Trace Elements, Food and Nutrition Policy

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Considerations Regarding Future Trace Element Dietary Reference Intakes

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Introduction

Since 1941, the Food and Nutrition Board of the National Academy of Sciences has issued reports periodically providing “standards to serve as a goal for good nutrition” (IOM 1994). The last edition of these standards, called the Recommended Dietary Allowances (RDAs), was published in 1989 (IOM 1989). That edition included recommendations for four trace elements — zinc, iron, iodine and selenium, and estimated safe and adequate daily dietary intakes for five other trace elements — copper, manganese, fluoride, chromium, and molybdenum. Since the standards were first proposed in 1941, their uses have expanded from guidelines for the planning and procurement of food for groups of people to standards serving as the basis of food labeling, federal food assistance programs, food fortification policies, assessment of dietary survey data, and the design of nutrient supplements and special dietary foods. The RDAs are frequently used to assess the diet intakes of individuals or to provide dietary guidance to a person. Nutrition science has also undergone a number of changes since the last edition was prepared. The role of diet in reducing the risk of chronic disease now is a major emphasis within the field. This development, along with the expanding uses of the RDAs, led the Food and Nutrition Board to conclude that a new paradigm is needed for the next set of dietary recommendations that incorporates data on the reduction of risk for chronic disease and provides several reference intakes for each nutrient in order to meet the expanding list of uses. Since the next set of standards will be based on a new paradigm, the Food and Nutrition Board proposes to change the name from “Recommended Dietary Allowances” to “Dietary Reference Intakes.”

Use of Risk Reduction as a Criterion for Dietary Reference Intakes

In past editions of the RDAs, recommendations were only established for essential nutrients, which were defined as chemical substances found in food that cannot be synthesized in the body and are necessary for life, growth and tissue repair. More recent research has shown, however, that there are a number of components in food that are not considered to be essential nutrients but which are important for maintenance of health and, possibly, the risk reduction for chronic disease. Examples of those substances include dietary fiber, carotenoids, lycopene, choline, and some of the ultra trace elements, such as boron and vanadium. Thus, new criteria need to be established for identifying those components in foods which have a Dietary Reference Intake (DRI). Criteria for making that decision may include the following questions: 1) Is the substance a normal component of the food supply? 2) Has a biological function for this substance
been identified in humans? 3) Are data available on levels of intakes that maintain tissue homeostasis and biologic function? 4) Is there evidence of inadequate or excessive intakes in some population groups?

Application of those criteria to boron would probably lead one to conclude that more information is needed before a DRI can be established for this element. It is known that boron is a normal component of the food supply, but an essential biological function has not been identified, intakes that maintain homeostasis and normal function are not well defined, and it is unknown if there are population groups consuming too little or too much boron because an indicator of nutritional status has not been defined. Alternatively, one might decide that sufficient data are available to establish a DRI for manganese. It is commonly found in the food supply. It is required to activate several types of enzymes and it is a constituent of several other enzymes. Some information regarding tissue homeostasis and amounts needed in the diet to maintain normal function are available, and there are reports of manganese toxicity due to the inhalation of manganese fumes and dust. The degree of risk for inadequate or excessive intakes of manganese are unknown, however, due to the lack of a biomarker of manganese nutritional status.

To establish a DRI, therefore, three types of information regarding a food component should be integrated when making a dietary recommendation. Those three types of information include: 1) Data on the biological function and the functional response to inadequate or excessive intakes, 2) Data on the mechanisms for regulating tissue nutrient homeostasis and adaptations in those mechanisms with changes in intake, and 3) Specific, quantitative data on changes in nutritional status with shifts in nutrient intake.

Functional endpoints of nutritional adequacy are needed to establish an intake that reduces the risk for chronic disease. Traditionally, functional endpoints have not been used to establish nutrient recommendations and very few quantitative, specific functional endpoints are available for assessing nutritional status. Research is needed to establish functional endpoints for nutrient requirements that reflect a dose response relationship, are consistent across a variety of studies, and are temporally correct (i.e., a change in nutrient intake occurs before the functional change).

Studies of zinc depletion in humans illustrate the need to use functional endpoints along with studies of homeostasis when estimating nutrient requirements. For example, when dietary zinc was reduced from 15 to 5.5 mg/d in a group of healthy men, zinc balance was achieved within nine days (Wada et al. 1985). Although adaptations in zinc homeostasis permitted zinc balance when low zinc diets were fed, this was not without some functional consequences. Circulating concentrations of serum albumin, pre-albumin, retinol-binding protein, thyroid stimulating hormone, and free thyroxine declined significantly (Wada et al. 1986). All of these functional changes occurred without a fall in plasma zinc concentration. Thus, without these functional endpoint data, one might conclude that the dietary zinc requirement is only 5.5 mg/d.

**Establishment of DRIs For Populations And Individuals**

As stated above, the use of the RDAs has expanded considerably during the last 50 years. Today, they are used to prescribe diets for populations (e.g., food planning and procurement, federal food assistance) and to assess the intakes of populations (e.g., evaluation of dietary survey data). RDAs are also used to prescribe diets for individuals and to assess the intakes of individuals. Two different types of DRIs are needed, therefore. One standard that can be used to prescribe and assess diets for populations and another set for prescribing and assessing intakes of individuals. Standards for both the population and individual require an estimation of the mean requirement for the nutrient. Establishment of an individual DRI also requires knowledge of the variance in that requirement among a group of individuals of the same gender, age, and health status. The population DRI, on the other hand, requires knowledge of the variance in intake of the nutrient in that population.

If the mean requirement for a nutrient and the variance of that requirement are known, an individual DRI can be set at the upper end of the distribution of the requirements so that the needs of practically all individuals in that population are met. This is the approach that has been used to establish RDAs in the past. This standard can be used to evaluate the intake of an individual. For example, if their intake is equal to or above the standard, one can conclude that the intake is adequate. An intake below the standard, however, does not denote an insufficient intake. An individual DRI at the upper end of the distribution of
requirements provides a goal for good nutrient intakes by an individual and would be an appropriate basis for dietary guidance.

In contrast to the individual DRI, a DRI for a population, requires knowledge of the distribution of intakes in that population. Knowledge of the distribution of intakes is necessary so that an adequate intake of all members of the population can be assured, even by those who eat small amounts of food. Using probability assessment, one can determine that the probability of an inadequate intake is low (about 2–3% of the population) if the population DRI is set so that subtraction of two standard deviations of the variance in intake from that standard equals the mean requirement (NRC 1989).

Using these definitions of an individual DRI and population DRI, hypothetical estimates of zinc DRIs for individuals and populations can be estimated. Let's assume that the mean requirement for zinc is 12.5 mg/d with a standard deviation of 1.25 mg/d. The individual DRI would be the mean requirement plus two standard deviations of that requirement or 15 mg/d. Let's also assume that the variance in zinc intake in a certain population is 2.5 mg/d, or a coefficient of variation in intake of 0.20. Using the definition that the mean requirement equals the population DRI minus two standard deviations of the variance intake, one can solve for the population DRI. A hypothetical estimate of the zinc population DRI, therefore, is 20.8 mg/d.

To establish both individual and population DRIs one must answer the question, requirement for what? Requirements for nutrients will vary with the level of nutritional status desired. For example, the requirement for prevention of the clinical symptoms of nutrient deficiency is lower than the amount needed for maintenance of biological function, for provision of body stores, or for support of a pharmacological role. The need for iron among adult men to prevent anemia is thought to be only 4 mg/d whereas the amount required to provide for some body stores is at least two-fold higher. One of the biggest challenges facing DRI committees will be to determine the criterion used to establish the mean requirement.

Summary

The Food and Nutrition Board of the Institute of Medicine recommends that a new paradigm be used to establish the next set of dietary recommendations and that those new standards be called Dietary Reference Intakes, or DRIs. The Board also proposes that data regarding risk reduction for chronic disease be used to establish the reference intakes; that a model integrating information on nutrient homeostasis, function, and static tissue or circulating concentrations be used to establish the requirements; that multiple reference intakes be established for individuals; and that guidance be provided on how to estimate reference intakes for populations based on knowledge of the mean requirement and distribution of intake.

Literature Cited


Discussion

Q1. Leslie Klevay, USDA-ARS, Grand Forks, ND, USA: Would you infer then that if we don’t have variance estimates for a nutrient will there be no DRI for it? And if this inference is correct will there be a shorter list of nutrients that will have DRIs?

A. No, we recognize that there is probably very limited information on the variance in requirement and that we will probably have to make some educated judgements of what that variance is in order to come up with DRIs.

Q2. Janet Hunt, USDA-ARS, Grand Forks, ND, USA: I may need to understand more about the population DRI calculations, but I am a little concerned about your example of 20 mg/day for zinc as a population standard. I think you
can’t ignore the political realities in the United States, where we have had bills proposed for dietary supplementation that criticize the scientific establishment of RDAs and claim that there is a need for additional kinds of recommendations that more optimize health, and that this movement is, I believe peddled mostly by the health food supplement industry. I think that to introduce this new concept will likely only add fuel to the fire for lobby groups critical of the process. In addition, from the scientific derivation of this intake variance, it will be very important to have good data for intake variances that do not rely on day-to-day variance in intake. For example, we should probably not use 24 hour recalls, but rather use 7- or 14-day averages. We should be ignoring the day-to-day variance.

A. First, let me clarify that we are not going to establish population DRIs, but we are establishing DRIs for individuals. We will provide guidance on how to determine what you should feed a population group, but you have the responsibility for doing that based on your knowledge of the variance of intake of nutrients within that population group. So there will be no document coming out that says the zinc population DRI is 20.8 mg/day. There will be an individual zinc DRI, and then guidance on how to convert that for the various population groups. Yes, I agree with you, we do need to have good information on variance of intake in the population group, in order to come up with appropriate standards, but that will be up to the individuals who will have to carry out that conversion. Requirements for dietary intake do vary between populations, so of course we will need good intake variance data.

Q3. Noel Solomons, Guatemala: I commend you for your clarity of explanation. However, I tend to dispute your description of Homo sapiens as having a homogeneous biology. There are differences in size and body compositions, in respect to environmental factors and not just diet (such as parasites, climate, etc.). Certainly there is genetic polymorphism, although it may be tough to identify all the details at present.

A. In the past there has not always been a clear basis of the recommendations, being sometimes based on biology, and other times on intake. My point was that variations in intake within a population will certainly be greater than variances in biology of the group of individuals. I’m sure that there will be things that will affect the requirement, as you pointed out but if we can clean it up a little bit by just focussing on the biology we’ve removed another major source of variability, which is intake. That’s our point.

Q4. John Bogden, New Jersey Medical School, Newark, NJ, USA: What about setting numbers that represent the threshold for frank deficiency? Did the committee discuss that?

A. We did consider this. At one point, we thought of having four reference intakes, with the fourth being at a level which would be deficient, but weren’t so sure it would be useful. Besides, given the mean and standard deviation of the requirement level, one can easily estimate the threshold. If we could be convinced that there is a need for it, I guess we would reconsider.

Q5. Gordon Klein, University of Texas, Galveston, TX, USA: Have you considered interactions between the nutrients? Has any consideration been given to possible effects of supplements on the bioavailability of nutrients? And finally, what effort will be made to disseminate this information to the public?

A. Yes, we have been considering nutrient interactions. That will be part of the analysis that we will have to consider in determining the mean requirements. Supplements will undoubtedly influence the variance in the intakes, but it’s not clear to me right now how that might influence the nutrient requirement. And finally, the dissemination of the information, will be coming out in increments. Probably the first report will be the calcium, vitamin D, magnesium and phosphorus report, and will be publicized in the same way that all the other reports from the National Academy of Sciences are publicized.

Q6. Forrest Nielsen, USDA-ARS, Grand Forks, ND, USA: If there is not enough information on a given element to allow the setting of a DRI (e.g. for boron, vanadium or fluorine), what will be done?

A. We may use an ESADDI approach, or something similar. This hasn’t really been decided yet, but we will not be ignoring those nutrients where there is some information, but insufficient to allow full determination of a DRI.