12 Vitamin D

12.1 Introduction

Vitamin D, also known as calciferol, is a fat soluble vitamin. It is different from all other fat soluble vitamins, in that the body can synthesise it with the help of sunlight, from a precursor that the body makes from cholesterol. Therefore, vitamin D can be regarded as a non-essential nutrient. Given enough exposure to the sunlight, we do not need vitamin D from foods.

The main biological function of vitamin D is to maintain normal blood levels of calcium and phosphate. This in turn sustains the normal mineralisation of bone, muscle contraction, nerve conduction and general cellular function in all cells of the body. The active form of vitamin D, 1,25-dihydroxyvitamin D or calcitriol, also regulates the transcription of a number of vitamin D-dependent genes coding for calcium transporting proteins and bone matrix proteins.

Vitamin D also modulates the transcription of cell cycle proteins that decrease cell proliferation and increase cell differentiation of a number of specialised cells in the body. This attribute may explain the actions of vitamin D in bone resorption, intestinal calcium transport and skin. Vitamin D also has immuno-modulatory properties that may alter responses to infection *in vivo.*

12.2 Deficiencies

Vitamin D deficiency is manifested as rickets in children and as osteomalacia in adults. Lack of the vitamin in adults may also contribute to the development of osteoporosis. Infants are the group most at risk of deficiency in vitamin D simply because of their high rate of skeletal growth. Although at birth, vitamin D is acquired *in utero,* the stores will only be sufficient for the first month of life. In temperate countries, infants born in the autumn months are especially at risk because they spend the first six months of their life indoors. Therefore they have less opportunity to synthesise vitamin D in their skin during this period. Infants who are breastfed are at higher risk of developing vitamin D deficiency as there is little vitamin D in human milk (Holick, 2004)

Although adolescence is another period of rapid skeletal growth, particularly at puberty, any risk of vitamin D deficiency can be overcome. Unlike infants, adolescents are usually outdoors, thus are usually exposed to ultraviolet light adequate for synthesising vitamin D for their needs.

In the elderly, clinical research studies have suggested age related decline in many key steps of vitamin D action (Holick, 1994). This included rate of skin synthesis, rate of hydroxylation leading to activation to the hormonal form, and response of target tissues (bone) as well as reduced skin exposure. Other studies from around the world have indicated that there appears to be vitamin deficiency in a subset of elderly population (Chapuy & Meunier, 1997). A few groups have found that modest increases in vitamin D intakes (10 to 20 µg/day) reduce the rate of bone loss and fractures (Chapuy & Meunier, 1997; Dawson-Hughes *et al.,* 1991). These results have led to recommendations of an increase in vitamin D intakes for the elderly to a value (10-15 µg/day) that is able to maintain normal vitamin D levels.

12.3 Food sources

Vitamin D occurs naturally in animal foods. It is found in small and highly variable amounts in butter, cream, egg yolk and liver. The best food sources are fish liver oils. The intake of foods fortified with vitamin D such as milk, cereals and orange juice can increase vitamin D in the diet. Some food sources of vitamin D are given in Table 12.1.

Table 12.1 Food sources of vitamin D

Food	Serving	Vitamin D (µg)
Milk, cow fortified	1 cup	2.5
Sardines, canned	1 oz	2.1
Liver, chicken,cooked	3 oz	1.1
Liver, calf, cooked,	3 oz	0.4
Egg yolk	1 egg yolk	0.6

Source: USDA (1986)

12.4 Factors affecting requirements

Most adults, especially in the equator (sunny regions) do not have to obtain vitamin D from food. Most of the world's population can rely on natural exposure to sunlight to maintain adequate vitamin D nutrition. Prolonged exposure to sunlight, however, can degrade vitamin D precursor in the skin, thus preventing its conversion to the active vitamin.

The pigments of dark skin can provide some protection from the sun, but they also reduce vitamin D synthesis. Darker–skinned people require longer sunlight exposure than light-skinned people. The latitude, season and time of day can affect vitamin D synthesis. The ultraviolet rays that promote vitamin D synthesis are blocked by heavy clouds, smoke or smog. For people who are unable to go outdoors frequently, dietary vitamin D is essential.

12.5 Setting requirements and recommended intakes of vitamin D

There is no local data on vitamin D requirements that could be used by the Technical Sub Committee (TSC) on Vitamins to arrive at the RNI for vitamin D. Thus the TSC referred to the FAO/WHO (2002) consultation report as well as the IOM (1997)

DRI recommendations. These organizations had made the same recommended intakes for the vitamin. The rationale and steps taken in setting the requirements and the levels recommended by these organisations and available reports on vitamin D status of communities in the country were considered. The TSC on Vitamins agreed to adapt the FAO/WHO (2002) values as the revised RNI for Malaysia, given in bold in the following paragraphs according to age groups and summarised in Appendix 12.1.

It must be recognised that Malaysia, which is around the equator, the most physiologically relevant and efficient way of acquiring vitamin D is to synthesise it endogenously in the skin by sunlight (UV) exposure. In most situations, approximately 30 minutes of skin exposure (without sunscreen) of the arms and face to sunlight can provide all the daily vitamin D needs of the body (Holick 1994).

Infants

Some studies have shown that a minimum intake of 2.5 µg/day will likely prevent rickets. However, even at this level of intake, particularly if there is an absence of sunlight many infants will still have serum concentration of 25-hydroxyvitamin D [25(OH)D] within the range found in cases of rickets. Human milk has also been shown to contain low amounts of vitamin D. Thus, for the above reasons and assuming that infants are not getting any vitamin D from sunlight, IOM (1997) recommended an intake of at least 5 µg/day for infants 0-6 months. Similarly, for infants 7-12 months, it has been observed that in the absence of any sunlight exposure, an intake of 5 µg/day will result in most of the infants with serum 25(OH)D above 11 ng/ml level. This amount was thus accepted as the adequate intake for infants 7-12 months. The FAO/WHO Consultation had agreed with this approach and had recommended the adoption of these intakes as the accepted RNI.

RNI for infants

0 - 5 months	**5 µg/day**
6 - 11 months	**5 µg/day**

Children and adolescents

There are no data on the amount of vitamin D that is required to prevent vitamin D deficiency in children aged 1 to 8 years. The IOM DRI Committee observed from available data from different countries where the children were not exposed to adequate sunlight, that children who had a mean dietary intake of 1.9-2.5 µg/day showed no evidence of vitamin D deficiency and had normal serum 25(OH)D values (IOM, 1997). Thus an actual intake of 5 µg/day, which is double the mean dietary intake value is recommended to cover the needs of the children in this age group regardless of sunlight exposure.

There is no scientific evidence that shows an increased requirement for vitamin D in boys and girls during puberty. Children during their pubertal years maintained a normal serum of 25(OH)D level with dietary intakes of 2.5-10 µg/day. Children who consumed less than 2.5 µg/day vitamin D had mean serum 25(OH)D concentration that was consistent with vitamin D deficiencies. With regular sun exposure, there would not be any dietary need for vitamin D. However children who do not get out in the sun may not synthesise enough vitamin D in their skin. To cover the needs of the adolescents in this age group regardless of sunlight exposure, the ingested value of 2.5 µg is doubled for an actual intake of 5 µg/day.

RNI for children

1 - 3 years	**5 µg/day**
4 - 6 years	**5 µg/day**
7 - 9 years	**5 µg /day**

RNI for adolescents

Boys	**10 - 18 years**	**5 µg/day**
Girls	**10 - 18 years**	**5 µg/day**

Adults and elderly

Available literature reviewed by the DRI Committee showed that both sunlight and diet play an important role in providing vitamin D to the adults. A study on male submariners who were not exposed to sunlight showed that males who received 15 µg/d vitamin D maintained their serum 25(OH)D concentration similar to those measured before entering the submarine. Those males who did not receive any vitamin D supplementation had a 38% decline in serum 25(OH)D concentration. Strict vegetarian demonstrated a significantly lower serum 25(OH)D concentration compared to their omnivorous counterparts. In a recent study in Nebraska, USA it was reported that most women consumed mean intake of 3.3 to 3.4 µg/d vitamin D and had serum 25(OH)D greater than 30 nmol/day. To cover the needs of adults ages greater than 19 years to 50 years, regardless of sunlight exposure, the mean value of 3.3-3.4 was rounded down to 2.5 µg and then doubled for an actual intake of 5 µg/day.

RNI for adults

Men	**19 - 50 years**	**5 µg/day**
Women	**19 - 50 years**	**5 µg/day**

Vitamin D is the only vitamin which has different intakes recommended for older adults and the elderly groups. For the older adults group (>51 years), bone loss is used as an indicator of adequacy. Data of studies among women showed that dietary intake of 2.5 µg/day is inadequate. Women supplemented with 2.5 µg/day vitamin D demonstrated a higher loss of bone mineral density of the femoral neck compared to women supplemented with 17.5 µg/day. At an intake greater than 5.5 µg/day there was no seasonal variation in serum PTH concentration. Based on the few data from the various studies, the value of 5 µg/day was chosen as a value between 2.5 µg and 17.5 µg. To cover the needs of adults ages 51 years through 65 year, the value of 5.0 µg was doubled for an actual intake of 10 µg/day (IOM, 1997).

RNI for adults

Men	**51 - 65 years**	**10 µg RE/day**
Women	**51 - 65 years**	**10 µg RE/day**

Upon reviewing available data, IOM (1997) felt that evidence is strong that the elderly are at high risk for vitamin D deficiency, which causes secondary hyperparathyroidism and osteomalacia and exacerbates osteoporosis, resulting in increased risk of skeletal fractures. Based on the available literature, a value of 7.5 µg/day was felt prudent for individuals over 70 years of age with limited sun exposure and stores. In order to cover the needs of adults over age 70, regardless of exposure to sunlight and stores, the above value was doubled and an intake of 15 µg/day recommended.

RNI for elderly

Men	**> 65 years**	**15 µg/day**
Women	**> 65 years**	**15 µg/day**

Pregnancy and lactation

Placental transfer of vitamin D from mother to fetus is relatively small and does not appear to affect the overall status of pregnant women. Women, whether pregnant or not, who receive regular exposure to sunlight do not need vitamin D supplementation. Thus, IOM (1997) felt that there is no additional need to increase the vitamin D intake during pregnancy above that required for non pregnant women. Therefore the recommended vitamin D is similar to that of non-pregnant women ie 5 µg/day.

There is no evidence to indicate that lactation increases a mother's actual intake of vitamin D. For this reason the recommendation of vitamin D is extrapolated from non-lactating women that when sunlight exposure is inadequate, an actual intake of 5 µg/day is needed.

RNI for

Pregnancy	**5 µg/day**
Lactation	**5 µg/day**

Discussions on revised RNI for Malaysia

The RNI values for vitamin D for Malaysia adapted from FAO/WHO (2002) are similar to those adopted by the Working Group for the Harmonisation of RDAs in SE Asia (2002). Appendix 12.1 provides a summary of these revised RNI, compared with the previous Malaysian RDI of 1975, the FAO/WHO (2002) recommendations and the values recommended by IOM (1997).

These revised values for the infants and young children are lower than the previous Malaysian RDI (Teoh, 1975). This is acceptable because in studies carried out abroad, where sunlight is absent or minimum, infants and young children with minimum intake of 2.5 µg/day can still prevent rickets. Meanwhile for children 7 years and above to adulthood (50 years), the values have been set higher than the previous RDI. This is to cater for the pubertal years and also for adults who are not exposed to enough sunlight.

For pregnant and lactating women, the vitamin D intake is set at 5 µg/day which is lower than the previous value. This is based on recent data that there is no evidence which indicates additional needs for vitamin D for both pregnant and lactating women.

The revised values for vitamin D intake for the 51-65 years and the elderly 65 years have been increased four and six-folds respectively. This is deemed justified as data have shown that intake of 2.5 µg/day is inadequate and a higher bone loss of bone mineral density has been shown for these age groups.

12.6 Toxicity and tolerable upper intake levels

Serum 25(OH)D is a useful indicator of vitamin D status, both under normal conditions and in the context of hypervitaminosis D. The latter is characterised by a considerable increase in plasma 25(OH)D concentration to a level of approximately 160 to 500 ng/ml. Because changes in circulating levels of $1,25(OH)_2D$ are generally small and unreliable, the elevated levels of 25(OH)D are considered the indicator of toxicity. Serum levels of 25(OH)D have diagnostic value, particularly in distinguishing the hypercalcemia due to hypervitaminosis D from that due to other causes, such as hyperparathyroidism, thyrotoxicosis, humoral hypercalcemia of malignancy, and lymphoma.

The adverse effects of hypervitaminosis D are probably largely mediated via hypercalcaemia, but limited evidence suggests that direct effects of high concentrations of vitamin D may be expressed in various organ systems, including kidney, bone, central nervous system, and cardiovascular system.

The tolerable upper intake for vitamin D for various age groups as proposed by IOM (1997) are given in Table 12.2.

Table 12.2 Tolerable Upper Intake (UL) levels of vitamin D for various age groups

Age groups	µg/day of vitamin D
Infants	25
Children, 1-18 years	50
Adult > 18 years	50
Pregnant women	50
Lactating women	50
Adult > 18 years	50

Source: IOM (1997)

12.7 Research recommendations

The following priority areas of research are recommended:

- Evaluation of vitamin D status of groups at risk to deficiency, such as homebound elderly people.
- Include vitamin D content in Malaysian food composition table (perhaps adapted from other countries as analysis of vitamin D in food will be costly and unjustifiable).

12.8 References

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Appendix 12.1 Comparison of recommended intake for vitamin D: RDI Malaysia (1975), RNI Malaysia (2005), FAO/WHO (2002) and AI of IOM (1997)

Malaysia (1975)		Malaysia (2005)		FAO/WHO (2002)		IOM (1997)	
Age groups	RDI (µg/day)	Age groups	RNI (µg/day)	Age groups	RNI (µg/day)	Age groups	AI (µg/day)
Infants		Infants		Infants		Infants	
< 1 year	10	0 – 5 months	5	0 – 6 months	5	0 – 6 months	5
		6 – 11 months	5	7 – 11 months	5	7 – 12 months	5
Children		Children		Children		Children	
1 – 3 years	10	1 – 3 years	5	1 – 3 years	5	1 – 3 years	5
4 – 6 years	10	4 – 6 years	5	4 – 6 years	5	4 – 8 years	5
7 – 9 years	2.5	7 – 9 years	5	7 – 9 years	5		
Boys		Boys		Boys		Boys	
10 – 12 years	2.5	10 – 18 years	5	10 – 18 years	5	9 – 13 years	5
13 – 15 years	2.5					14 – 18 years	5
16 – 19 years	2.5						
Girls		Girls		Girls		Girls	
10 – 12 years	2.5	10 – 18 years	5	10 – 18 years	5	9 – 13 years	5
13 – 15 years	2.5					14 – 18 years	5
16 – 19 years	2.5						
Men		Men		Men		Men	
20 – 39 years	2.5	19 – 50 years	5	19 – 65 years	5	19 – 30 years	5
40 – 49 years	2.5	51 – 65 years	10	51 – 65 years	10	31 – 50 years	5
50 – 59 years	2.5	> 65 years	15	> 65 years	15	51 – 70 years	10
≥ 60 years	2.5					> 70 years	15
Women		Women		Women		Women	
20 – 39 years	2.5	19 – 50 years	5	19 – 65 years	5	19 – 30 years	5
40 – 49 years	2.5	51 – 65 years	10	51 – 65 years	10	31 – 50 years	5
50 – 59 years	2.5	> 65 years	15	> 65 years	15	51 – 70 years	10
≥ 60 years	2.5					> 70 years	15
Pregnancy		Pregnancy		Pregnancy		Pregnancy	
1^{st} trimester	10.0		5		5	14 – 18 years	5
2^{nd} trimester	10.0					19 – 30 years	5
3^{rd} trimester	10.0					31 – 50 years	5
Lactation		Lactation		Lactation		Lactation	
1^{st} 6 months	10.0		5		5	14 – 18 years	5
2^{nd} 6 months	2.5					19 – 30 years	5
						31 – 50 years	5

Notes: 1 µg = 40 IU