

Introduction

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The Nutrition Research Foundation of the University of Sydney and ILSI Australia combined to have this special international symposium at the time of the annual symposium of the Foundation. The last time that the Nutrition Research Foundation and ILSI Australia combined to put on a symposium, it eventually developed into the International Conference on Dietary Guidelines held on the Algarve, Portugal in 1986, and published as a large supplement of the *American Journal of Clinical Nutrition*¹. Lists of previous symposia held by the Nutrition Research Foundation and by ILSI Australia appear on pages 53 and 54 of this Supplement.

The Nutrition Research Foundation is an organization which supports the work of the Human Nutrition Unit in the University of Sydney. ILSI Australia is an off-shoot of International Life Sciences Institute USA, which incorporates the former Nutrition Foundation (USA).

The first point I have to make, mainly for the journalists, is that the ideas in this symposium represent a gradual accumulation of information rather than a breakthrough. These ideas, the scientific experiments, the epidemiological observations that are reported in this Supplement, have been emerging over the last 25 years. Linus Pauling² wrote this 23 years ago:

Unsaturated fatty substances play an important part in the functioning of our biochemical machinery and in cell membranes and other tissues. These substances are converted by oxidation into peroxides that are harmful. Vitamin C and vitamin E are natural antioxidants. An increased intake of these vitamins provide protection against cardiovascular disease. Vitamin E may be the more important of these two natural antioxidants, but vitamin C is also important. A proper intake of vitamin C and vitamin E may help to prevent premature aging, especially if one's diet is rich in polyunsaturated fats.

Some of us in a committee of the Australian National Health and Medical Research Council worked over eight years to develop the present set of recommended dietary intakes (RDIs) for Australians^{3,4}. The RDIs in Australia, although they were worked out independently, are mostly very close in numbers to the better-known RDAs in the United States. The definition we used was that the RDI is the amount of a nutrient judged to be adequate to meet the known nutritional needs of practically all healthy people and the orthodox concept is that above the RDI there is no further health benefit to be gained (Figure 1). If you go far above it you can start,

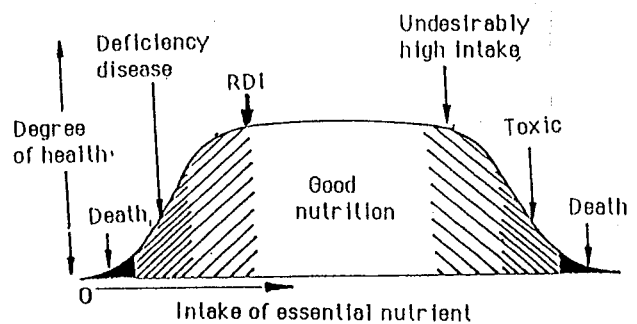


Figure 1. Plateau top diagram to illustrate the intended classical position of the RDI (recommended dietary intake) for an essential nutrient. Note: there is no further improvement in health beyond the RDI.

with some nutrients, to get into trouble from undesirable effects, but for other nutrients, the range between adequate and toxic is very large.

The concept discussed in this symposium is that perhaps this is not quite right. Perhaps for some nutrients there is an intake above the RDI (ie the amount that prevents deficiency disease or subclinical deficiencies) where the state of health is further enhanced, eg by partial protection against the degenerative diseases of old age. This higher intake level can be called the optimal intake (range) for a nutrient. To express this visually, the graph of health against intake for some nutrients would be thought of not as a plateau between the RDI and the start of undesirable effects, but still curving upwards for some way above the RDI level (Figure 2). Now it is relevant that the British committee which revised their equivalent of the RDAs has renamed these Dietary Reference Values⁵. These classical numbers – RDAs, RDIs and now Dietary Reference Values have, I believe, their main value as references (like anthropometric references) to give an idea of the relative size of requirement of nutrients⁶, because of some nutrients we require about 1 μ g (vitamin B-12), of others 100mg (iodine), of others 1mg (thiamin), and of others we require much larger, about 1 gram (calcium) and of others 50g (protein) or 100g (carbohydrates).

In our work for the Australian Recommended Dietary Intakes we considered in the background papers the possibility that intakes about the amount that prevents deficiency could have beneficial effects for each of the

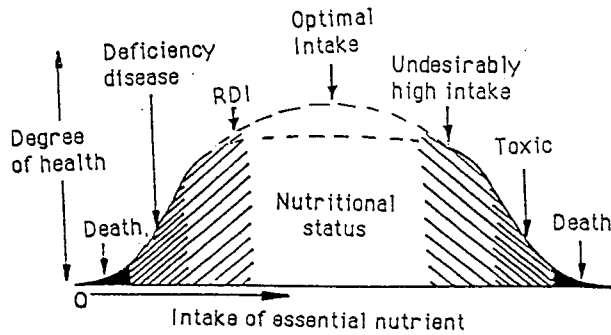


Figure 2. The alternative concept. Ingestion of the RDI should guarantee no deficiency disease but beyond the RDI there may still be additional health benefits (eg partial protection from a degenerative disease). The top of the dome beyond the RDI is then the optimal intake range.

four vitamins considered in this symposium: F (folate), A (or carotene), C (ascorbate) and E (tocopherols).

On folate (1984)⁷ 'an important and much-discussed question is whether folate deficiency in early pregnancy predisposes to foetal malformations, particularly harelip and neural tube defects'. The evidence, before the MRC trial was suggestive but incomplete.

Our background paper on vitamin A (1986)⁸ had four paragraphs on possible protective effects against cancer. 'Although there is considerable epidemiological and laboratory evidence to suggest that retinoids have a role in the prevention of cancer it is not yet clear which compounds are responsible for this effect. Ziegler et al. have recently reviewed several studies of diet and lung cancer and have found that inverse associations have been noted more frequently (in six out of seven studies) with indices of carotene intake or carotene containing foods. Again the evidence was incomplete and confusing, eg with some negative prospective serum levels.

'For vitamin C⁹ there were four criteria we considered when re-working the RDI for Australia:

- (a) intake that prevents scurvy,
- (b) intake to give tissue saturation,
- (c) intake that maximises absorption of non-haem iron,
- (d) intake that may minimise risk of gastric cancer.'

After careful consideration the committee decided on an intake to prevent scurvy in smokers and give 'reasonable' reserve in most people but not saturation. 'We thought the data about a protective effect of vitamin C against gastric cancer are not [in 1987] sufficiently quantitative for working out an RDI; it should be covered by the dietary guideline 'eat more vegetables and fruit'.

The background paper on vitamin E¹⁰ noted some reports of a therapeutic value of vitamin E for intermittent claudication and preliminary evidence suggesting possible protective effects against cancer of the stomach and of the breast. Clearly further research is needed in this important area.

The committee concluded at the end of the 1980s⁹

The *optimum nutrition* position sees a peak of physiological function rather than a plateau between deficient and toxic intakes and wants to include more recent

hypotheses about the role of generous intake of several nutrients in prevention of cancer, etc. This is something we all have to do at the practical level but in the present state of our knowledge we cannot use non-quantitative epidemiological evidence of a protective effect of (say) vegetables and fruits against certain cancers to change the RDI for vitamin C. This new tentative, provisional epidemiological information is suitable material to go into dietary guidelines, not the sort of continuous quantitative data that go to make up RDIs'.

In the last paragraph of 1990 editorial for the *British Medical Journal*, entitled 'Who should take vitamin supplements?'¹¹, having listed the sort of people (minorities) who would benefit from the right vitamin supplements, I noted that work was going on which might change the opinion that the majority of healthy people do not need vitamin supplements. We were waiting in 1990 for the results of the Medical Research Council's Trial on Prevention of Neural Tube Defects¹² and we needed to watch work going on about antioxidant vitamins.

The ideas for this Symposium come from the USA from the New York Academy of Science meeting in February 1992 called 'Beyond deficiency'¹³, which was very well summarized for the lay person in *Time* magazine¹⁴. They come from the 2nd International Symposium on Nutrition and Fitness in Athens in May 1992, which some of us attended, they come from work funded by the Ministry of Agriculture, Fisheries and Food in Britain and there is also an initiative near Sydney which I shall present.

Many people contributed to the organization of this symposium: Professor Ron Edwards, Dr Efi Farmakalidis, Mr Steve Kirkham for ILSI and Dr Chris Hudson who is on the Board of ILSI chaired the afternoon session. At the University of Sydney: Isa Hopwood, Zia Ahmad (who tape-recorded the talks), Peter Williams should be specially thanked, but the heaviest load of the administration was carried by Marianne Sylvada de Soza.

The symposium was originally held at the Stephen Roberts Lecture Theatre in the University of Sydney on 4 December 1992. Over 200 people attended and we have had many requests for a published version, which follows.

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