currently fit into our culture but it was how vitamin D was obtained for untold thousands of years before we became civilized and warned that sunlight was a carcinogen to be avoided.

Clinically, this fact has been clearly demonstrated in a recent publication from our group that effectively raised the antirachitic activity of human milk to a level that sustains the nursing infant with no harm to the mother[14]. Subsequently we received a large grant from the National Institutes of Health to study this approach further, in which we give mothers 50 or 150 μg vitamin D_3/d compared with controls receiving 10 μg vitamin D_3/d (and concomitant vitamin D_3 drops of 0 IU to the infants of mothers in the high-dose groups and 10 μg/d to the infants whose mothers are receiving 10 μg/d) to sustain not only maternal circulating levels of vitamin D and 25(OH)D, but also her nursing infant's. The 5-year project is nearing completion and we have not encountered a single adverse event related to high-dose maternal vitamin D supplementation. It should be noted, however, that we had to terminate the 50 μg/d arm of the trial because through our DSMC it was determined that this dose was 'inadequate' at supplying the nursing infant with sufficient amounts of vitamin D to maintain normal infant total circulating 25(OH)D level. Why, because a 5 μg/d intake even for a neonate is not an adequate amount. Just think, only a few years ago, that 50 μg/d dose was thought to cause vitamin D toxicity. Isn't science a wonderful force if one actually pays attention and follows the data?

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Vitamin D

Finding the appropriate referent for vitamin D

Madam

Organisms, as they evolve, come into an exquisite equilibrium with their environment. Those that inhabit starved environments depend upon them mainly as a source of water, energy and minerals. The vast array of organic molecules they need for metabolism they make for themselves. From the standpoint of energy that is expensive, and such organisms tend to be – and to remain – relatively simple. When the environment itself provides many of the compounds necessary for metabolism, organisms tend to shed the biochemical apparatus for making them for themselves. For man, examples are the essential amino acids, essential fatty acids and the array of compounds we call 'vitamins'.

It was not until World War II, when governments began to be concerned about ensuring optimal fighting status of their military, that the first nutrient intake recommendations were developed. For the most part, it seems that governments took as their starting point the prevailing intakes of populations that did not have the then-recognized explicit nutrient deficiency diseases. This is clearly the approach the Institute of Medicine (IOM) used in its recently released recommendations for calcium and vitamin D[1]. This stratagem is not altogether unreasonable if one's main concern is to ensure that beriberi and pellagra (for example) are not impairing the health of the population. By that criterion the diets of groups free of these disorders are, obviously, adequate. However, this approach makes no provision for

more subtle expressions of malnutrition, and for one nutrient, in particular, it fails altogether. That nutrient is vitamin D which, for most mammalian species, is not a food constituent at all, but is synthesized in the skin on exposure to solar UV-B radiation.

As the human race migrated north out of Africa, it became more and more deprived of what it could get only from the sun. Migrants could adapt to the cold by the development of clothing and shelter, but, of course, could not adapt to the lack of sun, the effect of which they could not readily perceive. The rapid loss of skin pigmentation would have helped to some extent, but even that required exposure to the necessary UV-B wavelengths which, unfortunately, do not reach the surface of the Earth for much of the year for latitudes such as those of northern Europe. Thus the gap between primitive and contemporary inputs became wider for vitamin D than for probably any other nutrient.

While most nutrients are essential for the optimal functioning of most tissues (in contrast with the original notion of each nutrient having a specific target effect and a specific deficiency disease), the multi-system activity of vitamin D in mammals is particularly striking. Advances in cell biology have revealed that: (i) most cells in most tissues are constantly accessing the information encoded in their DNA to enable the synthesis of biochemical compounds that mediate cellular response to various stimuli; and (ii) vitamin D (in the form of calcitriol synthesized intracellularly) is a key component of the signalling apparatus that opens up the genome to enable cellular responses[2]. Thus, suboptimal status of vitamin D means suboptimal functioning of most body systems.

The downstream consequences are much like the consequences of failure to do preventive maintenance on complex machinery (such as automobiles). While the apparatus continues to operate in a manner that seems adequate for a time, it wears out and breaks down prematurely. Medicine today is consumed with dealing with the consequences of chronic diseases, many of which have been strongly associated with low vitamin D status and have a now well-established basis in biology.

Rather than presuming that prevailing inputs at northern latitudes are adequate, one must start with the presumption that nutrient intakes experienced during the millennia over which human physiology evolved are the intakes to which that physiology is fine-tuned. The simple fact that humans experienced substantially greater inputs of vitamin D 100 000 years ago than we do now does not, of course, prove that we need today what we got then. Still, the burden of proof must fall on the proposition that lower intakes are safe, i.e. are without consequent dysfunction or disease. The IOM utterly failed to meet this criterion.

How can we know what the primitive vitamin D intake might have been?

One can start by examining the vitamin D status of individuals who get considerable sun exposure, such as summer outdoor workers or indigenous peoples who live where the human race first evolved and who maintain traditional lifestyles. The available evidence indicates that such individuals typically have serum 25-hydroxyvitamin D concentrations ranging from 100 nmol/l to as high as 225 nmol/l[3,4]. For a concentration towards the low end of that range, say 125 nmol/l, the average person requires inputs from all sources totalling 150 μg/d (CF Garland, CB French, LL Baggerly *et al.*[5]). While such intakes appear large in comparison with both current recommendations and prevailing values for vitamin D status, it is helpful to recall that a single minimum erythema dose (such as would be conferred on a light-skinned person in 15 min of midday July sun) produces upwards of 375 μg[6]. As there has never been a report of vitamin D intoxication from sun exposure, such inputs must be recognized as both physiological and non-toxic.

Because they failed to use a physiological referent, the new IOM vitamin D intake recommendations must be judged seriously deficient.

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doi:10.1017/S1368980011000279

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