Diagnosis and Management of Vitamin D Deficiency

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Introduction

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

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

Nomenclature and Reference Ranges

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

Reference ranges for vitamin D (25 0HD) Ashford and St Peters NHS trust

- <25 nmol/l deficient
- 25-75 nmol/l insufficient
- 75-200 nmol/l replete / normal
- 200-500 nmol/l high
- >500 nmol/l toxicity

Sources of Vitamin D

Sunlight

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

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

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

Recommended Daily Intake of Vitamin D

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

- All pregnant / breastfeeding women 400 IU/day
- Breastfed babies 1 – 6mths if mother is Vitamin D insufficient / deficient 340 IU/day
- All infants / toddlers from 6mths – 5yrs 280 IU/day
- Children with low sun exposure eg: confined indoors or with covered skin 400 IU/day
Presentation of Vitamin D deficiency in young children

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

Rickets

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

Symptoms and signs of rickets

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

Presentation of Vitamin D deficiency in Older Children/Adolescents

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

Who should be investigated?

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

Blood tests

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

Consider

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

Radiology

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

The X-ray appearances of rickets are characteristic:

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

It is possible to be significantly vitamin D deficient without obvious bony abnormality in older children and teenagers with vitamin D deficiency. The plain X-rays may show osteopenia.
Management of Vitamin D deficiency (<25 nmol/l)

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

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

**Doses (BNF)**

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

*These doses should be given for 12 weeks only.* The child should then be started on long term maintenance doses if considered to still be at risk.

- In circumstances of poor compliance, treatment with an intramuscular dose of Ergocalciferol can be given:
  - Child 6/12-12yrs  150,000IU
  - Child >12yrs  300,000IU

The Vitamin D level should be checked 3 months after the injection and if still suboptimal (<75 nmol/l) then another dose can be given.

**Daily maintenance supplements for children**

<table>
<thead>
<tr>
<th>Age</th>
<th>IU/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td>300-400</td>
</tr>
<tr>
<td>Child 1 month-12 yrs</td>
<td>400-800</td>
</tr>
<tr>
<td>12-18 yrs</td>
<td>800-2000</td>
</tr>
</tbody>
</table>

Management of Vitamin D insufficiency (25-75 nmol/l)

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

### Vitamin D Products (licensed)

<table>
<thead>
<tr>
<th>Product</th>
<th>Strength</th>
<th>Contents</th>
<th>Approx annual cost</th>
<th>Suitability for vegans</th>
</tr>
</thead>
</table>
| **Lamberts Vit D3**      | 400 unit/tablet                        | D3       | **£5.72** for 120
**£7.65** for 120 | Yes (NHS Surrey recommended)          |
|                          | 1000 unit/tablet                       |          |                            |                         |
| **Colecalciferol tablets/capsules** | 400 unit/tablet 1000 unit/tablet       | D3       | **£7.15 upwards** for 100 tabs/caps) | Prescribe gelatine free if required |
| **Calcichew D3**         | 200 units/capsule                      | Ca 12.5mmol/D3 | £55.26                    | No                      |
| **Calcichew Forte tabs** | 400 units/tab                          | Ca 12.5mmol/D3 | £56.00                    | No                      |
| **Adcal chewable/ effervescent tabs** | 400 units/tab                          | Ca 15mmol/D3 | £46.68                    | No                      |
| **Cacit D3 effervescent granules** | 440 units/sachet                      | Ca 12.5mmol/D3 | £97.44                    | No                      |
| **Calceos Chewable tabs** | 400 units/tab                          | Ca 12.5mmol/D3 | £43.44                    | No                      |
| **Calfovit powder**      | 800 units/sachet                       | Ca 30mmol/D3 | £103.68                   |                         |

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</tr>
</thead>
<tbody>
<tr>
<td><strong>Colecalciferol capsules</strong></td>
<td>20,000 units</td>
<td>D3</td>
<td><strong>£15</strong> to <strong>£90</strong> for 50 caps</td>
<td>No</td>
</tr>
<tr>
<td><strong>Ergocalciferol i.m injection</strong></td>
<td>300,000 units/ml</td>
<td>D2</td>
<td>1ml amp <strong>£9.35</strong></td>
<td>Yes</td>
</tr>
</tbody>
</table>
## Children’s products

<table>
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<th>Contents</th>
<th>Approx annual cost</th>
<th>Suitability for vegans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketovite liquid</td>
<td>400 units/5ml</td>
<td>D2 + multivits</td>
<td>£32.40</td>
<td>Yes</td>
</tr>
<tr>
<td>Dalivit drops</td>
<td>400 units/0.6ml</td>
<td>D2 + multivits</td>
<td>£35.76</td>
<td>Yes</td>
</tr>
<tr>
<td>Abidec drops</td>
<td>400 units/0.6ml</td>
<td>D2 + multivits</td>
<td>£26.40</td>
<td>Yes</td>
</tr>
<tr>
<td>Healthy Start Vitamin drops</td>
<td>300 units/5 drops</td>
<td>D2 + multivits</td>
<td>Free with “Healthy Start Vouchers”</td>
<td>Yes</td>
</tr>
</tbody>
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## Vitamin D Products (unlicensed)

Over the last few years there have been many intermittent supply problems with vitamin D preparations including the licensed tablets which have 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.

## Special liquids

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Colecalciferol liquid</td>
<td>3,000 units/ml</td>
<td>D3</td>
<td>£1013</td>
<td>Yes</td>
</tr>
<tr>
<td>Ergocalciferol liquid</td>
<td>3,000 units/ml</td>
<td>D2</td>
<td>£1708</td>
<td>Yes</td>
</tr>
</tbody>
</table>
**Monitoring**

After 3 months Vitamin D, serum calcium and ALP should be rechecked in all children prescribed Vitamin D. The aim of treatment should be to reach a total Vitamin D level of >75nmol/l with a normal ALP for age and resolution of radiological changes.

If the vitamin D level is not >75nmol/l continue treatment for a further 2-3 months and recheck.

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

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

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

- In patients with renal failure, serum calcium should be checked regularly for a few weeks after starting treatment.
References:
4. NHS Surrey PCT Guidelines for the Treatment of Vitamin D Deficiency and Insufficiency in Adults (June 2011)