects*** - delayed dentition (no teeth by 9 months, no molars by 14 months), enamel hypoplasia.
- ***Non osseus effects*** - myopathy.

Osteomalacia - accumulation of unmineralised osteoid at sites of bone remodelling (both adults and children)

Screening

There is very little evidence around frequency of screening, and families are often unwilling to have multiple blood tests. Some commercial assays do not measure D2 as well as D3; although D2 is no longer commonly used in supplements.

A reasonable approach is to:

- Screen all people at risk of low vitamin D
    - Screen all children within a family (and ideally parents).
    - Check Vitamin D levels, calcium, phosphate and ALP
    - Perform further investigations if there is clinical rickets (PTH, renal function, X-ray wrist).
    - Check PTH if there is a history suggestive of low calcium intake (even without bony deformity) or if Vitamin D level is < 25 nmol/L.

- In recent arrivals: if the initial Vitamin D level is normal, repeat at the end of the first winter in Australia.
- Repeat bloods (Vitamin D, ALP, Ca, PO4 and PTH) 3 months post treatment if clinical rickets or levels in the deficient range (< 25 nmol/L).
- Levels at the start and end of winter can be useful to make a clinical judgement on frequency of dosing.
- Use clinical photography to monitor bony deformity.
- If an X-ray wrist is performed there is limited value in repeating it within 12 months.

Management

- Symptomatic rickets/hypocalcaemia (including tetany, stridor, seizures) requires hospital admission for Vitamin D and intravenous calcium infusion, do *not* give Vitamin D in the outpatient setting to this group.
- Children with clinical rickets or abnormal serum calcium require specialist assessment
- RCH uses cholecalciferol (D3) 100,000 IU/ml in olive oil. The solution is light and temperature sensitive and degrades to inactive vitamin D. The shelf life is only 3 months if not kept in the fridge (with reduced potency at this time). It should be 90% potent at 3 months if stored < 4 degrees Celsius, but olive oil consolidates at this temperature.

In children aged > 12 months

- **Treat insufficiency** (Vitamin D = 25 - 50 nmol/L) with 150,000 IU oral then dosing 3 - 12 monthly depending on clinical situation.
  - A single dose raises Vitamin D levels by ~ 30 nmol/L but this varies.
  - Unpublished pharmacokinetic data on this solution in adults suggests giving doses at 0 and 6 weeks corrects low levels and does not cause toxicity.
- **Treat deficiency** (Vitamin D < 25 nmol/L) with 150,000 IU oral and consider repeat dosing in 6 weeks then dosing 3 - 12 monthly depending on clinical situation.

In children aged < 12 months

- **Treat insufficiency** (Vitamin D 25 - 50 nmol/L) with 50,000 IU oral then dosing 3 - 12 monthly depending on clinical situation.
- **Treat deficiency** (Vitamin D < 25 nmol/L) with 100,000 IU oral then dosing 3 - 12 monthly depending on clinical situation.

Other information

- **For breast fed infants of mothers at risk of low Vitamin D:** promote breast feeding and recommend 400 IU Vitamin D daily (e.g. Penta-Vite [TM] 0.45 ml oral daily) until at least 12 months of age
- **Ensure adequate dietary calcium intake** after Vitamin D is given. Calcium supplements may be needed in patients with low dairy intake and should be given in patients with hypocalcaemia. The Australian RDI for calcium intake varies according to age[5]:

Age	*RDI calcium*
< 6 months	210 mg/day
7-12 months	270 mg/day
1-3 years	500 mg/day
4-8 years	700 mg/day
9-11 years	1000 mg/day
12-18 years	1300 mg/d

Note: 1 cup cow milk contains ~ 300 mg calcium. One Caltrate [TM] tablet contains 600 mg elemental calcium; they can be dissolved in a tablespoon of hot water for administration to young children if needed.

- There is limited longitudinal data; treatment is likely to be needed lifelong while in Australia, particularly at lower latitudes.
- Although it is worthwhile recommending time outside, this may not ensure adequate levels in Melbourne.
- Although some low fat milk is fortified with Vitamin D (e.g. Physical [TM] 50 IU/250 ml), low fat milk is not recommended if age < 2 years or if there are concerns re: nutritional status. Milk intake should be limited to 500 ml/day in children > 12 months.
- There is very little data on high dose Vitamin D given to women during pregnancy[6]. Use daily supplementation instead. Guidelines are available

Recent National Guidelines

Recent national guidelines for infants/children suggest[2]:

- Penta-Vite [TM] 0.45 ml/d (standard dose, contains 400 IU Vitamin D) until 12 months for all breast fed infants of mothers at risk of low vitamin D.
- 400 IU/d Vitamin D or an annual dose of 150,000 IU orally for those at risk of deficiency[7]
- Screen siblings of children with low Vitamin D. (*Note: and parents*)
- Treatment of Vitamin D deficiency based on age (with concurrent treatment guidelines for hypocalcaemia):
    - < 1 month 1,000 IU daily 3 months
    - 1-12 months 3,000 IU daily 3 months or 300,000 IU over 1-7 days
    - > 12 months 5,000 IU daily 3 months or 500,000 IU over 1-7 days
    - Continuing with 400 IU/d after treatment of low Vitamin D complete

Most available oral supplements contain 1,000 IU per capsule/tablet; this represents a significant cost and inconvenience in most families. Capsules containing oil (e.g. Ostelin [TM] 1000 IU D3) can be punctured and the contents given directly or emptied into milk. Tablets (e.g. OsteVit-D [TM] 1000 IU D3) can be crushed for administration to small children. Higher dose formulations (e.g. 50,000 IU/tablet) are just becoming available.

Notes and other resources

[8]	**Breast milk**	**Formula**	**Cow milk**
Vitamin D	2.5 IU / 100 ml	40-53 IU / 100 ml	Only if fortified
Calcium	35 mg / 100ml	43 mg / 100 ml	120 mg / 100 ml

- Australian and New Zealand nutrient reference values: Vitamin D
- Australian and New Zealand nutrient reference values: Calcium
- Prevention and treatment of infant and childhood vitamin D deficiency in Australia and New Zealand: a consensus statement.
- Vitamin D and adult bone health in Australia and New Zealand: a position statement

High dose vitamin D initiative in Victoria

- GP prescribers [62 KB PDF]
- Pharmacies [40 KB PDF]

Translated handouts on Vitamin D (includes English versions).

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Immigrant health clinic protocols
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Hitwize

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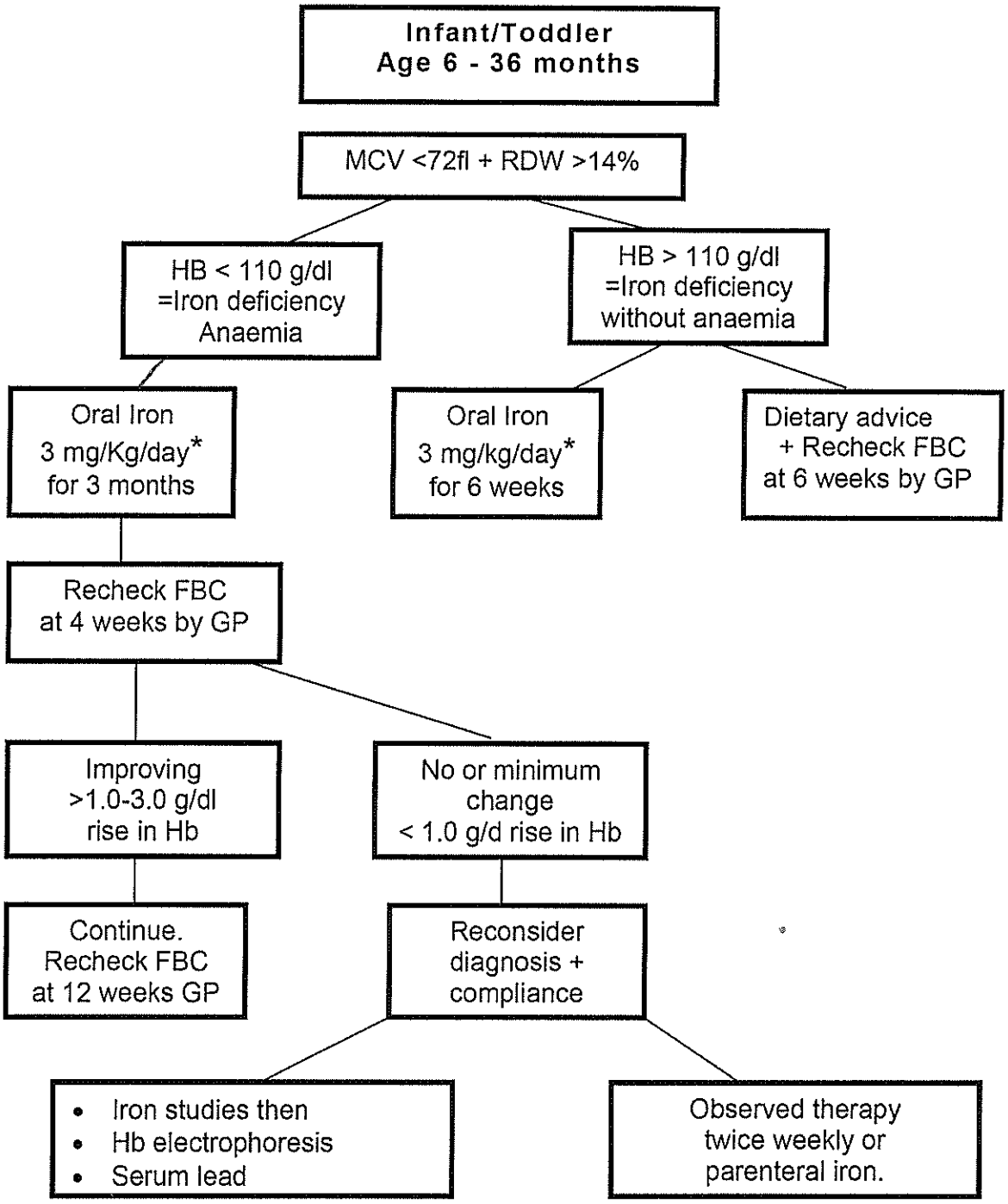
Iron Deficiency Anaemia



*Indicates the recommended daily dose of Oral Iron as Elemental Iron.

Iron Deficiency Anaemia

Iron deficiency is a very common nutritional deficiency. The prevalence of undiagnosed iron deficiency **anaemia** presenting to our department is between 10% and 20% in the at risk age group, between six months and two years. This is the period of rapid growth and high iron requirement, coincides with depletion of iron obtained in utero, potentially poor dietary iron intake and frequent infections.

Clinical Manifestations

Haematologic	Microcytic, hypochromic anaemia.
Immunologic	Impaired T cell and neutrophil functioning.
Neurologic	Current iron deficiency is associated with impaired cognitive function, depressed mood and irritability. Chronic deficiency is associated with impaired brain development and learning which may be permanent.
Gastrointestinal	Gastritis, fat malabsorption, abnormal appetite (pica).
General	Lethargy, poor weight gain, reduced exercise tolerance.

Many of these occur before anaemia develops and begin to improve within days of commencing iron treatment.

Investigations and Diagnosis: Infants age<3 years

Iron deficiency exists when **Serum Ferritin is <10 mcg/l.**
It is strongly indicated by low MCV <72fl + High RDW >14.0%.

Iron deficiency anaemia exists if in addition **Haemoglobin is <110 g/l.**

Problems with the diagnosis of iron deficiency anaemia include:

- ***Acute Infection:*** The serum ferritin is increased, iron saturation and haemoglobin are decreased, as a result of the inflammatory response. Iron studies are not recommended during an acute infection as they may be difficult to interpret. MCV and RDW are not so affected.

- ***Presence of Thalassaemia:***

  1 **Alpha Thalassaemia Trait:** Suggested by a normal RDW of <14.0% and low cord blood MCV <95 fl. All babies born at Middlemore Hospital have cord blood screening with 15% of Maori, 12% Cook Island and 5% Samoan infants having alpha thalassaemia trait. Also seen in Indian and SE Asian infants.

  2 **Beta Thalassaemia**: Hb drops at 4-6 months and is progressive. Will not be detected by Middlemore Hospital newborn screening. Therefore consider in microcytic anaemias developing <12 months with normal ferritin especially in Indian, South East Asian, African, Italian or Greek infants. Uncommon in Maori or Pacific Islanders.

NB A *therapeutic response to a trial of iron medication* given for four weeks is a sensitive "test" of iron deficiency anaemia in borderline or confusing cases and it will do no harm alternatively repeat FBC and iron studies 2-4 weeks after discharge when well to exclude the effect of acute sepsis.

Treatment Guidelines

Neurodevelopmental outcomes and Iron treatment:

Iron deficiency is a very common problem in our community and is strongly associated with social disadvantage and delayed cognitive development.

There is only limited evidence, however, that treatment improves these psycho-motor delays.

This should be born in mind before embarking on parenteral therapy.

1 *Iron deficiency without Anaemia ("Latent Iron deficiency")*

Give dietary advice on **iron rich** foods and the avoidance of **tea** and **whole unmodified cows milk** before the age of 12 months. Iron medication is optional. Repeat FBC in 4-6 weeks by GP as minimum.

2 *Iron Deficiency Anaemia*

Ferrous sulphate syrup 3 mg/kg/day of elemental iron as a single daily dose for three months. FERODAN contains 30 mg elemental iron per 5 ml. This, therefore, equates to a dose of 0.5 ml/kg per day.

Start iron at discharge. Iron supplementation does not increase the risk of infection. There is no need to wait until intercurrent infections have resolved.

Given at this "low" dosage indicated above, side effects from oral iron are uncommon. Warn the parents that treatment may result in dark faeces and stain the teeth.

Oral iron mixtures and tablets are toxic if taken in overdose.

Potentially fatal ingestions are those over 20 mg/kg. This is one week's supply! Therefore counsel parents about **safe storage of medicines** and prescribe in **child resistant containers.**

It is important that parents are encouraged to complete the full course of three months treatment and to visit their GP at four weeks for a FBC. This will both help confirm the diagnosis and review treatment response and compliance. The haemoglobin will rise by 1.0 g per week after an initial lag phase of 7-10 days in an infant with IDA who is compliant with treatment.

One would therefore expect a normal haemoglobin or, if initially very low, 3.0 g above discharge level after a month of treatment. It is unnecessary to recheck the FBC before four weeks of treatment.

"Non-responders"

If four weeks after starting treatment the haemoglobin has risen by <1.0 g/dl, you either have **non compliance** or the **wrong diagnosis.** Check iron studies and then thalassaemia screen if ferritin normal and ask family if iron given every day. The median duration of therapy in South Auckland is 14 days!

Management of Non compliance

Options either:

1 **Intramuscular Iron Injection FERROSIG 50 mg/ml**

Dose of FERROSIG in ml = (Weight in kg x (125-Hb in g/l) x 0.3/50) for deficit + (15 mg/kg/50) to replenish stores. Maximum single dose 1.5 ml.

This should be administered as 3-5 separate injections 1-2 days apart by IM injection in gluteal region, using a Z track injection to reduce skin staining and ooze; must be administered by a nurse familiar with this technique. Refer to Paediatric Homecare Nurses. Potential side effects include pain, skin discolouration, anaphylaxis (<1%), abscess formation and delayed systemic reactions.

Or

2 **Twice Weekly Observed Therapy**

Oral iron medication at dose of 3 mg/kg/dose of elemental iron administered at home twice weekly by a nurse or health care assistant. Haemoglobin will rise more slowly than daily treatment but an acceptable response occurs after three months of treatment. Discuss on a case by case basis with primary care provider.

3 Intravenous Iron Infusion

Not yet recommended treatment in children. Only four clinical trials with 120 total children reported. Only one trial used a Total Dose Infusion (TDI) regime. Six of 70 children given IV DEXTRAN as TDI had adverse events (~10%). Iron polymaltose complex (FERROSIG) is available in New Zealand for IV use, Iron sucrose (VENOFER) only on section 29. No data on TDI regimes for these newer agents in children. Use at consultant discretion after informed parental consent.

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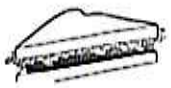
MEAL PLAN TO BOOST IRON

TODDLERS OVER 12 MONTHS OLD

Breakfast: 	1 weetbix with blue top milk ½ banana 1 slice toast with spreads Glass of milk, infant formula or breast feed 
Snack:	Yoghurt/Dairy Food
Lunch:	Sandwich with marmite or vegemite  Slice of meat/sausage Piece of fruit Glass of milk, infant formula or breast feed
Snack:	Cheese on crackers
Dinner: 	Lean beef, lamb or chicken casserole  Chopped potato, taro or kumara Silverbeet, spinach and carrots Custard and fruit
Snack:	Glass of milk, infant formula or breast feed

IRON DEFICIENCY

Introduction

Iron deficiency is the most common micro-nutrient deficiency in the world. Between 13% - 23% of urban New Zealand children less than 3 years of age have iron deficiency anaemia.

Iron deficiency results in widespread impairment in body functions. The most important adverse effect iron deficiency has during childhood is on learning, behaviour and cognitive function. Iron deficiency also results in abnormalities in weight gain, appetite, gastrointestinal function, exercise tolerance and immune response to infections as summarised in Table 1.

Table I. The more important adverse effects of iron deficiency

Site of adverse effect	Adverse effect
Brain	Impaired learning which may be permanent: see text
Weight gain	Impaired weight gain
Appetite	Reduced and abnormal appetite. Pica in particular pagaphagia (excessive ice eating)
Gastrointestinal system	Gastritis Gastric achlorhydria Fat and fat soluble vitamin malabsorption Impaired iron absorption.
Muscle	Reduced exercise tolerance. Increased muscle fatigability
Immune function	Impaired t-cell response to antigens Impaired neutrophil response to bacteria
Haematological	Anaemia

Children between the age of 6 and 24 months are at higher risk of iron deficiency than at any other age in their life. Iron stores at birth are adequate to maintain normal iron status to approximately 4 months of age. Premature infants are at risk of iron deficiency from 2 to 3 months of age. In addition to the high iron needs associated with rapid growth, children in the first few years of life are at greater risk of iron deficiency because their iron intake is largely dependent upon what foods are offered to them by their parents. Therefore parent education is important in trying to prevent young children from becoming iron deficient.

Three foods that are optimal sources of iron for children in the first year of life are breast milk, iron fortified milk formula and meat Breast milk is the optimal food for the first 4 to 6 months of age and when given exclusively provides sufficient iron to maintain normal body iron status to age 6 months. Breast milk contains similar concentrations of iron to cows milk but is much more readily

absorbed. If breast feeding is not possible or when a child is weaned from breast milk an iron fortified formula should be given until 12 months of age.

Two key food items to avoid giving are cow's milk for infants < 12 months of age and tea for any pre-school aged children. Homogenised milk should not be given until after 12 months of age. Not only is this milk a poor source of iron but it also can cause increased blood loss from the gastrointestinal tract. The tannins in tea bind dietary iron preventing it from being absorbed. Tea is not an appropriate beverage for young children.

Children between the age of 6 and 24 months are at higher risk of iron deficiency than at any other age in their life. Iron stores at birth are adequate to maintain normal iron status to approximately 4 months of age. Premature infants are at risk of iron deficiency from 2 to 3 months of age. In addition to the high iron needs associated with rapid growth, children in the first few years of life are at greater risk of iron deficiency because their iron intake is largely dependent upon what foods are offered to them by their parents. Therefore parent education is important in trying to prevent young children from becoming iron deficient.

Diagnosis

The definition of iron deficiency used in large national health and nutrition surveys in the United States is based on measures of the 3 body iron pools. A full blood count, serum ferritin and iron saturation provides measures of: storage iron (ferritin), transport iron (iron saturation) and iron in the red cell pool (haemoglobin concentration and measures of red cell size). A person is iron deficient when measures of 2 of these 3 pools are abnormal. Cut-off values for these measures of iron status are summarised in Table 2.

The mean cell volume is reduced in iron deficiency but is also reduced in a-thalassaemia trait. As approximately 15% of Polynesian New Zealanders have a-thalassaemia trait a low mean cell volume is not specific for iron deficiency. The red cell distribution width (RDW) is a measure of the variability in size of red cells. In normal children the RDW is between 11.5 and 14.5 percent. An elevated RDW appears to be the earliest haematologic manifestation of iron deficiency. The RDW is normal in people with a-thalassaemia trait.

A major difficulty in diagnosing iron deficiency in children is the confounding effect of acute infection. Even mild acute infections can make the diagnosis of mild iron deficiency anaemia difficult by causing a decrease in haemoglobin concentration, a decrease in iron saturation and an increase in serum ferritin. It is preferable to delay blood testing of iron status until 4 to 6 weeks after resolution of the infection.

Table 2. Cut Off Values For Laboratory Tests Of Iron Status.

Age in years	Red cell pool		Transport iron	Storage iron
	Hb (g/L)	RDW %	Iron saturation %	Serum ferritin µg/L
1 - < 2	< 110	> 14.0	<16	≤ 15
2 – 5	< 111	> 14.0	<16	≤ 15

IRON DEFICIENCY

Treatment

The standard therapy is oral iron elixir. The only prescription preparation available in New Zealand is ferrous sulfate (Ferro-liquid® brand) in a concentration of 150 mg/5ml. Each 5 mls contains 30 mg of elemental iron. The recommended dose is 3 mg/kg/day of elemental iron given once daily with a drink containing vitamin C. For a 10 kg child this dose is equivalent to 5 mls once a day. Giving the iron medicine with a meal can also reduce the frequency of these side effects.

If iron deficiency is sufficiently severe to result in anaemia most children will require at least 3 months of oral iron. In order to limit the potential for accidental ingestion of large volumes it is preferable to prescribe this in monthly volumes. Parents need to be reminded to continue the medicine for the full course and to store the medicine carefully. Potentially fatal side effects occur with acute ingestions of > 20 mg/kg.

Rickets

Osteomalacia is a generalized skeletal disorder characterized by the accumulation of osteoid matrix, which fails to mineralize. Mineral deficiency prevents the normal process of bone mineral deposition. When this occurs at the growth plate, growth slows and bone age is retarded. This condition is called Rickets.

Rickets is only found in growing children before fusion of the epiphyses whereas osteomalacia can be present at any age.

Aetiology

1 Calcium deficiency

Commonly associated with abnormalities of Vitamin D metabolism.

a] Inadequate exposure to ultraviolet light.

b] Inadequate dietary Vitamin D (cultural or in LBW or preterm infants).

c] Malabsorption of fat soluble vitamins (liver disease or malabsorption).

d] Enhanced catabolism of 25 OH D in liver and kidney into inactive metabolites secondary to chronic calcium deprivation or enzyme induction due to drugs such as phenytoin or phenobarbitone.

e] Abnormalities of the 1 alpha hydroxylase enzyme in the kidney which changes 25 OH D to 1,25 (OH)2D. This can either be inherited (Vit D dependant rickets type 1) or acquired (chronic renal failure).

f] Failure of 1,25 (OH)2D to act due to receptor abnormality (Vit D dependant rickets type II).

2 Phosphate deficiency

Commonly associated with impaired renal tubular phosphate reabsorption.

a] Usually congenital involving phosphate transport alone (X linked hypo-phosphataemic rickets, previously known as Vit D resistant rickets).

b] Can occur with multiple renal tubular defects (Fanconi syndrome).

c] It can also be acquired (tumour osteomalacia).

3 Osteoblast failure

The osteoblasts are the cells which lay down the osteoid and are responsible for mineralizing it. (Osteogenesis Imperfecta).

Clinical Presentations

These will vary depending on the underlying diagnosis, the age of the child and the severity of the disease (particularly in Vitamin D deficiency). The child may be asymptomatic and diagnosed following an incidental finding on x-ray or laboratory investigations.

Skeletal findings

- Craniotabes, delayed fontanelle closure.
- Enlargement of costochondral junctions (rachitic rosary).
- Scoliosis and kyphosis.
- Enlargement at the wrists and ankles.
- Genu valgum (bowlegs).
- Frontal and/or parietal bossing.
- Fractures in osteopenic bone.
- Impaired development of teeth.

General findings

- Failure to thrive/small for age.
- Delayed development.

Hypocalcaemia

- Seizure.
- Tetany.
- Weakness or reduced muscle tone.
- Drowsiness.
- Cardiomegaly.
- Arrhythmia (prolongation of QT interval is an early abnormality).
- Stridor.

Family history

- Sibling who has/had rickets.
- Mother may have osteomalacia or short stature.

Investigations of Rickets

1 First line

Blood:

- Calcium, Phosphate, Magnesium, ALP.
- LFT, Urea and Creatinine.
- Bicarbonate (low in Fanconi syndrome or other causes of renal tubular acidosis).
- 25-hydroxyvitamin D.
- Store serum for PTH and 1,25 (OH)2D (expensive, often unnecessary).

X-ray:

- Hand and wrist.
- Knee in infants.

X-ray signs of rickets include generalized osteopenia, splaying or cup shape of the metaphyses, fractures.

2 Second line. (Selective in atypical case or failure or response to treatment).

Urine:

- 'Spot' Calcium, Phosphate, creatinine and Urine Ca/Creat ratio to look at renal handling of phosphate and assess if Ca excretion is inappropriately high for low plasma Ca. A Urine Ca/Creat ratio >0.3 mmol/mmol on a spot sample in the presence of hypocalcaemia suggests inappropriate secretion.
- pH.
- Protein and glucose.

PTH & 1,25 (OH)2D.
Parental/sibling biochemistry.
Maternal Vitamin D status (in less than 6 months old).
Karyotype.
Autoantibody screen.
Thyroid function.
Low molecular weight proteins.
Renal Ultrasound.
EDTA sample for genetic studies.
Skull radiograph.

Treatment of Rickets

- When Rickets is suspected it is imperative to treat hypocalcaemia to prevent complications (Hypocalcaemia Protocol).
- Vitamin D therapy may be started once laboratory tests and radiological tests confirm the diagnosis.
- In addition to treatment of hypocalcaemia and Vitamin D replacement, it is essential to provide appropriate nutritional advice.

Options for treatment in Vitamin D deficiency

1 Vitamin D:

a] Single dose Vitamin D (STOSS therapy).
Treatment 600,000 IU given as Ergocalciferol tablets 12 x 1.25 mg tablet (50,000IU).

There is a theoretical risk of worsening hypocalcaemia therefore
(i) Do not commence till child is normocalcaemic; and
(ii) Give Calcium supplements in first two weeks after treatment.

OR

Daily Vitamin D.

EITHER

1,25 (OH)VITD3 (ROCALTROL) 1 ug/ml. Treatment 0.03-0.06 ug/kg/D, maximum1-2 ug daily.

OR

1alpha (OH)VITD3 (ONE ALPHA) 2 ug/ml. Treatment 0.06-0.12 ug/kg/D, maximum 2-4 ug/daily.

These latter agents are expensive, the risk of hypercalcaemia is significant and the risk of non-compliance is high. The temptation to do unnecessary blood calciums is common.

2 **Calcium 800-1200mg/day:**

e.g. CALCIUM SANDOZ (1000 mg effervescent tablet). Treatment 50-100 mg/kg/day in 2-4 divided doses.

Follow up

Review in clinic or ward in 6 weeks with repeat x-rays, serum Ca++, P04 and ALP.

1 If x-ray demonstrates a zone of provisional mineralisation and all blood tests are normal and ALP is normalizing, no further follow up is required.

2 If no improvement on x-ray or biochemistry and Serum Vit D2 is NORMAL, a single or repeat dose of STOSS therapy can be given.

3 If there is no improvement in any indices after STOSS therapy, further investigations are required to diagnose the rare inherited forms of rickets (the commonest is X Linked Hypophosphataemic rickets Incidence 1:10,000).

4 Consider maternal osteomalacia (screen siblings and mother).

5 Screen for other nutritional deficiencies.

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APPENDIX 1 Biochemical findings in various forms of Rickets

	Calcium	Phosphate	PTH	25-OH D	1,25-OH D
Vit D deficiency					
Early	Low	Normal	Normal	Low	Normal
Intermediate	Normal	Low	High	Low	Low, Normal, high
Late	Low	Low	High	Low	Low
X linked hypophosphate-aemic Rickets	Normal	Very low	Normal	Normal	Normal or ↓
Vitamin D dependent rickets Type 1 pseudovitamin D deficiency (lack 1α hydroxylase). Type 2 (severe calcitriol resistance)	Low	Low	High	Normal	Low High

APPENDIX 2 Terminology and abbreviations

Vitamin D2	Ergocaciferal
Vitamin D3	Cholecalciferol.
Calcidiol	25-hydroxycholecalciferol. 25-hydroxy vitamin D3 or 25OH Vit D.
Calcitriol	1,25-dihydroxycholecalciferol. 1,25-dihydroxy vitamin D3 or $1,25OH_2$ Vit D.
PTH	Parathyroid hormone.

APPENDIX 3 Brief summary of vitamin D metabolism

Vitamin D3 (cholecalciferol) is synthesized in the skin from cholesterol precursors by the action of UV light. This inactive prohormone undergoes 25 hydroxylation in the kidney and 1α hydroxylation in the liver to form the metabolically active form of vitamin D or 1,25 dihydroxycholecalciferol.

Dietary ergocalciferol (vitamin D2) also undergoes hydroxylation to become metabolically active.

1,25OH_2 Vit D:

Synthesis is controlled by PTH; serum calcium and phosphate have feedback regulatory role and there is a direct negative feedback effect by itself.

1,25OH2 Vit D **increases** serum calcium by"

- ↑ absorption of calcium by the GI tract.
- ↑ resorption of calcium from bone *(but if serum Ca^{2+} is high there is ↑ deposition in bone).*
- ↑ renal tubular reabsorption of calcium.

PTH:

Stimulates activity of cyclic AMP, secreted in response to reduced serum calcium (also secreted in response to ↑ phosphate, ↓ magnesium).

PTH ***increases*** serum calcium by

- ↑ renal tubular reabsorption of calcium (↑↑ PO4 excretion resulting in phosphaturia).
- ↑ resorption of calcium from bone.
- ↑ activity of 25 hydroxylase enzyme → ↑ Vit D3.

This information is to be supplied to the community pharmacist with the prescription for Stosstherapy.

Background

Stosstherapy is a European method in which a dose of up to 600,000 units of ergocalciferol is administered at once or in divided doses during a 24-hour period to treat rickets[1]. In New Zealand ergocalcicferol is available as Calciferol Strong tablets (PSM) containing 1.25 mg ergocalciferol[2].

Pharmaceutics

Ergocalciferol = calciferol = vitamin D_2.
1,000units = 25 microgram ergocalciferol.
Therefore, 1.25 mg calciferol strong tablet contains 50,000 units ergocalciferol per tablet [3].
N.B. Other forms of vitamin D cannot be substituted.

Administration

Ergocalciferol is practically insoluble in water but soluble in fatty oils. To prepare an oral formulation suitable for an infant containing 600,000 units ergocalciferol, 12 calciferol strong tablets should be crushed to powder with a mortar and pestle. This powder can then be dissolved in olive oil[3]. There is limited stability data for storage so this solution should be prepared as close to the day of administration as possible.

Alternatively, the powder from the crushed tablets could be sprinkled onto a spoonful of soft food e.g. apple puree, yoghurt, etc.

References

1. Shah B and Finberg L. Single-day therapy for nutritional vitamin D-deficiency rickets: a preferred method. The Journal of Pediatrics 1994;125(3):487-90.
2. Adis International. New Ethicals Catalogue Nov 2002-May 2003.
3. Sweetman SC (Ed). Martindale: the complete drug reference. Pharmaceutical Press, UK 2002.