

CHAPTER -

Progress in Megavitamin and Orbomolecular Science

Limes Baking

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 ~~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 single 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 ~~group~~

~~the~~ 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 Dietetics² the authors, Sir Stanley Davidson and R. Passmore, mention that the ^{different} recommendations of the national committees of Britain and the USA are related to the customary diets of the two countries (p. 243). They

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also say (p. 213) that the chief argument against recommending an intake of vitamin C that would ~~lead to~~ ~~provide~~ 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 ^avitamins 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 wrote³ 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
~~given~~ 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 363 students who received
vitamin C or a placebo, with
31% less respiratory illness
in the vitamin C group than in
the placebo group, ~~described~~
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.

Megavitamin therapy
was developed in 1952

by A. Hoffer 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, ^{of 30} schizophrenic patients a comparison was made of a placebo, nicotinic acid, and nicotinamide (each as an adjunct to standard schizophrenia treatment). The patients receiving vitamin

B3 (nicotinic acid or
nicotinamide) fared better
than those given a placebo:

★ second double-blind study
with 82 patients, follow-up

(Ref H, p. 207)

Hofier, states ~~that~~ ~~A~~

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 megavitamins, tranquilizers, anti-depressants, and electroconvulsive therapy, combined with psychotherapy within the framework of the medical model. An example of independent corroboration is the work of Hawkins (Ref. 4, pp. 571-673). He and his clinic have treated ~~2~~ over 4,000 cases, and the vast majority were restored to normality."

This ^{more} 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 be 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 Hoffer (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. Hoffer and Diamond, Hawkins, and ~~the~~ 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} ~~in~~ enzyme ^{systems} ~~systems~~.

Nicotinamide is a constituent ~~of the coenzymes~~

of nicotinamide-adenine dinucleotide (NAD) and nicotinamide-adenine dinucleotide phosphate (NADP), which serve as coenzymes in many enzyme systems.

Another early investigator in the megavitamin field was Fred P. Klenner. Following the 1935 report by Tungeblat of the inactivation of poliomyelitis virus by ascorbate ion⁵, 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 day⁶⁻¹⁰. The 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~~ ~~these~~ prophylactic
and therapeutic use in
amounts far larger than
the RDA^{11,12}.

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.U. of vitamin A might be lethal.

Because the vitamins ^{and some other substances} have 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 TDA.
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.¹³

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 extramolecular substances, as are also various other substances, such as choline, β -aminobenzoic acid, the ubiquinones, and human proteins such as insulin and interferon.

Orthomolecular medicine is the achievement and preservation of the best of health ~~the~~ 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, that for the B vitamins, ^{and vitamin E} about 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 Stone¹² and by Pauling^{3, 14}.

The idea that the amounts of vitamins provided by an

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are adequate
ordinary good diet seems
to be based on two arguments.
One is that people on a poor
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
~~the~~ 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 ~~and animals~~ that are the source of the ^{vitamin-containing} 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^{13,15} is that an organism that synthesizes a vital substance ~~does not~~ synthesizes a somewhat smaller daily amount than the optimum, because to synthesize the optimum amount would require supporting the burden of additional synthetic

~~with~~ machinery, with only a smaller compensation.

The Food and Nutrition Board recognizes that the RDAs do not apply to persons with vitamin-related genetic ^{diseases} ~~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^{15, 16, 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 ~~of the~~ enzymes of amino-acid metabolism, and the

effects of deprivation are attributed to the decreased functioning of the enzymes. The fact that ~~the~~ ordinary health is restored by administration of pyridoxine in amounts ~~not~~ 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 ~~when~~ in persons receiving the

RDA intake of the vitamin. Recent work by John M. Ellis, Earl 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} ~~vitamin~~ helped to control rheumatism, edematous conditions, carpal tunnel syndrome, menopausal arthritis, clinical disturbances following the use of

anticoagulatory pills, and some other problems^{18, 19}.

The doses used were usually between 50 and 300 mg per day. He and Folbers, co-author of a treatise on vitamins²⁰, found that many subjects with the ordinary intake of B_6 had ~~a low~~^{an} activity of the B_6 -dependent enzyme EGOT (erythrocyte glutamic oxaloacetic transferase) far lower than that achieved with a high

B₆ intake. 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.²¹ 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
~~now~~ with pyridoxine therapy
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 cardio-
vascular disease

Arthritis

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