ABSTRACT   Dietary reference intakes (DRI), like its predecessor, the recommended dietary allowances (RDA) and the Recommended Nutrient Intakes (RNIs), are reference values, based on the best scientific evidence available. They serve as reference amounts of specific nutrients and food components for use in assessing the adequacy of and planning for nutritious diets. They have been used for over 50 y as the basis for national nutrition monitoring and intervention programs in the United States, Canada, and other countries and as the basis for dietary guidance developed for both individuals and for targeted groups of people. Thus, although not developed for specific policy applications, they have represented the best scientific perspectives regarding what should be the basis for nutrition and public health policy related to foods and supplements. In determining DRIs, as was the case with the RDA, significant attention must be paid to the form of the nutrient or food component that is evaluated. Research conducted to determine how much of a nutrient is needed must evaluate the chemical form provided, the matrix in which it is given and the effect of other food components on absorption and/or utilization. Because the DRI recommendations will be used in population-wide policy development, assumptions must be made explicitly about what is expected for all of these factors in a typical diet. At the same time, where data exist relative to nontypical but potentially very significant effects on bioavailability, these must also be delineated to be of use in a variety of settings. Finally, one of the most important aspects of determining bioavailability in developing reference intakes is that as new information emerges, new complexities enter into the process. As more chemical complexes of nutrients and food components become available in the marketplace, new bioavailability factors may need to be established. Examples of such changes exist in the DRI reports already published for vitamin B-12 and folate and in previous RDA for iron and protein. It is often the different assumptions related to bioavailability that alter the reference intakes used as the basis for public health policy in different countries, rather than the basic science from which the recommendation is derived. J. Nutr. 131: 1331S–1334S, 2001.

KEY WORDS: • dietary reference intakes • recommended dietary allowances • DRI • RDA

The new dietary reference intake (DRI)1 activity (Institute of Medicine 1994) of the Food and Nutrition Board, and its predecessors, the recommended dietary allowances (RDA) (National Research Council 1989a), and similar reference standards from other scientific bodies, are designed to be used as quantitative reference intakes for a variety of purposes and are based on consensus based on the best science available. The new DRIs provide reference amounts of specific nutrients and food components for use in assessing the adequacy of and in planning for nutritious diets.

RDA have been used for over 50 y as the basis for national nutrition monitoring and intervention programs in the United States and other countries and as the basis for dietary guidance developed for both individuals and for targeted groups of people (Institute of Medicine 1994). Thus, although not developed for specific policy applications, they have represented the agreement of a group of experts of the scientific basis for nutrition and public health policy related to foods and supplements.

The DRI process has evolved as a methodology to provide quantitative reference intakes for the many uses related to nutrition and public health policy development. Some of the uses include serving as the scientific basis for planning meals for groups, such as school lunch programs and menus for correctional facilities, the basis for food assistance and nutrition education programs, and as a reference point for nutrition labeling of food and dietary supplements. In this manuscript, an overview of the DRI process, the development of DRI
values, and examples of the impact of bioavailability on reference values and subsequent evaluation of diets or intakes are briefly discussed.

**DRI**

The RDA (Institute of Medicine 1989a) report was first issued in 1941 and contained recommendations for nine nutrients and energy; the last edition of RDA in 1989 (the 10th edition) contained recommended or safe intakes for 26 nutrients and energy. In 1989 the Food and Nutrition Board also issued the report, "Diet and Health" (National Research Council 1989b), which discussed the role of food components in risk factors for chronic disease. In the early 1990s, it seemed appropriate to broaden the framework for determining RDA to include concepts of chronic disease in addition to deficiency diseases. Thus, the DRI process was undertaken. It consists of a number of panels of experts brought together under the oversight of the standing committee on DRIs to deliberate on the scientific evidence available to determine quantitative reference points for use in specific applications. Assisting in the overall process are two subcommittees. One subcommittee assists the panels in developing one of the reference points, the tolerable upper intake level, and the other subcommittee assists in providing the statistical and theoretical basis for applying the various multiple reference points to specific uses and in interpreting to the various users how to apply the DRIs.

The DRI framework requires the estimation of average requirements for nutrients and food components reviewed, the definition and justification for criteria used to assess dietary adequacy in meeting that requirement, estimation of the variation of the requirement in the population for which the requirement is developed, and is fairly specific that the functional RDA is to serve as a goal for an individual and, thus, is not the most suitable reference value to be used in other possible roles in nutrition policy and programs (Yates et al. 1998).

To briefly review the DRI, there are currently four categories of reference intakes: the estimated average requirement (EAR), RDA, tolerable upper intake level (UL), and the adequate intake (AI). The EAR is the average requirement for healthy individuals in which some type of functional or clinical assessment has been conducted and adequacy determined. Not all nutrients reviewed to date have EAR, because there have not been adequate studies available upon which to develop estimates of average requirements. The EAR is related to the RDA by increasing the EAR by the variation in the population in order that the RDA meet the needs of 97-98% of the population group for whom it is developed. Thus, two standard deviations of the requirement or two coefficients of variation (if the standard deviation can not be estimated) are added to the EAR to develop the RDA.

Thus, the RDA is based on the EAR. In the case that data are inadequate to estimate an average requirement, no RDA is provided. In this case, an AI is given, which in the judgment of the experts convened should meet or exceed the needs of those in the healthy population for whom it is intended. Thus, there is significantly more judgment involved in setting the AI and, thus should be used as a guide for intake but cannot be used for all of the applications for which the EAR is designed (Institute of Medicine 1997).

In determining DRIs, as was the case with past efforts to develop RDA, significant attention must be paid to the form of the nutrient or food component that is evaluated. Research conducted to determine how much of a nutrient is needed must include evaluation of the chemical form provided, the matrix in which it is given, and the effect of other food components on absorption and/or utilization. Because the DRI reference values will be used in population-wide policy development, assumptions must be made explicitly about what the expected effect of all of these factors in a typical diet is on availability of the nutrient to meet cellular demands. At the same time, where data exist relative to atypical diets but which result in potentially very significant effects on bioavailability, these must also be delineated to be of use in a variety of settings.

Finally, one of the most important aspects of including bioavailability in developing reference intakes is that as new information emerges, new complexities enter into the development of reference values and standards. As more chemical forms or combinations of nutrients and food components become readily available in the marketplace and as new data are published demonstrating differences in absorption or metabolism of various forms, new bioavailability factors may need to be established. Examples of such changes exist in the DRI report already published for vitamin B-12 and folate and in previous RDA efforts for iron and protein.

**Vitamin B-12**

A number of assumptions related to bioavailability were made by the panel responsible for developing DRIs for vitamin B-12. First, they determined that absorption of vitamin B-12 varied substantially depending on the food from which it came, although there were very few studies available (Institute of Medicine 1998). In fact, there were only five published studies at the time that provided intrinsically labeled vitamin B-12 and determined rates of absorption. The variation is in part thought to be due to the saturation of ileal receptors when ~1.5–2.5 µg of vitamin B-12 per meal is given (Scott 1997) and, thus, foodstuffs, such as liver, which have a high content of vitamin B-12 (112 µg/100-g serving), quickly saturate the transport system resulting in low rates of absorption—in this case, 11%. Other foodstuffs, such as mutton, provide a much higher percentage absorbed (65%), but in terms of content only contain ~1/50th as much, ~2.5 µg/100-mg serving.

Thus, for vitamin B-12, as for many nutrients, absorption is dependent on available transport mechanisms and the load put on the system. This is particularly important with a complex organic compound such as methylcobalamin, which requires a number of steps for absorption: an intact stomach that secretes acid and pepsin for initial dissociation from food proteins, R proteins (haptocorrins) secreted by the salivary glands, gastric mucosa that binds released vitamin B-12, intrinsic factor (secreted by parietal cells of the stomach after food stimulation), pancreatic sufficiency that provides pancreatic proteases that partially degrade the R proteins, released vitamin B-12 to bind with intrinsic factor and a normally functioning terminal ileum, where absorption actually occurs.

Estimates of vitamin B-12 absorption from food indicate that with normal gastric secretion, ~50% is assumed to be absorbed; however, crystalline vitamin B-12 at low doses results in 60% absorption (Adams et al. 1971), whereas at high doses (>500 µg), only 1% is absorbed (Berlin et al. 1968).

The EAR and corresponding RDA derived for vitamin B-12, thus, is based on normal gut function, until the reference intakes for those >50 y of age, in whom it is estimated that 10–30% have atrophic gastritis, which decreases gastric acid secretion and, thus, may have decreased ability to absorb protein-bound vitamin B-12 from food. Therefore, although it appears that in national surveys in the United States, few have inadequate intakes, it is possible that the absorption of bio-
available vitamin B-12 is actually decreased in some. Thus, the most recent DRI recommendation states that for those > 50 y of age, who may not be aware of decreased acid secretion or the presence of atrophic gastritis, most of their vitamin B-12 should come from crystalline sources (such as that usually added to foods or in supplements) because such sources do not depend on acid action on proteins to release the vitamin B-12 for combination with intrinsic factor.

The lack of data on the absorption of vitamin B-12 and the true prevalence of atrophic gastritis in the population makes these assumptions need further substantiation; because of the lack of data on absorption from dairy foods and most forms of red meat and fish, a conservative adjustment, 50%, for the bioavailability of naturally occurring vitamin B-12 was used in the DRI activity. What is important to note here is that quantitative reference values provided by the DRI process, as well as other scientific processes that define reference values, where only small amounts of data regarding food composition, absorption or influences on absorption of other food components are available, will be under review and possible revision as the assumptions used to develop them are changed due to new data and information.

Folate

With regard to folate, the DRI panel on B vitamins took the step to recognize the significant importance of bioavailability in evaluating folate requirements (Institute of Medicine 1998). They recommended that reference values be given in units of dietary folate equivalents (DFE) to recognize the significant differences in absorption demonstrated by the various sources of folate. The pteroylmonoglutamates (the naturally occurring form of folate found in food) are approximately one half as bioavailable as that of folate from supplements or fortified foods, which is in the form of pteroylmonoglutamate.

In previous reviews of reference values, the difference has not always been taken into account, because folate content of foods has been provided as composites of all sources of folate. In addition, older techniques for folate analysis, which have depended on enzymatic digestion of food folate before determination, are now thought to significantly underestimate folate content of many foods. Thus, being able to estimate accurately from various sources and differentiate the monoglutamate form taken with food (as in fortified foods) or individually as a supplement, from naturally occurring polyglutamates found in food will determine the amount of truly available folate in the diet. DFE have been introduced to address these concerns. However, it must be noted that again, these are estimates, and await significant efforts for additional studies to determine the accuracy of the equivalencies provided.

Estimates of prevalence of inadequacy of dietary folate based on the EAR of folate (in DFE) show that if the total intake is adjusted to include both the new equivalents and the presence of fortified foods not available when surveys were conducted, the percentage of the population that appears to be deficient in folate dropped from 10 to 15% per d.

If 10% absorption is used, then men would need 13 mg/d in the diet; if 15% were the factor for absorption, then men would need less, ~8.7 mg/d. Similarly, for women, if 10% were used, then they would need 18 mg/d, but if 15% were used, then 12 mg/d would be needed. The RDA decided upon would be equivalent to 12.5%: 10 mg for men and 15 mg for women, which was chosen in part based on review of data on prevalence of iron deficiency anemia and estimated intakes in the United States.

If one were looking at a group with other types of diets containing little animal protein and low in ascorbic acid, higher amounts of food iron would be needed; for example, a diet of cereal grains and no heme iron, with absorption of only 4% would theoretically increase the recommended intake to 32 mg for men and to 45 mg for menstruating women. Thus, assumptions and knowledge about the bioavailability have profound effects on the quantitative reference values used for both planning diets and for assessing the adequacy of diets of specific groups of people.

Protein

Protein requirements in the 1989 RDA activity were based on meeting the body’s needs for nitrogen and for essential amino acids (National Research Council 1989a). Based on experimental nitrogen balance data in young men using high quality reference proteins (such as, egg, casein or meat) at levels below and near predicted adequate intakes, an estimated average requirement of 0.6 g/kg was obtained (World Health Organization 1985). The CV for the average daily requirement was 12.5% in participants measured, and, thus, to develop an RDA, twice the CV (equivalent to two standard deviations) above the average requirement was added to the average requirement to develop the allowance of reference protein of 0.75 g/kg per d. This level of protein would be expected to meet both the nitrogen and essential amino acid needs for adults. The RDA was rounded to 0.8 g/kg per d for both men and women.

Assumptions about the U.S. diet involved in determining the RDA for protein included the following: the amino acid score of the typical U.S. diet was 100 for adults and most age groups; data from national surveys, Nationwide Food Consumption Survey 1977–1978 (U.S. Department of Agriculture
1983) and 1985 (U.S. Department of Agriculture 1986), showed 14–18% of energy coming from protein and despite wide variations in energy intake, the proportion of protein as a percentage of energy remained similar; 65% of dietary protein was from foods of animal origin [Nationwide Food Consumption Survey 1977–1978, 1985, National Health and Nutrition Examination Survey II (48% from meat, fish and poultry; 17% from dairy; and 4% from eggs = 67%)]; and digestibility of the typical diet was equal to reference proteins. Based on these assumptions, adjustment for allowances for dietary quality for typical U.S. diets “would rarely be warranted....” Would the protein RDA for adults need to be adjusted if the reverse in terms of animal protein (two-thirds plant, one-third animal) was the predominant diet? Based on an amino acid score of 100 and a lower assumed digestibility of 92 compared with the reference proteins, the RDA for adults would change little, to 0.82 g/kg, thus, still within the rounding of the RDA for higher levels of intake of animal protein.

However, for a young child, 3 y old, the increased need would be more pronounced because of a greater need for essential amino acids as a proportion of relative total nitrogen needs. The amino acid score for this predominantly plant-based diet for a young child would equal 88 (51/58, due to lysine being the limiting amino acid). The adjusted RDA for the 3-y-old child would increase to 1.4 g/kg per d, an increase of ~27%, based on comparison with the typical U.S. diet.

Given the number of uses identified as being dependent on scientifically based quantitative estimates of reference intakes, the importance of accurate and specific data on bioavailability to develop sound nutrition and public health policy and programs cannot be understated. Also, it is often the different assumptions relative to bioavailability that alter reference intakes used as the basis for public health policy in different countries, rather than differences in interpretation of the basic science from which the recommendation is derived. As with other aspects of science, the increasing complexity of reference intakes and equivalency of various forms based on bioavailability may be perplexing to the policymaker but is crucial to the scientific integrity of the policy or program developed.

Note: unless otherwise attributed, the views expressed by the author are not necessary those of the National Academy of Sciences or the Institute of Medicine.

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