CHAPTER -

Progress in Megavitamin and Orthomolecular Science

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During the first half of the 20th century, the several fat-soluble and water-soluble vitamins were identified, isolated, and characterized and methods for their synthesis were developed. By 1943, the Recommended Dietary Allowances (RDAs)
were formulated and published by the Food and Nutrition Board of the U.S. National Academy of Sciences-National Research Council, which has revised its recommendations about every five years. The RDAs are defined in the following way: "Recommended Dietary Allowances (RDA) are the levels of intake of essential nutrients..."
considered, in the judgment of the Committee on Dietary Allowances of the Food and Nutrition Board on the basis of available scientific knowledge, to be adequate to meet the known nutritional needs of practically all healthy persons.

The Board states that the RDAs are intended to be met by a variety diet of a wide variety of foods rather than
by supplementation or by extensive fortification of
mingle foods, and that they apply to healthy
populations, not to those people with problems
such as premature birth, inherited metabolic
disorders, infections, chronic diseases, and the
use of medications requiring special dietary and
therapeutic measures.
During the second half of the 20th century it has been recognized that there is a fallacy in the definition of the RDAs. The fallacy lies in the last words of the definition, "... to meet the known nutritional needs of practically all healthy persons." Thus the "nutritional needs" are the amounts ingested by the control
A subpopulation of people in "ordinary good health." Since the nutrient intake of these people is an average one, the definition of RDA leads to values of the RDA equal to the amounts in the average diet.

With this definition, there is no possibility that the RDAs would be given values that would improve the health of all the people.
This fallacy is well known, even though the U.S. Food and Nutrition Board does not tell the American people about it. In their book *Human Nutrition and Dietetics* the authors, Sir Stanley Davidson and R. Passmore, mention that different recommendations of the national committees of Britain and the USA are related to the customary diets of the two countries (p. 242). They...
also say (p. 213) that the chief argument against recommending an intake of vitamin C that would lead to full saturation and improve the general health is that it would require a revolution in British habits to eat sufficient fruit and vegetables to provide the vitamin in this amount.
The value of megavitamins

The recognition of the value of an intake of vitamin larger than the intake that prevents manifestations of the corresponding deficiency disease has come mainly during the second half of the 20th century. In 1937 Albert Szent-Györgyi wrote that "Vitamins, if properly understood and applied, will help us to reduce human suffering to
on extent which the most fantastic mind would fail to imagine.” In the period from 1940 on values of intake of vitamins somewhat larger than the RDAs were tested for prophylactic and therapeutic value. The amounts used were at first early investigators were conservative; for example, Cowan, Diehl, and Baker, who in 1942 reported that
in their double-blind study of 333 students who received vitamin C or a placebo, with 31% less respiratory illness in the vitamin C group than in the placebo group. He described the daily dose of 200 mg (four times the RDA) as a "massive" dose. A dose of 20,000 mg is now considered a massive dose.

Meganutritional therapy was developed in 1952.
By A. Hofer and H. Diamond, in Saskatoon, Saskatchewan, who reported then began the first double-blind study ever made in the field of psychiatry. In this study, schizophrenic patients a companion was made of a placebo, nicotinic acid, and metimamide (each as an adjunct to standard schizophrenia treatment). The patients receiving vitamin
B3 (nicotinic acid or nicotinamide) fared better than those given a placebo.

A second double-blind study with 82 patients, follow-up (Ref 43, p. 207).

Studies since 1952, and clinical experience with on nearly 2,000 cases treated between 1952 and 1969 have clearly established for me that the treatment of choice for schizophrenia is a
combination of megavitaminic, tranquilizers, anti-depressants, and electroconvulsive therapy, combined with psychotherapy within the framework of the medical model. An example of independent corroborations is the work of Hawkins (Ref. 4, pp. 571-673). He and his clinic have treated over 4,000 cases, and the vast majority were restored to normality. This recent work may
be considered to be the logical consequence of earlier studies by many investigators of the value of this vitamin, which had been recognized in 1933 to the pellagra-preventing vitamin, in controlling the psychosis associated with pellagra and also in controlling depression and other psychotic states. The
Early studies are described by Koffler (Ref. 4, pp. 203-205). The RDA of vitamin B3 is 17 mg per day. In the early studies daily amounts from 100 mg to 1000 mg per day were used. Koffler and Diamond, Hawkins, and 13 other psychiatrists prescribe 3,000 or more mg per day, usually together with an equal amount of ascorbic acid and often with other vitamins.

The biological importance
of vitamin B3 results from its involvement with enzymatic systems. Niacinamide is a constituent of the coenzymes 3-nicotinamide-adenine dinucleotide (NAD) and nicotinamide-adenine dinucleotide phosphate (NADP), which serve as coenzymes in many enzyme systems.
Another early investigator in the megalovitamin field was Fred P. Klenner. Following the 1935 report by Tungeblut of the inactivation of poliomyelitis virus by ascorbate in vivo, Klenner before 1949 began the treatment of patients seriously ill with viral pneumonia, poliomyelitis, and other viral diseases by oral administration or venous infusion of ascorbate, often
in amounts as large as 100 g per day. He recommended 10 to 20 g per day for prophylaxis. The biochemist Irwin Stone also played an important part in this development by marshalling the arguments about the optimum intake of vitamin C and advocating its use prophylactically and therapeutically in amounts far larger than the RDA.
Orthomolecular Substances and Orthomolecular Medicine

Most drugs have little physiological activity at doses far less than those at which they show pronounced activity, and the doses of drugs usually prescribed for the treatment of a serious illness are usually rather close to the lethal dose. In these respects the vitamins are much different. A daily intake
of 5 mg of nicotamide is enough to prevent pellagra from developing in most people, but 50 g, 10,000 times as much, can be taken without harm. Similarly, 5 mg of ascorbic acid per day is enough to prevent scurvy in most people, but 10,000 or even 50,000 times this amount can be taken without harm. No lethal dose is known for these vitamins or for
Other—most of the others—it is estimated that a single dose of 10,000,000 I.C. of vitamin A might be lethal, and sometimes substances and other physiological activity over a great range of tolerated intakes, an important question may be asked: what is the optimum intake?

For a vitamin the optimum intake may be
far greater than the IPDA. Only during recent decades has there been serious interest in determining the optimum intakes.

In order to differentiate them from drugs, the vitamins and similar substances have been given the name *orthomolecular substances.* An orthomolecular substance is a substance that is normally present in the
human body and that serves some purpose. The vitamins, essential amino acids, essential fats, essential minerals, and various other constituents of foods are on-homoeolausal substances, as are also various other substances, such as choline, \( p \)-aminobenzoic acid, the ubiquinones, and human proteins such as insulin and interferon.
Orthomolecular medicine is the achievement and preservation of the best of health and the prevention and treatment of disease by varying the concentrations of the orthomolecular substances in the human body. Reaching the goal may involve either increasing the concentration (e.g., for example, high-density lipoprotein in the blood) or decreasing the concentration (e.g., for example, low-density lipoprotein)
Optimum intakes of vitamins

During recent years the effort has been made to estimate the optimum intakes of vitamins. The curve expressing wellbeing as a function of the intake of a vitamin is expected to have a rather flat top, and the optimum intake depends on the genetic constitution of the person and on the state of his health. For a person in ordinary
health the optimum intake of vitamin C may be 100 or 200 times the RDA, and vitamin E 25 times the RDA, and that for vitamin A about 10 times the RDA. Evidence supporting the high values of the optimum intake of vitamin C is discussed by Stone and by Pauling.

The idea that the amounts of vitamins provided by an
are adequate ordinary good diets, seem to be based on two arguments. One is that people on a good diet show manifestations of deficiency diseases that disappear when the diet is improved. The fallacy in this argument is that the health of the control population, receiving a good diet, may be improved further by increased intake of the
vitamins; that is, the intakes provided by an ordinary good diet are adequate for ordinary health but not for the best of health. The other argument is that the plants that are the source of the foods are similar in their biochemistry to human beings, and that accordingly the amounts of vitamins
that they manufacture, which are adequate for them, are also adequate for human beings. One of the fallacies in this argument is that human beings require vitamin C for the synthesis of the principal structural macromolecule of the human body, the protein collagen, whereas plants use a carbohydrate, cellulose, as their principal structural
macromolecule, and hence have a smaller need for vitamin C. Another fallacy is that an organism that synthesizes a vital substance synthesizes a somewhat smaller daily amount than the optimum, because to synthesize the optimum amount would require supporting the burden of additional synthetic...
machinery, with only a smaller compensation.

The Food and Nutrition Board recognizes that the RDAs do not apply to persons with vitamin-related genetic abnormalities. More than 100 of these diseases are known, most of them with strikingly serious manifestations. It is estimated that many thousands of less serious vitamin-related abnormalities occur, with nearly every person bearing one or more. The
biochemical individuality discussed by Roger J. Williams 13,15,17 may arise mainly in this way. Much of the improvement in health resulting from optimum nutrition may result from control of minor genetic defects.
Vitamin B6 and the carpal tunnel syndrome

Either a low intake of vitamin B6 (pyridoxine, pyridoxal, pyridoxamine) or the administration of an antagonist (deoxypyridoxine) leads to serious problems - convulsions, depression and confusion, dermatitis, stomatitis, and cheilosis. Pyridoxal phosphate and pyridoxamine are coenzymes including those for many amino-acid metabolism, and the
effects of deprivation are attributed to the decreased functioning of the enzymes. The fact that vitamin C is restored by administration of ascorbic acid in amounts not much greater than the RDA (2.2 mg per day for an adult male) has given rise to the belief that the various enzyme systems dependent on B-6 function at nearly their maximum level in persons receiving the
RDA intake of the vitamin. Recent work by John M. Ellis, Paul Folkers and their collaborators has shown that this conclusion is not justified.

In his practice in a small Texas community, Ellis discovered that an increased intake of pyridoxine helped to control rheumatism, edematous conditions, carpal tunnel syndrome, menopausal arthritis, clinical disturbances following the use of
anticoagulant pills, and some other problems 18,19. The doses used were usually between 50 and 300 mg per day. He and Folkers, co-author of a treatise on vitamins 20, found that many subjects with the ordinary intake of 50 had an activity 23 of the B6-dependent enzyme EGT (erythrocyte glutamic oxaloacetic transferase) far lower than that achieved with a high
It was shown in a double-blind controlled trial with patients with carpal tunnel syndrome that the administration of 100 mg of pyridoxine per day, about 50 times the RDA, led to control of the disease, whereas administration of a placebo did not. The mechanism of action may involve the shrinking of the synovial membranes adjacent to the nerve. The authors conclude that clinical
Improvement of the syndrome may frequently obviate hand surgery, and mention that carpal tunnel syndrome is often associated with rheumatoid arthritis, obesity, myxedema, diabetes, pregnancy, and rheumatoid conditions such as "tennis elbow", Dupuytren contracture, deQuervain disease, "trigger fingers", bursitis, and periarthritis of the shoulder.
These conditions are so common as to suggest that nearly everyone would benefit by the orthomolecular intake of this vitamin.
Vitamin C and cancer
Vitamins and cardiovascular disease
Arthūrs


   62, 517-52 (1935).

   and Surg. 159, 60-63 (1948).


   and Surg. 163, 197-207 (1951).
