



DIETARY REFERENCE INTAKES (RDIs): A STEP IN THE RIGHT DIRECTION

INTRODUCTION

Since their inception in 1943 by the National Research Council of the USA, the Dietary Recommended Allowances (RDAs) have been updated on a number of occasions and undoubtedly have served as useful guidelines for individuals, institutions, populations and population subgroups. Nevertheless, their original objective, namely “to provide standards to serve as a goal for good nutrition”, has always been hampered by the important limitation that the RDAs were developed primarily from minimalist criteria aimed at the prevention of clinical deficiencies, and in the case of micronutrients the respective deficiencies and their overt clinical signs. This limitation became more acute and indeed provided added momentum to the repeatedly expressed need for the establishment of a more precise and customised approach to defining requirements better and to setting more quantitative recommendations for nutrient intake, because of the increasing realisation of the beneficial role of micronutrients in the prevention of disease as well as the impact such factors as lifestyle (smoking, alcohol abuse, self-imposed weight reduction), occupation, environment, genetic variation and nutrient interactions may have on their requirements.

Dietary Reference Intakes (DRIs)

The approach by the Food and Nutrition Board of the Institute of Medicine of the United States to have defined DRIs represents a paradigm shift from ***avoiding of deficiency states***, as determined by clinical manifestation and status, to ***maximising health and improving quality of life***. The latter is determined by functional measures including the reduction of risk of chronic disease and by suggesting guidelines for groups and individuals.

The DRI framework includes:

- the objective to determine recommendations to meet a variety of uses
- the contribution by nutrients in the risk reduction of chronic disease
- the inclusion and review of other food components
- the use and the rationale for functional end points, and
- the assessment of estimates of upper safe level of nutrient intake

The term DRIs is a collective name and refers to a set of at least four nutrient-based reference values:

- **EAR** : Estimated Average Requirement
- **RDA** : Recommended Dietary Allowance
- **AI** : Adequate Intake
- **UL** : Tolerable Upper Intake Level

Each of these reference values has special uses:

Estimated Average Requirement (EAR)

The EAR is the nutrient intake value that is estimated to meet the nutrient requirements in 50% of the individuals in a given life-stage and gender group defined by a specified indicator of adequacy. At this particular level of intake, the remaining 50% of the respective group will not have its nutrient needs met. In deriving the EARs, contemporary concepts on the reduction of risk of chronic disease were among the factors considered. The EAR is being expressed as a daily value averaged over time, for most nutrients at least over one week.

Because the EAR is a dietary intake value, it includes an adjustment for an assumed bioavailability of the respective nutrient.

The EAR is used as the basis in setting the RDA. If sufficient scientific evidence is NOT available to establish an EAR, no RDA is set. The EAR may be used as one tool for assessing the adequacy of intakes of population groups, and for planning adequate intakes by groups.

Recommended Dietary Allowance (RDA)

The RDA is the daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97 – 98 %) individuals in a given life-stage and gender group (Table 1). It is important to recognise that the RDA applies to individuals and not to groups and is the goal for dietary intake by the individual. The EAR serves as the basis to calculate an RDA. If the standard deviation (SD) of the EAR is available, the

$$RDA = EAR + 2 SD_{EAR}$$

If data are insufficient to calculate an SD, a coefficient of variation [(CV_{EAR}); CV_{EAR} = SD_{EAR} / EAR] of 10% is assumed:

$$RDA = EAR + 2 (EAR \times 0.1)$$

$$RDA = 1.2 \times EAR$$

The assumption of a 10 % coefficient of variation is based on extensive data on the variation of the basal metabolic rate (10%) and on the comparable coefficient of variation of 12.5% for the protein requirement of adults. If the nutrient requirement is highly skewed, other approaches may be needed to establish the 97th to 98th percentile to set the RDA.

Adequate Intake (AI)

In a case where the scientific evidence is inadequate to set an EAR, the Adequate Intake (AI) reference is used instead of an RDA (Table 1). The AI is based on experimentally derived intake levels or approximations of observed mean nutrient intakes by a group of healthy people. For example, for young infants for whom milk is the sole source of food for most nutrients during the first 4 to 6 months of life, the AI is based on the daily mean nutrient intake supplied by human milk for healthy, full-term infants who are exclusively breastfed.

Both, the RDA and the AI are used as the goal for the nutrient intake of an individual. However, there is much less certainty about the numerical value of an AI than that of an RDA value. Since the AI is dependant to a greater extent on judgement than is the case in determining an EAR, and subsequently an RDA, the AI value is expected to be numerically larger than an EAR and possibly even larger than the respective RDA. An AI is seen as an indication that substantially more research is required in order to have an EAR established and to have an RDA calculated.

Tolerable Upper Intake Level (UL)

The UL is the highest level of nutrient intake that is considered unlikely to pose any risk of adverse health effects to almost all individuals in the general population. If the intake of a given nutrient increases above the UL, then the risk of adverse effects is thought to gradually increase as well. ULs are based on the total intake of a nutrient derived from food, fortified food and food supplements. The need for setting ULs has arisen because of the increasing practice to fortify foods with nutrients as well as the increased use of dietary supplements by a larger number of people. The UL applies to long-term (chronic) nutrient intake and it is based on risk assessment. In this regard, it should always be borne in mind that scientific uncertainties are always an inherent part of the risk assessment process, especially when estimates of adverse health effects in humans are based on the extrapolation of data obtained from experimental studies.

Key issues in the development of a model for safety of nutrients include the concept of safety versus risk, the limitation of traditional models, and the unique characteristics of nutrients such as:

- the absence of dose-response data
- the availability of limited human or animal long-term studies
- the availability of limited surveillance studies to establish a no-observed-adverse-effect-level (NOAEL)
- the ready availability of information on supplemental nutrient intake, but relative paucity of data on total nutrient intake, and

- the available data on issues of bioavailability

The risk assessment model proposed by the National Research Council of the United States, which is widely used in public health and in making regulatory decisions includes the following steps:

- **Hazard identification.** This involves the collection, organisation, and evaluation of all information that can be related to adverse effects of a nutrient in humans. It also includes the relevance of any available experimental data, causality considerations, mechanism of the adverse effect, and the identification of distinct and highly sensitive sub-populations.

- **Dose-response assessment:** This is the relationship between the level of nutrient intake and the occurrence of adverse effects as well as the identification of the highest level of daily nutrient intake associated with no risk of adverse effect (UL). When

possible, the UL is based on the NOAEL, which is the highest intake or experimental oral dose of a nutrient at which no adverse effects have been observed in the individuals investigated. If there is insufficient data to demonstrate a NOAEL, then the lowest-observed-adverse-effect-level (LOAEL) may be used. The LOAEL is the lowest intake at which an adverse effect has been identified. The derivation of a UL from the NOAEL (or the LOAEL) may incorporate the so-called Uncertainty Factors (UF), which reflect or refer to or consider the gaps in our knowledge on a given relationship. Different ULs may be developed and, for instance, may be applied in dealing with various age groups.

- **Exposure assessment:** This evaluates the distribution of the usual total daily nutrient intakes among the members of a particular population group.

- **Risk characterisation:** It defines the fraction of the exposed population, if any, which is known to have nutrient intakes larger than the estimated UL as well as any uncertainties regarding the UL in relation to the nutrient intake estimates under consideration.

- **Risk management:** This includes the debate on any recommendations made in order to reduce associated risks, if a substantial part of the exposed population has intakes higher than the set UL. If the available data analysis reveals that the basis for estimating an UL is not given, ULs cannot be set. For instance, in the recent publication of the Food and Nutrition Board Panel although no ULs were set for thiamin, riboflavin, B₁₂, biotin and pantothenic acid, such ULs were set for some other nutrients and choline using the following indicators:

Nutrient UL	Indicator for setting UL	(adults)/day
Calcium	Milk/alkali syndrome	2500 mg
P	Elevated serum phosphate concentration	4 g
Mg	Osmotic diarrhoea	0.35 g (non-food)
Vitamin D	Elevated serum calcium concentration	50 µg (2000 IU)
Vitamin B ₆	Sensory neuropathy	100 mg
Folic acid	Precipitation or exacerbation of neuropathy in vitamin B ₁₂ -deficiency	1000 mg
Niacin	Vasodilatory effects (flushing)	35 mg

Application of DRIs

In diagrammatic terms (Fig. 1), the EAR of the DRIs is the intake at which the risk of inadequacy for a *selected group* is 50%. With intakes at the RDA level, the risk of inadequacy for an *individual* is rather negligible (only about 2-3 %). The AI has actually no relationship either to the EAR or the RDA, because a given nutrient requirement had to be estimated on an incomplete database. At intakes between the RDA and UL (distance B-C in the “observed level of intake” axis) the risk of inadequacy as well as of any adverse effect is practically not existent, since both are close to 0% risk. However, at intakes above the UL (distance C-D in the “observed level of intake” axis) the risk of adverse effect gradually increases. It should also be noted that the actual shape of the risk curve at intake levels in excess of the ULs has not been determined for all nutrients and may indeed be different from nutrient to nutrient. Moreover, the distances between the various given points of the “observed level of intake” may also differ for different nutrients. The risk for adverse effects is increased beyond the UL

(Fig. 2) depending on the size of the uncertainty factor (UF) deemed to be appropriate to adjust for the uncertainty in deriving the UL either from the NOAEL or from the LOAEL as the case may be. Nevertheless, there is a range of safety, which may vary from nutrient to nutrient.

For an individual's assessment of status, the RDA can be used to evaluate any nutrient inadequacy, but the true nutritional status of an individual requires in addition biochemical, clinical, and/or anthropometric data. Likewise, the UL can be used as a yardstick for an individual to obtain information on an eventual "over-consumption" and on the risk of adverse effects. For a given life-stage group, the EAR can be used in the assessment of prevalence of inadequate intakes (Fig.3). The percentage of people with usual intakes less than the EAR is an indicator of the prevalence of inadequacy of a certain nutrient in a given population. It should, however, be borne in mind that the strength of such data is augmented, if the day-to-day variations in the intake of a nutrient are lessened by a more frequent measurement of the intake of a given nutrient, usually averaged over a week. When using food intake data, it should also always be borne in mind that overestimation of the prevalence of inadequate intakes as well as the prevalence of adverse effects in those individuals having a higher than the UL level of intake may occur.

For planning purposes, an individual should aim at meeting the suggested RDA for his gender and life-stage group, or, in absence of an RDA, the AI may be used as the yardstick. Similarly, the individual can use the UL as a guide that higher intakes increase the risk of adverse effects. The EAR may again be used as the basis for planning or making recommendations for the nutrient intakes of free-living population groups (Fig.4). For instance, the mean nutrient intake for a group with a low prevalence of inadequate intake (approximately 2-3 % receiving less than the EAR for a given nutrient), can be based on the EAR and the respective variance of this particular group. In order to plan for an adequate dietary intake of this particular group, the average nutrient intake of the group must be planned to be far higher than the EAR in order to meet the envisaged nutrient intake for the overall population. Similarly, the variation of the intake distribution should be interpreted in relation to the respective UL for a given nutrient.

Current initiatives and future developments

Two panels of experts dealing with the Food and Nutrition Board's DRI evaluation process have successfully completed DRIs for the following nutrients^{1,2}:

Calcium Panel: Ca, Mg, vitamin D, F, P

B-Vitamins and Choline Panel: Vitamins B₁, B₂, B₆, B₁₂, niacin, folate, pantothenic acid, biotin, niacin, and choline

At present, the Panel on Dietary Antioxidants and related compounds is at work and the pre-publication of its report is expected to be issued next September. It is planned that a number of other Panels will soon be dealing with trace elements, vitamins A and K, fluid and electrolytes, macronutrients including energy as well as other food components such as phytochemicals found in tea and garlic, fibre and phytoestrogens.

At present RDA re-assessments as well as evaluations are being conducted in several countries, such as The Netherlands, Germany and Japan. The Nordic Recommendations (Sweden, Denmark, Finland, Norway and Iceland) have also been published recently. The WHO in collaboration with the FAO is continuing its series of Expert Consultations to formulate guidelines and recommendations for nutrient intakes and requirements as the basis for monitoring and improving nutrition-related health, especially in developing countries.

REFERENCES

1. Institute of Medicine: Food and Nutrition Board. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride. Washington, DC. National Academy Press:1997.
2. Institute of Medicine: Food and Nutrition Board. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B₆, Folate, Vitamin B₁₂, Pantothenic acid, Biotin and Choline. Washington, DC. National Academy Press:1998.