# 8 Niacin (Vitamin $B_3$)

## 8.1 Introduction

Niacin is a water-souluble vitamin, also known as vitamin $B_3$. Niacin is the generic term for nicotinic acid (pyridine 3-carboxylic acid) and nicotinamide (nicotinic acid amide) and the coenzyme forms of the vitamin.

Nicotinamide is the active form, which functions as a constituent of two coenzymes, namely, nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). In the forms of these coenzymes, niacin functions in many biological redox reactions which activate about 200 dehydrogenases essential to electron transport and other cellular respiratory reactions. NAD functions as an electron carrier for intracellular respiration as well as a co-factor for enzymes involved in the oxidation (catabolism) of fats, proteins, carbohydrates and alcohol to produce energy. NADP functions as a hydrogen donor in reductive biosynthesis (anabolism), such as in fatty acid and steroid synthesis. Like NAD, NADP is a cofactor for enzymes, such as in the oxidation of glucose-6-phosphate to ribose-5-phosphate in the pentose phosphate pathway.

In non-redox reactions, NAD is the substrate for two classes of enzymes that separate the niacin moiety from NAD and transfer ADP-ribose to proteins. A third class of enzymes catalyses the formation of cyclic ADP-ribose. This molecule also functions within cells to provoke the release of calcium ions from internal storage sites and may also plays a role in cell-signaling

## 8.2 Deficiencies

Clinical evidence of niacin deficiency includes fatigue, poor appetite, diarrhea, irritability, headache, emotional instability and possible memory loss. These may lead to changes in the skin, mucosa of the mouth, stomach and intestinal tract and the nervous system. These changes are called “pellagra”, which means “raw skin” and are most pronounced in the parts of the skin exposed to sunlight. Other signs and symptoms include dizziness, vomiting, constipation or diarrhoea, and inflammation of the tongue and gastric mucosa. The neurological symptoms can include fatigue, sleeplessness, depression, memory loss and visual impairment. If untreated, pellagra is ultimately fatal.

Presently, pellagra is rarely seen in most industrialized countries except among chronic alcoholics and individuals with conditions that disrupt tryptophan pathways. In more recent times, pellagra has been reported in India, and parts of China and Africa, and was reported among Mozambican refugees in Malawi (Malfait *et al.,* 1993).

## 8.3 Food sources

Important sources of preformed niacin include beef, liver, pork, fish, anchovies, peanuts and other nuts, whole grains and whole-meal wheat flour. In general, food rich in protein, with the exception of tryptophan-poor grains, can satisfy some of the requirement for niacin. Human milk contains a higher concentration of niacin than cow's milk. In plants, especially in mature cereal grains like corn and wheat, niacin may be bound to sugar molecules in the form of glycosides, thus significantly reducing niacin bioavailability. In unprepared foods, niacin is present mainly in the form of the cellular pyridine nucleotides NAD and NADP. Enzymatic hydrolysis of the coenzymes can occur during the course of food preparation. Significant amounts of niacin can be lost if large quantities of liquid are used in preparation and cooking of food sources. Table 8.1 provides examples of food with substantial amounts of niacin in 100 g portion of the food:

**Table 8.1 Niacin content of selected Malaysian foods**

| Food | Niacin (mg/100g) |
|---|---|
| Peanut | 11.7 |
| Anchovy, dried | 13.2 |
| Liver | 11.5 |
| Wheat flour, whole-meal | 10.2 |
| Beef extract | 5.6 |
| Pomfret, black (bawal hitam) | 4.2 |
| Sardine, canned | 3.5 |
| Beef, lean | 3.4 |
| Mackerel (Tenggiri batang) | 3.2 |
| Chicken, breast meat | 3.1 |

(Source: *Tee et al.*, 1997)

Besides dietary niacin as a source for the synthesis of NAD, it may also be synthesised in the liver from tryptophan, an essential amino acid. The synthesis of niacin from trytpophan also depends on enzymes that require vitamin $B_6$ and riboflavin, as well as an enzyme containing heme. On average, 1 mg of niacin can be synthesised from 60 mg of tryptophan. Thus, 60 mg of tryptophan can be considered to be 1 mg of niacin equivalent (NE) (Horwitt *et al.,* 1981).

## 8.4 Factors affecting requirement

Bioavailability of niacin varies depending on the food sources. From mature cereal grains, only 30% of niacin is available because it is largely bound. The bioavailability can be increased by treating the grains with alkali. For enrichment and fortification of food, free form of niacin is used, thus making it highly available. Foods that contain niacin in the free form include beans and liver.

The conversion of tryptophan to niacin may be affected by a number of factors. There are several dietary, drug and disease factors that reduce this conversion, such as use of oral contraceptives. The requirement for pre-formed niacin is increased by factors that reduce the conversion of tryptophan to niacin. It tends to be lower with higher tryptophan intakes and during pregnancy, when conversion is more efficient. There is also an interdependence of enzymes within the tryptophan-to-niacin pathway where vitamin $B_6$ (as pyridoxal phosphate), riboflavin (as FAD) and iron are functional. Further, riboflavin (as FMN) is required for the oxidase that forms coenzymic pyridoxal 5'-phosphate from the alcohol and amine forms of phosphorylated vitamin $B_6$. Therefore, inadequate iron, riboflavin, or vitamin $B_6$ status decreases the conversion of tryptophan to niacin.

Variation in the levels of energy intake may influence niacin requirement. However, there are no directly relevant data that examined this relationship. Despite this lack of direct experimental data, the known biochemical function of riboflavin in the metabolism of carbohydrate suggests that at least a small (10%) adjustment be made to the estimated requirement to reflect differences in the average energy utilisation and size of men and women (IOM, 1998). A 10% increase in the requirement is also suggested to cover increased energy utilisation during pregnancy, and a small increase in the requirement to account for the efficiency of niacin use during lactation.

## 8.5 Setting requirements and recommended intakes of niacin

There are no local data available to help establish niacin requirements. The Technical Sub-Committee (TSC) on vitamins reviewed the consultation report of FAO/WHO (2002) and the IOM (1998) DRI recommendations. In reviewing these reports, consideration were given to the rationale and steps for arriving at the RNI for niacin, the levels of niacin recommended for different age categories. The TSC on Vitamins decided to adapt the FAO/WHO (2002) values as the revised RNI for Malaysia, given in bold in the following paragraphs according to age groups. The proposed RNI are summarised in Appendix 8.1.

### *Infants*

The adequate intake for niacin for infants ages 0 through 6 months is based on the reported mean volume of milk (0.78L/day) consumed by this age group, the estimated niacin concentration in human milk of 1.8 mg/l and the tryptophan content of human milk (210 mg/l). Thus the IOM (1998) recommended intake for niacin for infants (0-6 months) is 2 mg of preformed niacin.

One of the method that can be used to determine adequate intake of niacin for infants 7-12 months is to use the estimated niacin content of human milk as 1.1 mg/l and a mean milk volume of 0.6L, and adding the amount of niacin provided by solid foods (8 mg). The amount of niacin equivalents (NE) thus obtained would be 9 mg/day. The DRI

Committee felt that this amount was too high and used the approach of extrapolating from estimated average requirement of adults to estimate adequate intake for this group of infants. Thus, IOM (1998) set the adequate intake for infants 7 through 12 months as 4 mg/day of NEs.

**RNI for infants**

| | |
|---|---|
| **0 - 5 months** | **2 mg/day of NEs** |
| **6 - 11 months** | **4 mg/day of NEs** |

***Children and adolescents***

Since there was no available data on which to base the requirements for children or adolescents, the DRI Committee of IOM (1998) had based the recommended intakes for these groups on extrapolation from adult values. The recommended intake was determined as 130% of the EAR.

**RNI for children**

| | |
|---|---|
| **1 - 3 years** | **6 mg/day of NEs** |
| **4 - 6 years** | **8 mg/day of NEs** |
| **7 - 9 years** | **12 mg/day of NEs** |

**RNI for adolescents**

| | |
|---|---|
| **Boys 10 - 18 years** | **16 mg/day of NEs** |
| **Girls 10 - 18 years** | **16 mg/day of NEs** |

***Adults and elderly***

The metabolites of niacin excretion, $N^1$-methyl-nicotinamide and its 2-pyridone derivative are thought to be the best biochemical measure for estimating niacin requirement. An average niacin requirement can be estimated as the niacin intake corresponding to an excretion of $N^1$-methyl-nicotinamide that is above the minimal excretion at which pellagra symptoms occur. A urinary excretion value for $N^1$-methyl-nicotinamide of 1.0 mg/day has been chosen as the level of niacin excretion that reflects a niacin intake that is minimal or barely adequate.

Upon reviewing data from four experimental studies, the IOM DRI Committee observed that the overall average intake equivalent to the excretion of 1 mg/day of $N^1$-methyl-nicotinamide was 11.6 ± 3.94, with a CV of 34%. It was also assumed that women have a slightly lower requirement than men because of their size and average energy utilization. The average requirement was estimated to be 12 mg/day NEs for men and 11 mg/day of NEs for women. There are insufficient data to determine whether the niacin requirement changes with age in adults. The FAO/WHO consultation also felt that there are insufficient data to justify changes in requirements for the elderly for most of the B vitamins, including niacin.

Taking into consideration the wide variation in the efficiency of converting tryptophan to niacin, the DRI Committee assumed a higher coefficient of variation (CV) of 15%. The daily recommended intake for adults was thus calculated as 130% of the estimated requirement or 16 mg NEs for men and 14 mg NEs for women.

**RNI for adults**

| | | |
|---|---|---|
| **Men** | **19 – 65 years** | **16 mg/day of NEs** |
| **Women** | **19 – 65 years** | **14 mg/day of NEs** |

**RNI for elderly**

| | | |
|---|---|---|
| **Men** | **> 65 years** | **16 mg/day of NEs** |
| **Women** | **> 65 years** | **16 mg/day of NEs** |

***Pregnancy and lactation***

During pregnancy, it is estimated that the need for niacin increases by 3 mg/day of NEs to cover increased energy utilisation and growth in maternal and fetal compartments, especially during the second and third trimesters. Thus, the estimated niacin requirement is 14 mg/day of niacin equivalents during pregnancy with no adjustment being made for the woman's age. As has been explained for adult requirement, a CV of 15% is assumed for niacin requirement. The calculated recommended intake for niacin during pregnancy is thus 130% of the requirement or 18 mg NEs per day.

For lactating women, an estimated 1.4 mg of preformed niacin is secreted daily into breast milk. To cover the energy expenditure involved in milk production, 1 mg is further added. Therefore, for women who are exclusively breastfeeding an infant, the additional amount of niacin needed is 2.4 mg/day of NEs. Taking into consideration the CV for niacin requirement, the recommended intake during lactation is 17 mg/day of NEs.

**RNI for**

| | |
|---|---|
| **Pregnancy** | **18 mg/day of NEs** |
| **Lactation** | **17 mg/day of NEs** |

***Discussions on revised RNI for Malaysia***

The RNI values for niacin for Malaysia, adapted from FAO/WHO (2002), are also the same as those adopted by the Working Group for the Harmonisation of RDAs in SEAsia (2002). Appendix 8.1 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 (1998).

Amongst children and adolescent boys, the revised RNIs are lower than the previous RDI (Teoh, 1975) values. For adolescent girls and the adults, the revised RNI are similar or slightly higher than the previous RDI. For pregnant and lactating women, the revised RNI are higher than the previous RDI to accommodate for increases in energy requirement and replacement of secretion losses. These values are almost identical to the values proposed by IOM (1998), with the exception for age groups 9-13 and 14-18 years. These changes in the revised recommended intake for Malaysia compared with the previous values should not be a cause for concern. The proposed RNI can be easily met by adopting the recommended dietary guidelines. Moreover, deficiency of this vitamin has not been reported in the country of over 50 years.

## 8.6 Toxicity and tolerable upper intake levels

Niacin toxicity is rarely observed at doses generally consumed and niacin from foods is not known to cause adverse effects. Nevertheless, considerations should still be given to intake of niacin as a supplement, fortified foods or as a pharmacological agent.

Pharmacological doses of nicotinic acid (but not nicotinamide) (1-2 g three times a day) is used as a cholesterol-lowering drug. Nicotinic acid therapy has been found to result in markedly increased HDL-cholesterol levels, as well as decreased serum Lp(a) lipoprotein concentrations, and a shift from small dense LDL particles to large, buoyant LDL particles, all of which are considered cardioprotective changes in blood lipid profiles. At this level of intake, histimine release may be triggered resulting in flushing of the skin which can be harmful to patients with asthma or peptic ulcer disease. Most adverse effects are dose-related and generally subside with a reduction in dose or the cessation of treatment.

Symptoms of acute toxicity include flushing, itching of skin, nausea, vomiting and gastrointestinal disturbances. In addition, jaundice, hyperglycaemia, abdominal pain, elevated serum bilirubin, alkaline phosphatase and aminotransferase levels can be seen with ingestion of high levels of nicotinic acid (generally intakes of 3,000 mg/day or more) for long periods of time.

The Tolerable Upper Intake Level (UL) of 35 mg/day as proposed by IOM (1998) was adopted by the FAO/WHO Consultation Group (2002). This value was also set for pregnant and lactating adult women. The UL of 35 mg/day was adjusted for children and adolescents on the basis of relative body weight and using revised reference weights. The UL is not meant to apply to individuals who are being treated with a nutrient under medical supervision, such as for lowering of cholesterol levels. The UL recommended by IOM (1998) are as given in Table 8.2.

**Table 8.2 Tolerable Upper Intake Levels (UL) of niacin for various age groups**

| Age groups | mg/day niacin equivalents |
|---|---|
| Infants, 0-12 months | Not possible to establish |
| Children | |
| 1 - 3 years | 10 |
| 4 - 8 years | 15 |
| 9 - 13 years | 20 |
| Adolescents, 14-18 years | 30 |
| Men, 19 years and older | 35 |
| Women, 19 years and older | 35 |
| Pregnant women | 35 |
| Lactating women | 35 |

## 8.7 Research recommendations

The following priority areas of research are recommended:

- Determination of niacin status and extent of deficiency among high risk groups
- Identification of more sensitive and specific biochemical measures of niacin status
- Identification of specific roles or functions of niacin in disease prevention
- Determine effects of food preparation and cooking methods on niacin content of selected foods to enable establishing conversion factors for calculating niacin losses for a wide variety of foods

## 8.8 References

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Teoh ST (1975). Recommended daily dietary intakes for Peninsular Malaysia. *Med J Mal* 30: 38-42.

**Appendix 8.1 Comparison of recommended intake for niacin: RDI Malaysia (1975), RNI Malaysia (2005), FAO/WHO (2002), and RDA of IOM (1998)**

| Malaysia (1975) | | Malaysia (2005) | | FAO/WHO (2002) | | IOM (1998) | |
|---|---|---|---|---|---|---|---|
| **Age groups** | **RDI (mg/day)** | **Age groups** | **RNI (mg/day)** | **Age groups** | **RNI (mg/day)** | **Age groups** | **AI (mg/day)** |
| Infants | | Infants | | Infants | | Infants | |
| < 1 year | 6.6 | 0 – 5 months | 2 | 0 – 6 months | 2 | 0 – 6 months | 2 |
| | | 6 – 11 months | 4 | 7 – 11 months | 4 | 7 – 12 months | 4 |
| | | | | | | | **RDA (mg NE/day)** |
| Children | | Children | | Children | | Children | |
| 1 – 3 years | 9.0 | 1 – 3 years | 6 | 1 – 3 years | 6 | 1 – 3 years | 6 |
| 4 – 6 years | 12.1 | 4 – 6 years | 8 | 4 – 6 years | 8 | 4 – 8 years | 8 |
| 7 – 9 years | 14.5 | 7 – 9 years | 12 | 7 – 9 years | 12 | | |
| Boys | | Boys | | Boys | | Boys | |
| 10 – 12 years | 17.2 | 10 – 18 years | 16 | 10 – 18 years | 16 | 9 – 13 years | 12 |
| 13 – 15 years | 16.2 | | | | | 14 – 18 years | 16 |
| 16 – 19 years | 17.0 | | | | | | |
| Girls | | Girls | | Girls | | Girls | |
| 10 – 12 years | 15.5 | 10 – 18 years | 16 | 10 – 18 years | 16 | 9 – 13 years | 12 |
| 13 – 15 years | 14.5 | | | | | 14 – 18 years | 14 |
| 16 – 19 years | 13.9 | | | | | | |
| Men | | Men | | Men | | Men | |
| 20 – 39 years | 16.7 | 19 – 65 years | 16 | 19 – 65 years | 16 | 19 – 30 years | 16 |
| 40 – 49 years | 15.8 | > 65 years | 16 | > 65 years | 16 | 31 – 50 years | 16 |
| 50 – 59 years | 15.0 | | | | | 51 – 70 years | 16 |
| ≥ 60 years | 13.0 | | | | | > 70 years | 16 |
| Women | | Women | | Women | | Women | |
| 20 – 39 years | 13.0 | 19 – 65 years | 14 | 19 – 65 years | 14 | 19 – 30 years | 14 |
| 40 – 49 years | 13.0 | > 65 years | 14 | > 65 years | 14 | 31 – 50 years | 14 |
| 50 – 59 years | 13.0 | | | | | 51 – 70 years | 14 |
| ≥60 years | 13.0 | | | | | >70 years | 14 |
| Pregnancy | | Pregnancy | | Pregnancy | | Pregnancy | |
| 1st trimester | 13.0 | | 18 | | 18 | 14 – 18 years | 18 |
| 2nd trimester | 15.3 | | | | | 19 – 30 years | 18 |
| 3rd trimester | 15.3 | | | | | 31 – 50 years | 18 |
| Lactation | | Lactation | | Lactation | | Lactation | |
| 1st 6 months | 16.6 | | 17 | | 17 | 14 – 18 years | 17 |
| 2nd 6 months | 13.0 | | | | | 19 – 30 years | 17 |
| | | | | | | 31 – 50 years | 17 |