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Editorial

Unacceptable Losses: Hospital-Caused Deaths

_I find medicine is the best of all trades because whether you do any good or not you still get your money._

(Moliere: “A Physician in Spite of Himself” 1664)

Indeed, it is likely that adverse reactions are systematically under-reported.10

If we now consider the results of medical error, the figures provide increased concern. In the United States, medical errors result in between 44,000 and 98,000 unnecessary deaths each year, and one million direct injuries.11

Note that these deaths are in addition to those from adverse drug reactions indicated above. Similarly, in Australia medical error results in about 18,000 unnecessary deaths, and disabled more than 50,000 patients.12

A reasonable (low) estimate for medical deaths per year in the United States is between 225,000 and 284,000, making medicine at least the third largest cause of death in the United States.13

However, this estimate is conservative. Some authors estimate the number of deaths to be far higher, about 780,000 deaths per year, which would make conventional medicine the number one leading cause of death in the US.14 Compare this with all deaths from cancer, numbering 553,251 in 2001.15 It is clear that “the toll of medical injury is truly appalling.”16

When Doctors Strike

An objection to pointing out the high incidence of medical-related deaths is that doing so ignores the benefits provided. It is frequently suggested that the number of lives saved greatly outweighs the number of deaths.17 However, in developed countries, mortality increases with the number of doctors.18,19

When conventional doctors withdraw their services in a strike, there is a brief but dramatic lowering of mortality rates as surgery for elective operations is suspended.20 Such a decrease (about 18%) occurred in Los Angeles in the 1970s.21,22 When the strike ended, the death rate returned to more normal values. At about the same time, a strike
occurred in the Colombian city of Bogota and the mortality was reduced by about 35%.\textsuperscript{23} A strike in Israel produced a reported 50% drop in deaths.\textsuperscript{24} A later strike, in 2000, produced a similar result (93 funerals compared with 153), and lead to complaints by funeral parlors. The director of Jerusalem’s burial society reported “the number of funerals we have performed has fallen drastically.”\textsuperscript{25} The \textit{British Medical Journal} suggested the strike might be beneficial to health. A recent study of a strike in Croatia showed no effect on mortality figures.\textsuperscript{26} It seems strange when a study showing no increase in deaths during a physicians’ strike is reassuring.

\textbf{Treatment or Prevention?}

Filling hospital beds is much like filling hotel rooms or airline seats: maximum occupancy means maximum profitability. Treating illness is profitable. Often treatments are cost insensitive, as a patient with a severe or life-threatening disease has a profound impetus to pay whatever is necessary to become well again. A person in good health has less motivation to pay out-of-pocket to maintain wellbeing, but is often insured either directly or indirectly against sickness.

For decades conventional medicine has espoused the benefits of preventive medicine, but the immediate economic benefits to the medical providers are not apparent. Indeed, a declining proportion of sick people in a population means a reduced role for the most profitable medical interventions. Hospitals stays are not for preventive care.

There are ready alternatives to continued tolerance of iatrogenic deaths. History more than suggests that most gains in public health arise from sanitation, hygiene, and nutrition. Hospital food, long mocked for poor quality, has been just as long tolerated. This too could be radically and promptly improved. One cost-effective way to enhance nutrition is with routine vitamin supplementation to institutional diets. Adding suitable supplements with a patient’s meal would add only pennies to a hospital’s costs, but greatly enhance the patient’s healing. A healthier patient means a shorter hospital stay and a lower bill. Shorter stay? Lower bill? A cynic might perceive a vested interest in hospital undernutrition.

Hospital stays have always been dangerous, and they remain dangerous. Hospitals collect our very sickest people into close proximity. Very sick patients require optimum nutrition. Even a glance at what is served up on any hospital food-service tray indicates a pressing need for orthomolecular supplementation. Delay is unjustified at best and fatal at worst. Let us provide patients with superior hygiene, and actively protect them from unnecessary surgery and excessive drug therapy. In not doing so, hospitals are clearly breaching their duty of care, and the death toll is horrendous.

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\textbf{References}

20. Bunker JP: The role of medical care in contrib-
Orthomolecular Psychiatry

The journal Science published a revelatory article in its April 19th, 1968, issue. The author, Linus Pauling, was not a stranger to the pages of Science, but his article, “Orthomolecular Psychiatry,” heralded a dramatically new direction in his thinking and research. Pauling had enjoyed widespread fame as the world’s greatest chemist and tireless peace advocate for many decades, but his venture into the field of nutrition, especially concerning micronutrients and their role in maintaining mental and physical health, attracted new attention and ignited controversy. In a letter published in the June 14th issue of Science, Donald Oken, a psychiatrist in the National Institutes of Health, wrote:

“The article, “Orthomolecular Psychiatry” (19 April, p. 265), illustrates elegantly the pitfalls which occur when an expert in one field enters another area. With his characteristic brilliance, Linus Pauling describes a biochemical mechanism which could be responsible for some forms of mental illness (or, indeed, for illness of many other types). Remote plausibility, however, no matter how intriguing and creative its nature, should not be confused with evidence. Unfortunately for Pauling’s thesis, there is no adequate evidence to back up his view.”

In response, Pauling noted that he had been working for 12 years on the molecular basis of mental illness with his research supported by the NIH, the Ford Foundation, and private donors, implying that he was not a newcomer to the field of brain chemistry. Indeed, he had published his theory on the molecular mechanism of anesthetic agents, particularly the inert gases, in 1959 and had begun working on biological molecules in the late 1930s. Those efforts culminated in the discovery of the structural themes of proteins, including the alpha-helix and pleated sheet, and the cause of sickle-cell anemia—the first disease to be characterized as a molecular disease—and established Pauling as the major founder of molecular biology. Pauling also remarked that psychiatrists had a duty, in his view, to employ the techniques of orthomolecular psychiatry in addition to the standard therapies.

Oken was certainly justified in his praise of Pauling’s brilliance but missed entirely the point of his genius: the ability to span diverse scientific and medical fields and synthesize original, compelling perspectives into perplexing issues. Pauling, the only person to have won two unshared Nobel Prizes, was one of history’s greatest embodiments of the interdisciplinary approach, decades before it became considered essential. In the “Millennium Essay” published in Nature in 2000, Gautam Desiraju characterized Pauling as “one of the great thinkers and visionaries of the millennium”, ranking him alongside Galileo, Da Vinci, Faraday, Newton, and Einstein. Desiraju noted that “Pauling’s ingenuity and awesome intuition permeated quantum mechanics, crystallography, biology, medicine and, above all, structural chemistry” and that modern chemistry, unlike biology or physics, is utterly dependent on the work of a single scientist—Linus Pauling.

What, then, was Pauling’s paper, “Orthomolecular Psychiatry,” about, and why did it generate such criticism? Written while Pauling was a professor in the chemistry department in the University of
California at San Diego, “Orthomolecular Psychiatry” established the theoretical basis for treating cerebral avitaminosis by “the provision of the optimum molecular environment for the mind, especially the optimum concentrations of substances normally present in the human body.” Somewhat later, Pauling broadly defined orthomolecular medicine as preserving good health and treating disease by “varying the concentrations in the human body of substances that are normally present in the body and are required for health.”5 Drawing on evidence from microbial genetics and molecular reaction rates, Pauling suggested that the brain’s sensitivity to its biochemistry affects the mind. While this concept seems as intuitive and obvious as some of Pauling’s other discoveries like biological specificity or the molecular clock, it was very controversial when first introduced. Many nutritionists and psychiatrists like Oken felt that Pauling was trespassing on their domains and adopted an almost reactionary stance. Pauling’s encyclopedic knowledge and awesome memory, as well as his great personal charm, served him extremely well in debates with his detractors over the next decades.

In 1945 Pauling had postulated the cause of sickle-cell anemia as an abnormal hemoglobin that combines with itself in deoxygenated blood, forming long rods that distort the shape of red blood cells into the characteristic sickle shape observed in the disease. Four years later, he and colleagues published a paper in *Science* that confirmed this mechanism and heralded the new era of molecular medicine.6 Pauling returned to the concept of molecular disease in “Orthomolecular Psychiatry”, noting that phenylketonuria is a molecular disease in which phenylalanine accumulates in the tissues of afflicted children because of a genetic defect in the enzyme that catalyzes the conversion of phenylalanine to tyrosine. The resultant pathology includes mental manifestations and physical problems, such as severe eczema, but can be attenuated by replacing a normal diet with one that is limited in phenylalanine—an example of orthomolecular medicine.

In “Orthomolecular Psychiatry”, Pauling noted the mental manifestations of the B vitamin deficiency diseases that produce physical pathology, supporting his thesis that these vitamins play crucial roles in mental health. He explained that evolution may favor the loss of certain functions, such as the synthesis of vitamin C, if the environment supplies sufficient amounts of the critical substance. A mutant that synthesizes an adequate but suboptimum amount of a vital substance may also outcompete the wild-type organism if the energy saved by diminished synthesis can be applied advantageously elsewhere. To support this point, Pauling discussed the *Neurospora* work of his friends, Beadle and Tatum. They showed that the growth rate of a pyridoxine-requiring mutant strain, produced by irradiation, actually increased to about seven percent greater than the parental strain when large amounts of pyridoxine were supplied in the medium. Similar results were obtained for a *p*-aminobenzoic-acid-requiring strain. Citing the work of Zamenhof and Eichhorn on *Bacillus subtilis*, Pauling elaborated on observations that when nutrilite-requiring mutants were grown together with the parental strain in a medium containing the nutrilite, the mutants exhibited a selective advantage, outcompeting and overpopulating the parental strain, owing to gene deletion rather than point mutations, since the intermediate steps, including the synthesis of mRNA, would be lost.

Pauling then discussed the dependence of reaction rates on molecular concentrations. Echoing his interest in the 1950s on the potential role of abnormal
enzyme function in mental illness, Pauling noted that enzyme-catalyzed reaction rates are proportional to the concentration of the reactant, assuming that there are no enzyme inhibitors present. The rate decreases as the enzyme becomes saturated. If the enzyme is defective, as may be the case with those involved in abnormal brain function, the saturating concentration is larger because the enzyme has less affinity for its substrate. However, the rate may be normalized by increasing the concentration of the substrate. This provides the rationale for supplying high-dose vitamins to treat biogenic mental illness. Building on this concept, in a paper published in the *American Journal of Clinical Nutrition* in 2002, Bruce Ames discussed the remediation of about 50 human genetic diseases caused by defective enzymes with high-dose B vitamins and other micronutrients.7

To illustrate his hypothesis, Pauling focused on vitamin B12, niacin, vitamin C, and glutamic acid. He cited a Norwegian study that found abnormally low levels of B12 in the blood of about 15% of patients admitted to a mental hospital, compared to values observed in the general population. He then recounted the successful application of niacin in the southeastern United States that alleviated psychosis in thousands of pellagra patients. Citing the work of Sydenstricker and Cleckley and the work of Hoffer and Osmond, he discussed the use of high-dose niacin and, in the case of Hoffer and Osmond, the combination of high-dose niacin and vitamin C, to treat schizophrenia without the side effects typically seen with drugs. Vitamin C deficiency in schizophrenics has often been reported and is also associated with depression in patients with scurvy. Pauling briefly noted that Stone estimated the optimum intake of vitamin C at 3 to 15 grams per day, based on cross-species comparisons and other arguments. A few years later, the first paper from the newly founded Linus Pauling Institute of Science and Medicine, “Results of a Loading Test of Ascorbic Acid, Niacinamide, and Pyridoxine in Schizophrenic Subjects and Controls”, reported that almost all of the schizophrenic patients examined excreted abnormally low amounts of one or more of the orally administered vitamins given in doses over one gram each, compared to controls.8 Pauling explained that several investigators in the 1940s reported that large doses of L-glutamic acid had beneficial effects in subjects with convulsive disorders or mental retardation. The effective dosage was found to be 10 to 20 grams per day, higher than the estimated intake from food of about 5 to 10 grams per day.

In the penultimate section of “Orthomolecular Psychiatry”, *Localized Cerebral Deficiency Diseases*, Pauling argued that a simple model of fluid dynamics in the body leads to calculations demonstrating that localized deficiencies of vital substances could occur in specific reservoirs. In his model, such substances are used up at characteristic rates in various reservoirs, such as blood and cerebrospinal fluid; the rate of absorption from the gastrointestinal tract is constant; and the diffusion across the blood-brain barrier is a function of permeability, area of the barrier, and the difference in concentration of the substance in blood and cerebrospinal fluid. Given these parameters, the steady-state concentration of a vital substance in the brain could be much less than its concentration in blood. In schizophrenia the situation would be aggravated by genes affecting the regulation of vitamin metabolism or other critical functions so that massive doses of certain vitamins may be required to normalize cerebral concentrations and, therefore, mental function.

Pauling elaborated on and extended the concept of orthomolecular psychiatry and medicine in many publications over the next decades. In “Some Aspects of
Orthomolecular Medicine,” published in 1974, he introduced new examples of orthomolecular medicine, such as the treatment of diabetes with injected insulin, the use of iodine to prevent goiter, and methylmalonicaciduria, which is treated by supplying large amounts of vitamin B12 (1,000 times the normal concentration) to normalize the conversion of methylmalonic acid to succinic acid.9 In How to Live Longer and Feel Better, published a dozen years later, he added another example: the treatment of galactosemia—a genetic disease characterized by a deficiency of an enzyme that metabolizes galactose in lactose—by the provision of a diet free of milk sugar.10 Pauling stressed that he used the adjective orthomolecular “to express the idea of the right molecules in the right concentrations” and contrasted orthomolecular medicine with the use of potentially dangerous drugs used in conventional allopathic medicine. Pauling believed that the biological plausibility of his arguments was evident and that the available evidence was supportive. Of course, as is the case with many revolutionary ideas, “Orthomolecular Psychiatry” was not greeted with universal acclaim. The American Psychiatric Association, in particular, was skeptical and dismissive.

In the Fall of 1974, Pauling contributed an article, “On the Orthomolecular Environment of the Mind: Orthomolecular Therapy,” to the American Journal of Psychiatry, which provided an opportunity to comment on the American Psychiatric Association’s Task Force Report: Megavitamin and Orthomolecular Therapy in Psychiatry, issued in 1973.11 He was clearly dismayed with the negative reaction of conventional psychiatry to his ideas and the scientific evidence and criticized what he considered to be specious arguments and fallacies in the report. After discussing the probability that abnormal enzyme function may cause mental illness and listing examples of successful orthomolecular treatment with vitamins, some of which effectively shift the equilibrium rate for the formation of an active enzyme from the apoenzyme and coenzyme, Pauling faulted the APA report for ignoring evidence on vitamin C and pyridoxine; misunderstanding simple biochemistry, including the nature of vitamins and how a population of molecules can easily serve several functions—they don’t all have to be committed to one reaction as implied by the task force; and intentional or unintentional bias, resulting in “a sort of professional inertia that hinders progress.”

Setting the Stage

Several childhood experiences and later episodes set the stage for Pauling’s codification of orthomolecular medicine and his fascination with vitamin C. His father was a druggist and, in the era before the Food and Drug Administration, concocted many medicines in his store, where Linus was exposed to this medicinal chemistry as a youngster. Later, he set up a laboratory in his basement where he carried out exciting chemical reactions. He was deeply impressed by the transformation of substances during reactions, and those early experiments stimulated an intense desire to learn more about chemistry, which was fulfilled as an undergraduate in Oregon Agricultural College (now Oregon State University) and in graduate work in the California Institute of Technology (Caltech). When Pauling and his wife were in Europe on a Guggenheim Fellowship in 1926, after earning his doctorate in chemistry and mathematical physics, his mother, Belle, died from pernicious anemia in a hospital for the insane in Salem, Oregon. Pernicious anemia, caused by a deficiency of vitamin B12, is characterized by neurological problems and loss of normal mental function, resulting in delusions known as
“megaloblastic madness” and, ultimately, death. In the year that Belle Pauling died, Minot and Murphy discovered that eating raw liver reversed pernicious anemia. In 1934, they won the Nobel Prize in Medicine or Physiology for their work, and 14 years later, vitamin B$_{12}$ was isolated independently by Pauling’s friends, Karl Folkers and Alexander Todd. Another of Pauling’s friends, Dorothy Hodgkin, won the Nobel Prize in Chemistry in 1964 for elucidating the molecular structure of B$_{12}$ by X-ray crystallography in 1956.

In 1938 Pauling gave a speech at the dedication of the Crellin laboratory in Caltech in which he said:

“There is, however, a related field of knowledge of transcendent significance to mankind which has barely begun its development. This field deals with the correlation between chemical structure and physiological activity of those substances, manufactured in the body or ingested in foodstuffs, which are essential for orderly growth and the maintenance of life, as well as of the many substances which are useful in the treatment of disease.”

Pauling remarked on the structural complexity of many vitamins and predicted that, given the rapid progress in the synthesis of vitamins in the preceding decade, “success will soon reward the men who are now carrying on the attack on vitamin E”. Clearly, in the heyday of vitaminology, Pauling was thinking about the virtues of these vital substances. Indeed, the early part of the twentieth century, especially the 1930s, was the prime time for the discovery of vitamins and their use to correct and prevent associated deficiency diseases. For example, vitamin A was identified as a vitamin in 1914 and structurally characterized in 1930. Vitamins D$_2$ and D$_3$ were chemically characterized in 1932 and 1936, respectively. Vitamin E was discovered in 1922 but not isolated until 1936. Vitamin K was discovered in the early 1930s and identified in 1939. Pauling’s friend Albert Szent-Gyorgyi first isolated vitamin C in 1928. Thiamin was isolated in 1911 by Casimir Funk, who coined the term ‘vitamine’, and structurally characterized by R.R. Williams in 1936. Williams’s brother, Roger J. Williams, first identified the structure of pantothenic acid in 1940 and later proposed important concepts about biochemical individuality that greatly influenced Pauling. In his classic book, *Biochemical Individuality*, Roger Williams described significant anatomical and biochemical variations due to genetic polymorphisms among humans and postulated, “practically every human being is a deviate in some respects.” He noted that if 95% of the population is normal with respect to one measured value, only 0.59% of the population would be normal with respect to 100 uncorrelated measured values. In December 2007, the journal *Science* heralded human genetic variation (polymorphisms) and its implication for disease risk and personal traits as the “Breakthrough of the Year.” Riboflavin, the first vitamin to be recognized as a co-enzyme, was isolated in 1933. Vitamin B$_6$ (pyridoxine and related forms) was isolated in 1938, and its structure was determined a year later. Niacin was isolated in 1867 but not identified as the anti-pellagra factor until 1937. As mentioned previously, vitamin B$_{12}$ was not isolated until 1948, five years after another group of pharmaceutical scientists isolated folic acid. Biotin was first isolated in 1936, and its structure was elucidated in 1942. Many early vitamin pioneers won accolades for their work that spared millions of people from the ravages of debilitating and fatal deficiency diseases. From the 1920s until the mid-1960s, 16 Nobel Prizes were awarded to scientists who discovered, isolated, synthesized, or structurally characterized vitamins.

While Pauling was well aware of these developments in biochemistry and nutrition in the 1930s, his only relevant...
research in that era concerned the molecular structures of some carotenoids and the flavonoid anthocyanidin. In 1939, the year in which he published papers on hemoglobin, the structures of benzene and proteins, and \textit{The Nature of the Chemical Bond}—the most cited scientific book of the twentieth century and work for which he was awarded the 1954 Nobel Prize in Chemistry—Pauling published a quantum-mechanical explanation of the intense colors in flavonoids, carotenoids, and dyes,\textsuperscript{15} as well as a discussion of the use of resonance theory to understand anthocyanidin and carotenoid structures.\textsuperscript{16} “A Theory of the Formation of Antibodies” followed in 1940, after which Pauling published papers with Zechmeister on the structure of prolycopene, an isomer of lycopene obtained from the tangerine tomato, with comments on the structural characteristics of lutein, zeaxanthin, and the carotenes, among other isomers.\textsuperscript{17,18} However, Pauling’s interest in these carotenoids and flavonoids was confined to their chemical structures and the influence of structure on optical properties; he did not address their health functions.

In 1941 Pauling was diagnosed with Bright’s disease, or glomerulonephritis, which was at the time an often-fatal kidney disorder. On the advice of physicians at the Rockefeller Institute, he went to San Francisco for treatment by Thomas Addis, an innovative Stanford nephrologist. Addis prescribed a diet low in salt and protein, plenty of water, and supplementary vitamins and minerals that Pauling followed for nearly 14 years and completely recovered. This was dramatic first-hand experience of the therapeutic value of the diet.

Revelations

When Pauling cast about for a new research direction in the 1950s, he realized that mental illness was a significant public health problem that had not been sufficiently addressed by scientists. Perhaps his mother’s megaloblastic madness and premature death caused by B\textsubscript{12} deficiency underlay this interest. At about this time, Pauling’s eldest son, Linus Jr., began a residency in psychiatry, which undoubtedly prompted Pauling to consider the nature of mental illness. Thanks to funding from the Ford Foundation, Pauling investigated the role of enzymes in brain function but made little progress. When he came across a copy of \textit{Niacin Therapy in Psychiatry} by Abram Hoffer in 1965, Pauling was astonished to learn that simple substances needed in minute amounts to prevent deficiency diseases could have therapeutic application in unrelated diseases when given in very large amounts. This serendipitous and key event was critically responsible for Pauling’s seminal paper in this emergent medical field. Later, Pauling was especially excited by Hoffer’s observations on the survival of patients with advanced cancer who responded well to his micronutrient and dietary regimen, originally formulated to help schizophrenics manage their illness.\textsuperscript{19,20} The regimen includes large doses of B vitamins, vitamin C, vitamin E, beta-carotene, selenium, zinc, and other micronutrients. About 40\% of patients treated adjunctively with Hoffer’s regimen lived, on average, five or more years, and about 60\% survived four times longer than controls. These results were even better than those achieved by Ewan Cameron, Pauling’s close clinical collaborator, in Scotland.

After a long and extremely productive career in Caltech, Pauling left under political pressure in late 1963 after winning the Nobel Peace Prize for his efforts to ban the atmospheric testing of nuclear weapons. Following a short tenure in the Center for the Study of Democratic Institutions in Santa Barbara, California, Pauling became professor of chemistry in the University of California at San Diego in 1967. Two years later, he accepted an
appointment as professor of chemistry in Stanford University in Palo Alto, California, where he remained through 1973. His ideas about orthomolecular medicine had been incubated at a number of institutions over the course of over 15 years, but it wasn’t until he and two colleagues founded the independent Institute of Orthomolecular Medicine, shortly renamed the Linus Pauling Institute of Science and Medicine, in 1973 that they began to flourish. Stanford had provided an academic base while Pauling continued to develop his arguments for supplemental vitamin C, culminating in an important paper, “Evolution and the Need for Ascorbic Acid”, published in the Proceedings of the National Academy of Sciences USA in 1970 and a book, Vitamin C and the Common Cold, also published in 1970, that won the Phi Beta Kappa Award as the best science book of the year and sold well. Lack of adequate laboratory space in Stanford prompted Pauling to establish the Institute, which was financed by donations and the transfer of federal grants on metabolic profiling from Stanford. The Institute remained his base until his death in 1994.

Pauling’s fascination with his favorite molecule—vitamin C—led to numerous papers and was the focus of hundreds of his speeches from the 1960s until his death. Pauling was stimulated to think deeply about vitamin C after being contacted by Irwin Stone in 1966. Stone had been in the audience in 1966 when Pauling gave a talk at the reception for his acceptance of the Carl Neuberg Society for International Scientific Relations Medal in New York City. In his speech, Pauling remarked that he hoped and expected to live a long time. Stone wrote to Pauling about hypoascorbemia (a genetic disease affecting all humans and caused by the inability to synthesize vitamin C) and suggested that he might well live for a long time, perhaps enjoying another fifty years of good health, by taking supplemental vitamin C. In his reply to Stone, Pauling cited his 1962 paper with Zuckerkandl on molecular diseases in which they argued that the loss of the endogenous synthesis of a vitamin can be considered to be a molecular disease, corrected by a palliative diet. Pauling reviewed the evidence supplied by Stone and decided to take three grams of vitamin C per day, partly for optimum health and partly to prevent the serious colds that had afflicted him for many years, seriously interfering with his work. His wife, Ava Helen, also began to take supplemental vitamin C, and both reported better health and a greatly reduced incidence of colds, in accord with the scant clinical literature. Pauling was so impressed that he decided to write a book on the use of vitamin C to prevent and treat the common cold. The book was also a response to a letter from a critic, Victor Herbert, who complained about “vitamin hucksters” and challenged Pauling on statements he made in a talk at the dedication of the Mt. Sinai Medical School in 1968 on the efficacy of vitamin C in preventing and ameliorating colds. Herbert asked for evidence from properly controlled trials, and Pauling discussed evidence from four such trials in his book. In a new edition of that book, Vitamin C, the Common Cold, and the Flu, published in 1976, Pauling added material on influenza, especially concerning the work of Jungeblut and Murata on the inactivation of viruses by vitamin C and the work of Klenner, Morishige, Murata, and others on the prophylactic and therapeutic effect of vitamin C in viral diseases. Pauling noted that in 1935 Jungeblut was the first to report that high-dose vitamin C inactivates poliomyelitis virus, and he was intrigued by Klenner’s use of very high-dose vitamin C, usually given intravenously, to treat viral diseases like hepatitis, poliomyelitis, and pneumonia, and toxicological conditions like venomous snake bites. Klenner
Linus Pauling and the Advent of Orthomolecular Medicine

had published his work in regional medical journals since 1948. In the late 1980s, Pauling’s attention returned to infectious disease and vitamin C. On the basis of in vitro and clinical evidence, he and his associates argued that vitamin C should be used in conjunction with newly introduced antiviral drugs like AZT, which prevents the de novo infection of cells, to inhibit replication of HIV and prevent the formation of abnormal giant T lymphocytes called syncytia, which are markers of viral infectivity and cytopathology.25 Pauling and Cameron completed a draft of a new book, never published, on vitamin C and AIDS.

Szent-Gyorgyi and Pauling shared the opinion that the optimum intake of vitamin C is much larger than the RDA, the amount set by the Food and Nutrition Board to prevent scurvy. Pauling wrote to Szent-Gyorgyi in 1970, asking about Stone’s ideas. Szent-Gyorgyi replied:

“As to ascorbic acid, right from the beginning I felt that the medical profession misled the public. If you don’t take ascorbic acid with your food you get scurvy, so the medical profession said that if you don’t get scurvy you are all right. I think that this is a very grave error. Scurvy is not the first sign of the deficiency but a premortal syndrome, and for full health you need much more, very much more....there is an enormous scattering in the need of vitamins and it is quite easily believable that many diseases which have not been connected til now with vitamins are really expressions of a lack of vitamins.”26

Robert Cathcart, an orthopedic surgeon in California, read Pauling’s book on vitamin C and the common cold in 1971 and began taking large doses of vitamin C to prevent colds from developing. Based on his success, he treated patients with high-dose oral vitamin C and observed the “bowel tolerance” threshold effect, which refers to a laxative function of high-dose vitamin C that depends on the health status of the subject.27 Cathcart used this observation to titrate the therapeutic dose of vitamin C. A recent study suggested that vitamin C, by stimulating the cystic fibrosis transmembrane conductance regulator (CFTR), increases fluid secretion in epithelial cells, such as those found in the lung and intestine.28 This may account for the observed laxative effect and could be variable depending on the individual’s health status.

Pauling’s public celebrity became increasingly associated with the advocacy of high-dose vitamin C to prevent and treat infectious diseases, even though he continued to work productively for the rest of his life on theoretical problems in chemistry and physics, notably his closed-pack spheron theory of atomic nuclei, as well as on solving chemical structures of organic and inorganic substances. Of course, he also continued to honor a commitment to his wife and himself to advocate for peace among nations at every opportunity. A collaboration with the Scottish surgeon Ewan Cameron on the adjunctive use of high-dose oral and intravenous vitamin C in advanced cancer that began in 1971 continued until Cameron’s death in 1991. Cameron had written a book, Hyaluronidase and Cancer, in 1966 about the quest for a physiological hyaluronidase inhibitor (PHI) that would interfere with the action of the enzyme hyaluronidase in attacking hyaluronic acid in the ground substance that permits the growth of tumors.29 Such a strategy might enhance “host resistance” to cancer and slow the growth of solid tumors, making cancer a manageable disease. Cameron read about Pauling’s statements on the putative value of vitamin C in controlling cancer and wrote to him in 1971.30 Cameron began to give his patients hospitalized with advanced cancer about 10 grams of vitamin C per day for about 10 days or longer, typically by slow-drip intravenous administration.
followed by oral dosage. Pauling and Cameron argued that vitamin C benefits cancer patients by stimulating the synthesis of a PHI or by being incorporated into one, augmenting the immune system, and optimizing collagen synthesis, thus encapsulating tumors and enhancing tissue integrity. Pauling also thought about the cytotoxicity of vitamin C, involving copper and redox chemistry, as early as 1975 and in 1983 published a paper with Japanese colleagues implicating hydrogen peroxide as the cytotoxic molecular species, based on in vitro and animal studies. Despite repeated denials of federal grant requests over eight years, Pauling and his colleagues managed to publish scores of papers on vitamin C and cancer encompassing in vitro research, animal experiments, and clinical work. In 1979, he and Cameron published Cancer and Vitamin C, which remains in print in an expanded and updated edition.

With funding from the National Cancer Institute, the Mayo Clinic conducted two randomized controlled trials of high-dose vitamin C and advanced cancer. Both studies failed to demonstrate any benefit of supplemental vitamin C, which was given only orally and for a short period. Pauling, Cameron, and others noted serious methodological flaws in the Mayo studies, which have been amply discussed elsewhere. In recent years, Mark Levine and colleagues in the NIH have studied the pharmacokinetics of vitamin C in young, healthy men and women. Based on their results demonstrating dramatic differences in plasma concentration of vitamin C depending on the mode of administration—intravenous administration produces plasma levels of 14,000 umol/L compared to about 220 umol/L with oral dosing—Levine considered the anticancer role of intravenous vitamin C extensively used by Cameron and by Riordan and colleagues. He published several papers showing that, with high concentrations attained by intravenous infusion, the ascorbate radical is formed in the extracellular milieu around cancer cells, helping to generate hydrogen peroxide that then diffuses into malignant cells, inducing apoptosis and pyknosis and disrupting mitochondrial function. This activity is selective—normal cells are unaffected—and appears to be dependent on the presence of an unidentified small molecular weight protein. Other recent papers have reported that vitamin C modulates hypoxia-inducible factor-1 (HIF-1), a transcription factor induced by hypoxia in cancer cells. Vitamin C inhibits HIF-1 induction and related gene expression, resulting in decreased growth of tumor cells. It’s possible that multiple mechanisms are involved in the anticancer effect of vitamin C and, based on Cameron’s results with oral vitamin C, that some types of cancer may be more therapeutically sensitive to vitamin C. Fortunately, interest in this area has been renewed, and phase 1 clinical trials have been published and are under way.

In the late 1980s, Pauling’s renewed friendship with a German cardiologist led to the formulation of a novel hypothesis on the possible cause of atherosclerosis: lipoprotein(a), a major constituent of atherosclerotic plaque, serves as a surrogate for vitamin C in chronic vitamin C insufficiency. A number of related concepts were derived from this putative surrogacy, including the role of lysine and vitamin C in ameliorating exercise-induced severe angina pectoris in patients with advanced heart disease. Indeed, Pauling wrote three case reports in the early 1990s that discussed such relief associated with the use of 3-6 grams per day each of lysine and vitamin C. Clinical studies in recent years have repeatedly demonstrated that high-dose vitamin C promotes relaxation of the arteries and improves blood flow—reversing endothelial dysfunction in
patients with heart disease or diabetes\textsuperscript{49,50} probably by stabilizing or increasing tetrahydrobiopterin, a molecule involved in nitric oxide synthesis.\textsuperscript{51} Other clinical studies have shown that high-dose vitamin C reduces systolic blood pressure in hypertensive subjects by about ten points.\textsuperscript{52} Of course, none of these beneficial effects are directly related to the classic role of vitamin C as a vitamin in preventing scurvy by promoting collagen synthesis.

The Work Continues–A Brief Survey

We have witnessed an explosion in research in orthomolecular medicine in the last 40 years. Nutritional epidemiological studies, mainly observational studies, have reported associations between many dietary factors and the risk for disease, and these initial associations have been followed up by biochemical and molecular biological studies to determine the substances and molecular mechanisms responsible for the putative benefits. While nutritional epidemiological studies do not prove a causal relationship, they do suggest possibly fruitful areas for further research. Foremost among epidemiological studies in the U.S.A. are the Nurses’ Health Study I, organized in 1976 with 122,000 women; the Nurses’ Health Study II, established in 1989 with 117,000 women; and the Health Professionals’ Follow-up Study, organized in 1986 with about 51,500 men. Subjects report periodically on their diet and health using food-frequency and health-status questionnaires, and some biological samples, such as toenail clippings, blood, and urine, have been collected. Compliance has been extremely good, with about a 90% response rate, and the value of the food-frequency and health questionnaires has been generally verified,\textsuperscript{53} although many scientists remain skeptical of associations derived from observational studies. One of the outcomes of the Nurses’ Health Study has been the discovery of the strong association between the intake of trans fat and coronary heart disease, which has led to the reduction of trans fat in the American diet through labeling and food industry practices. In the Netherlands, the work of Martijn Katan has been equally important in this area.\textsuperscript{54} Other large nutritional epidemiological studies have been organized, including the Netherlands Cohort Study (121,000 men and women, begun in 1986) and the European Prospective Investigation into Cancer and Nutrition (EPIC) study (440,000 men and women, begun in 1993), which found a link between the consumption of red meat and colorectal cancer, as well as myriad other findings, such as impressive inverse relationships between plasma vitamin C and all-cause mortality\textsuperscript{55} or risk of stroke.\textsuperscript{56}

Reports from these large-scale studies and others have identified associations between the consumption or avoidance of certain foods and supplements with disease risk, and scientific reductionism and biological plausibility have prompted the investigation of dietary constituents putatively responsible for the observed effects. Ellagic acid and anthocyanidins in berries; flavonoids like catechins in tea and chocolate and others in fruit and vegetables; isothiocyanates, including sulforaphane, and indole-3-carbinol from cruciferous vegetables; resveratrol in wine, grapes, and peanuts; chlorophyll and its derivative, chlorophyllin; carotenoids like lutein and lycopene; allicin and its derivatives from garlic; phytosterols; lignans; fiber; essential fatty acids; curcumin; and soy isoflavones are some of the dietary phytochemicals for which substantial literature has emerged in recent years. Research on the role of fish-derived omega-3 fatty acids in attenuating cardiovascular disease, inflammatory diseases, and mental illness has also been robust. The antioxidant function of flavonoids has been emphasized, but their poor absorp-
tion and rapid metabolism has led to the suggestion that fructose, not flavonoids, in ingested fruit increases the antioxidant capacity of plasma by stimulating the synthesis of uric acid, a strong physiological antioxidant, in the liver. A new focus on the cell-signaling properties of flavonoids and transient antioxidants like alpha-lipoic acid has emerged. The Micronutrient Information Center on the Linus Pauling Institute Web site provides a resource for updated and comprehensive information on micronutrients, phytochemicals, and other dietary substances and their roles in health and disease (http://lpi.oregonstate.edu/info center).

Interest in improving health span by dietary strategies has also accelerated, leading to remarkable studies with acetyl-L-carnitine and lipoic acid. Supplementation with these compounds has increased ambulatory activity and cognitive performance in old rats and old dogs, suggesting that they may be useful in slowing or even reversing age-related deficits in humans. Mitochondrial dysfunction, caused partly by oxidative damage and inflammation, has been implicated in neurodegenerative diseases, such as Parkinson’s, ALS, and Alzheimer’s, as well as in age-related decline, and therapeutic efficacy for coenzyme Q10, lipoic acid, and other antioxidants has been suggested.

Vitamin D is critical for cell differentiation, immune function, calcium utilization, and bone health, and it is required to prevent rickets and osteomalacia. A number of conditions, such as skin color, advanced age, fat malabsorption syndromes, obesity, and inflammatory bowel disease, are associated with increased risk for vitamin D deficiency. Concern about chronic suboptimum levels of vitamin D in northern latitudes, implicated in increased cancer risk, autoimmune disease, and osteoporosis, has prompted discussion of increasing the AI (Adequate Intake).

Clinical studies have also been conducted to determine if intervention with supplements identified by observational studies will attenuate disease risk. In 1993 two prospective studies from the aforementioned epidemiological research showed that the intake of vitamin E supplements significantly reduced the risk for coronary heart disease in men and women. While this had been common knowledge among those familiar with the Shute’s work in Canada and with Pauling’s writings, the papers stimulated much clinical interest in high-dose vitamin E and heart disease, leading to several randomized controlled trials. Results have been inconsistent, possibly owing to insufficient dose and/or duration, inadequate instructions about how to take vitamin E with fat-containing food for sufficient absorption, and the polypharmacy of patients with heart disease. For example, investigators have speculated that vitamin E may induce drug-detoxifying enzymes in the liver that could interfere with the therapeutic efficacy of certain drugs. Additionally, one recent study in hypercholesterolemic subjects found that oxidative stress, as measured by plasma F2-isoprostanes, was significantly suppressed (by 35% and 49%) only by daily doses of RRR-alpha-tocopherol of 1,600 IU or 3,200 IU, respectively, for at least 16 weeks. Smaller daily doses (400 IU or 800 IU) resulted in non-statistically significant reductions in plasma F2-isoprostanes.

Recent studies have also identified in vitro and in vivo anti-inflammatory roles for gamma-tocopherol in alleviating oxidative and nitrative stress, despite the more rapid metabolism and clearance of gamma-tocopherol compared to alpha-tocopherol, for which a transport protein has been discovered. About 70% of the vitamin E intake in the U.S. is in the form of gamma-tocopherol. One recent review of the role of gamma-tocopherol in the prevention of heart disease and
cancer noted that the results of prospective studies of gamma-tocopherol and the risk for heart disease are inconsistent, but some evidence suggests that high plasma gamma-tocopherol levels are associated with a decreased risk for prostate cancer.71 The media have compounded confusion about vitamin E and heart disease by not carefully distinguishing primary prevention trials in which subjects at baseline have not manifested heart disease from secondary prevention trials in which patients with heart disease have been supplemented with micronutrients to determine if supplementation decreases clinical events like myocardial infarction, stroke, or death.

Cellular transport mechanisms for vitamin C—the sodium vitamin C transporters (SVCT 1 and 2)—have been discovered in recent years.72 Dehydroascorbic acid (DHA) and glucose are facilitatively transported by GLUT1, GLUT3, and GLUT4.73,74 DHA has a half-life of only about seven minutes, and its levels in plasma are about 1000-fold less than circulating glucose, so its uptake is likely to be competitively inhibited by glucose.75 Ascorbic acid, on the other hand, is actively transported by the SVCT proteins, and the activity of one, SCVT1, declines with age,75 suggesting that older people need higher intakes to maintain a plasma status similar to young people at lower intakes of vitamin C.76 New biochemical functions have been reported for vitamin C, such as the ascorbylation reaction in which vitamin C combines with reactive aldehydes, potentially protecting biomolecules from damage.77 Mechanistic and pharmacokinetic studies on vitamin C and vitamin E and their roles in disease prevention and treatment will continue to be further explored in the near future.

Nutritionally essential minerals, such as selenium, zinc, and magnesium, have also garnered attention after inverse associations with risk for disease, especially cancer, emerged from epidemiological studies. Deficiencies of selenium or zinc impair immune function and increase susceptibility to infectious diseases, including HIV/AIDS.78,79 A long-term intervention trial found that daily supplementation with selenium-enriched yeast was associated with about a 50% reduction in prostate cancer incidence,80 although the risk for non-melanoma skin cancer was increased by 25%.81 In a large-scale randomized controlled trial, daily zinc supplements alone or in combination with antioxidant vitamins significantly reduced the risk for age-related macular degeneration by about 25% or more.82 In another large-scale, long-term study, high serum magnesium levels were associated with substantial decreases in all-cause mortality (40%), cardiovascular disease mortality (40%), and cancer mortality (50%), compared to low serum magnesium.83 Over half of Americans appear to ingest less than the daily Estimated Average Requirement (EAR) for magnesium, and a significant percentage of pre-menopausal American women ingest less than the daily EAR for iron, which increases vulnerability for heme deficiency and anemia.84

From these studies we can ascertain with certainty that relationships between micronutrients are complex and, in many cases, poorly understood. It is also clear that many people do not have adequate intakes of vital micronutrients, resulting in poor health and increased risk for disease. There is much to learn about the optimum intake of specific micronutrients or combinations of micronutrients, and new emphasis on translational research and evidence-based medicine will continue to stimulate research. Uncertainties propel research forward, and the future of orthomolecular medicine is bright. On the 40th anniversary of his paradigm-shifting paper, Linus Pauling would be pleased.
References


45. Rath M, Pauling L: Hypothesis: lipoprotein(a) is a surrogate for ascorbate. Proc Natl Acad Sci USA, 1990; 87: 6204-6207.


57. Lotito S, Frei B: The increase in human plasma antioxidant capacity after apple consumption is due to the metabolic effect of fructose on urate, not apple-derived antioxidant flavonoids. Free Radic Biol Med, 2004; 37: 251-258.


61. Lin M, Beal M: Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases.


Vitamin C and the Common Cold
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Straw man: a logical fallacy, based on misrepresentation of an opponent’s position. To “set up a straw man” means to create a sham position that is easy to refute, and then attribute that position to the opponent.

Introduction
The controversy over vitamin C and orthomolecular medicine began with the publication of Linus Pauling’s book, Vitamin C and the Common Cold. Since that time, a proportion of the population have been experimenting with high dose vitamin C, reflecting a belief in its efficacy as a treatment or preventative for this minor illness. However, some elements of conventional medicine continue to assume that vitamin C is ineffective. Here, we show that the available scientific evidence supports the use of this simple substance.

In their recently updated Cochrane review, “Vitamin C for preventing and treating the common cold”,1 Douglas, Hemilä, Chalker, and Treacy (2007) state their objectives as being to discover whether oral doses of 0.2 g or more daily of vitamin C reduce the incidence, duration, or severity of the common cold, when used either as continuous prophylaxis or after the onset of symptoms. This statement is their “straw man”. They conclude: “The failure of vitamin C supplementation to reduce the incidence of colds in the normal population indicates that routine mega-dose prophylaxis is not rationally justified for community use.”

The review’s conclusions were widely reported in the world’s press, with headlines, such as “Vitamin C useless for preventing colds” (Reuters, July 18, 2007), trumpeting the failure of vitamin C to prevent or cure colds. More recently, the Los Angeles Times (February 18, 2008) ran a similar headline, also based on the Cochrane review: “Cold sufferers mindlessly reach for vitamin C.” This article claimed that vitamin C may not be as beneficial as most Americans think.

As a result of this publicity, orthomolecular practitioners are likely to get questions from concerned patients, as to whether the Cochrane reviews’ data and analyses support such negative interpretations. This paper provides a robust answer to such questions.

Orthomolecular Claims for Vitamin C
The Cochrane review on vitamin C and the common cold has several shortcomings. Fundamentally, it fails to understand the orthomolecular claims for vitamin C in prevention and treatment of the common cold. Such claims for the actions of vitamin C against colds and other infections have been made over a period of at least 50 years.2-6 They specify a definitive and uniquely effective response.7-10 The clinical data upon which these claims are based have been replicated repeatedly.11-13 However, the claims are often wrongly stated and misunderstood.

The review by Douglas et al. is apparently based on such (admittedly widespread) misconceptions, rather than the original claims.14 It is important to stress that the doses Douglas et al. refer to as “mega-dose vitamin C supplementation” range from just 200 mg given once or twice daily. We would not consider these as high doses.

To avoid further misunderstanding, we must state the orthomolecular claims for vitamin C clearly.
Prevention of Common Cold

Vitamin C given to human subjects at frequent intervals (< 6 hourly) and sufficiently high doses (8+ grams per day) will prevent the common cold.

Klenner, one of the earliest clinical investigators, provides a quantitative indication of the dose required: 10 grams of vitamin C per day, given in divided doses, will prevent colds in 90% of individuals, but some people will require more. Hoffer indicates a similar dose response relationship (95% prevention at 8 grams per day or more, depending on individual variability). Reported dosing intervals vary slightly, but 4-6 doses a day would indicate a maximum interval of 4-6 hours.

Treatment of Common Cold

Vitamin C, given at short intervals and very high doses to a subject with the common cold, can eliminate the symptoms and may bring about a cure within hours.

These claims are based on high (pharmacological) doses and are subject to high levels of individual variation. Cathcart provides an indication of the dose and interval: 30-150 grams per day, in divided doses at intervals of one hour or less. The Vitamin C Foundation recommends 8 grams every 20 minutes, from the onset of symptoms.

Treatment Threshold Effect

The dose-response relationship for the treatment claim is described as a threshold effect; unless a minimum threshold dose is reached, little or no clinical response is achieved. For a mild cold, the threshold is close to the subject’s bowel tolerance level. Above this threshold, the symptoms are “quenched”; below it, there is little clinical benefit. In some individuals, with a virulent infection, reaching the threshold may be unfeasible with oral doses. However, recent research indicates oral liposomal formulations may be more effective.

Now that we have specified the orthomolecular claims explicitly, we can examine the Cochrane review in context.

Shortcomings of the Cochrane Review

It is clear that the Cochrane review fails to address the orthomolecular claims for vitamin C. Firstly, the reviewers base their view of the “failure of vitamin C” on inadequate dosing regimes. Secondly, the review relies on social and epidemiological medicine, rather than on a biological understanding of the proposed anti-viral effects of vitamin C. Thirdly, there are methodological defects: those selecting studies for inclusion or exclusion had knowledge of the results, therefore their choices were susceptible to bias. Finally, the reviewers extrapolated beyond their data, leading to over-generalisation of conclusions, particularly in their press releases. We will examine these points individually.

Inadequate Dosing Regimes

Dose Size

The review does not include data for intakes of the same order of magnitude as those described in the orthomolecular prevention claim. The intakes studied are too small. Similarly, the review does not consider intakes of the same order of magnitude as those claimed to be effective for treatment.

These objections were stated clearly by Hickey and Roberts, in response to an earlier version of the Cochrane review. Emerson, who also points out the discrepancy in the doses, has reinforced these early objections. Douglas et al. responded tangentially and failed to explain how their data could be extrapolated to cover the doses claimed to be effective.

Dose Frequency

The review covers longer dose intervals than those claimed to be effective. Hickey and Roberts published this
objection, and once again, the response by Douglas and Hemilä did not indicate how the data they presented could be extrapolated to more frequent doses. Furthermore, Douglas et al. failed to provide a specific explanation of how and why they ignored the dose-response mechanism; a rigorous response was required, as this failure breaches basic principles of pharmacology.

Lack of Scientific Understanding

Epidemiology lacks the power of direct and replicated observation; socially-based medical studies must comply with the underlying rules of science. Epidemiology is a secondary statistical discipline, and requires consistency with findings from fundamental sciences, such as chemistry or biophysics.

The Cochrane reviewers have ignored the pharmacokinetics of vitamin C. The half-life for kidney excretion of high-dose vitamin C from plasma is about 30 minutes. At the dose levels and intervals studied by Douglas et al., there would be little, if any, consistent increase in plasma ascorbate levels or body content. The antioxidant action of ascorbate depends on its ability to donate and transfer electrons (we are unaware of any other significant effects being postulated for this molecule). Clearly, a dose-response relationship requires the presence of the molecule in question: if the ascorbate has been excreted, as would be the case for the studies described in the Douglas et al. review, it cannot be expected to have a physiological effect.

Furthermore, the reviewers have excluded relevant published clinical data. They dismiss the observations of Cathcart and others, on the grounds that “their uncontrolled observations do not provide valid evidence of benefit”. This overlooks repeated, independent observations of large and easily replicated effects. Scientifically, such experimental results are more valid than large-scale clinical trials or epidemiological studies. By way of analogy, we might consider whether it would be necessary to carry out large-scale randomized double-blind controlled trials of the guillotine, to find out whether removing a person’s head results in death. Clearly, a single experiment would provide the answer to this question, and double blind controls would be superfluous.

On the clinical dose-response relationship, Cathcart claimed a reversible cessation of symptoms at the oral threshold near bowel tolerance: increasing the dose slightly removes the symptoms, while lowering the dose brings them back. However, Levy reports that he has not achieved this effect with standard oral doses and that intravenous, or liposomal, doses may be required. Levy claims intakes of 4-5 grams per hour of liposomal vitamin C, taken orally, have the reported effects with substantial biological variation in the doses required. This discrepancy may relate to carbohydrates inhibiting the absorption of ascorbate.

The scientific method involves hypothesis and refutation. Simple, easily replicable experiments, like those reported by internationally-known physicians, such as Cathcart, Klenner, Hoffer, Levy, Kalokerinos, and Brighthope, have greater scientific validity than the Cochrane meta-analysis. If the clinical observations of the above mentioned doctors were in error then, over the last half century, any physician or scientist could have refuted the claims directly, with little effort or cost. However, no such refutation exists in the scientific literature. This could be because the relevant doses have not been studied; alternatively, results obtained by conventional physicians attempting a refutation may have been declined for publication.
Methodological Issues

A sequence of systematic errors in the Cochrane review invalidates both its conclusions and the untenable extrapolations, associated particularly with comments from Hemilä, in the popular press.

Predetermined Opinion and Social Pressure

The Cochrane review provides a meta-analysis of low-dose studies of vitamin C and the common cold. Unfortunately, its authors have limited the range of intakes to low values, which are unlikely to be effective, and excluded clinical data on higher doses, which have been shown to provide positive results.

When choosing studies for a review paper, it is important to avoid selection errors. To avoid such errors, the studies should be selected on objective criteria, and without knowledge of the results. If the results of the studies are known before the selection criteria have been determined, then the people making the selection can be unconsciously biased. In the Cochrane review, the researchers were aware that the criteria used to select their studies would exclude all clinical reports of high (orthomolecular) doses.

Further selection bias can be introduced when papers are considered for inclusion. If a reviewer choosing a paper is aware of the author’s names, experimental details, and results, she can largely influence the outcome of the study by unfair selection. Such experimenter bias is well known and is the reason blind and double blind experiments are performed. Even the most honest experimenters are unconsciously subject to these effects. Moreover, obedience to authority (the Milgram effect), social pressures (Ashe conformity), and Groupthink can combine to produce erroneous results. In the Cochrane study, the reviewers who selected or excluded studies had prior knowledge of the literature on vitamin C and the common cold, as well as specific information about the papers under consideration.

These problems have been communicated to the Cochrane authors, though their response to date has been unsatisfactory. A clear and objective response, focusing on these specific objections, might provide reassurance that the potential for such bias was being addressed.

Exclusion of Non-placebo Controlled Trials

Although the review acknowledges that the placebo effect is not relevant except for minor subjective effects, it excludes data from any trials without placebo controls.

As described in another Cochrane review, and elsewhere, the placebo effect is irrelevant in the case of definitive and objective clinical effects. The effects claimed for vitamin C, as described above, are large, objective, and definitive, and have not been replicated using any other antiviral substance. Authors report complete, dose-related, reversal of symptoms, or rapid cure: these substantive results are unambiguous clinical observations.

The review required placebo controls on the basis that the authors considered “that with the expected small effects of vitamin C, and the greatly subjective outcome definitions, only placebo-controlled trials could yield information of adequate rigour to meet our study objectives.” Such an expectation is based on a misconception of the claims for vitamin C. The reported outcomes for appropriate doses are large and objective, rendering this explanation spurious. The reason provided was particularly inadequate for this review, as it restricted the doses studied to outliers of the range claimed to be effective.

Overgeneralization

The authors failed to make clear the limitations of their review. They did not specify clearly enough that their results
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relate to low doses. The doses studied were approximately an order of magnitude less than those claimed to be effective. Similarly, the review did not specify that its results and conclusions do not apply to the clinical claims for the effectiveness of vitamin C.

Taken as a whole, the review and its resultant media generalizations are misleading, as they deflect attention away from the actual claims for vitamin C’s effectiveness.

Discussion

Cochrane reviews generally provide an excellent scientific resource to medicine, as illustrated by the review of the placebo effect. However, with the review of vitamin C, the authors have failed to provide an effective response to objections. They have promoted their conclusions widely, resulting in media generalisations that are out of proportion to a scientific interpretation of the data.

The current Cochrane review exemplifies the dangers of systematic error. Bias and confusion can be primary sources of inaccuracy, even when a statistical analysis obeys the technical rules. The review by Douglas et al. is an example of “cargo-cult science,” as initially described by the physicist Richard Feynman: it has the appearance and techniques of proper science, while avoiding the constraints required for an effective and accurate investigation.35

In previous responses to objections on dose raised by Higgins, and Hickey and Roberts, Douglas et al. did not address the specific criticisms. Rather, their responses deflected the readers’ attention from a rational consideration of the central issues. In particular, by excluding high dose studies, the Cochrane reviewers set up a straw man, demolished it, and highlighted their “achievement” (or misleading claims) in the worldwide press.36,37

Linus Pauling’s initial pragmatism in suggesting lower dose levels was overly optimistic, particularly for preventing the common cold; his suggested daily doses increased with time, to a recommended optimal intake of 1-18 grams per day, depending on individual variation.38 Pauling was aware of the difference between intakes for prevention of infection and those for therapeutic intervention, and he reported the massive doses described by Cathcart.

Before the current minor review update, Hemilä and Douglas used their results to claim that the “lack of effect of prophylactic vitamin C supplementation on the incidence of common cold in normal populations throws doubt on the utility of this wide practice.”39 A widely quoted press release from Douglas’ university begins “vitamin C has been proven ineffective in combating the common cold in most people.” Douglas goes on to claim, “vitamin C has proven not to be a magic bullet to solve the common cold.”40

We can find no evidence in either version of the Cochrane review to support such unscientific claims, let alone provide anything close to “proof.”41 The hypothesis that appropriate doses of vitamin C can prevent or cure the common cold has not been refuted.

References

5. Klenner FR: Massive Doses of Vitamin C and
Introduction

Lipoic acid (LA), also known as alpha-lipoic acid, is a sulfur-containing fatty acid. It is found inside every cell of the body, where it helps to regenerate the energy that keeps cells alive and functioning. LA, an alipoamide, is a constituent of biological membranes and an important cofactor of mitochondrial dehydrogenases. LA is a key part of the process that turns glucose into energy.

LA, unlike other antioxidants that work only in water or fatty tissues, functions in both water and fat. This gives LA a broad spectrum of antioxidant actions. A healthy body makes enough LA to supply its own requirements. However, several medical conditions may be accompanied by low levels of LA.

LA is easily absorbed from the diet. It enters cells from the bloodstream and is readily converted to its reduced form, dehydrolipoic acid (DHLA). Both LA and DHLA act as antioxidants in vitro and in vivo.1-5

The specific effects of LA and DHLA include quenching of reactive oxygen species, such as superoxide radicals and hydroxyl radicals, and chelation of copper, zinc, and iron. It is important in the intracellular recycling of vitamin E through interaction with vitamin C. LA also increases levels of glutathione, a very important antioxidant normally found in cells.6

This powerful antioxidant is currently being studied to provide both preventive and therapeutic benefits in numerous conditions such as diabetes, heart disease, and neurological diseases (Parkinson’s and Alzheimer’s).7-15 For example, LA has been used for decades to treat diabetic peripheral neuropathy. Free radicals (oxidants) are thought to play a role in neuropathy. It has been shown that LA is effective in the prevention of early diabetic glomerular injury and has advantages over high doses of other antioxidants.13

Although hundreds of studies over the past years showed how LA energizes metabolism, our studies focused on a new aspect. We analyzed the differential effect of LA on energy metabolism of normal lymphocytes and leukemic lymphocytes and demonstrated inhibition of the energy metabolism of leukemic cells in comparison with normal cells. Analysis was performed for three leukemic cell lines and lymphocytes of healthy subjects. At similar concentrations, lipoic acid was toxic to leukemia cells and nontoxic to blood lymphocytes. Exposure of cells to 200-800 µM of LA was followed by a decrease of ATP production and increased apoptosis of leukemia cells. These experiments may be useful to prove the effectiveness of lipoic acid in the treatment of leukemia.

In addition, we demonstrated that supplementation of lymphocytes under oxidative stress can restore the functional activity of cells and improve the level of mitochondrial functioning and mitochondrial potential. The experiments suggest that lipoic acid has a beneficial effect in pathological conditions involving impairment of the immune system due to oxidative stress.
Methods

1. Method of ATP Measurements in Cells

Levels of ATP in cells were determined by the CellTiter –GLO Luminescent Cell Viability Assay Kit (Promega Company). This assay generates a luminescence glow type signal produced by a luciferase reaction, which is proportional to the amount of ATP present in the cells. Levels of ATP were proportional to luminescent output and ATP was determined from a standard curve by measuring the level of luminescence for different concentrations of pure ATP (Sigma).

2. Measurements of Mitochondrial Potential

Mitochondrial potential was measured by using the fluorescent potentiometric dye JC-1. JC-1 is able to selectively enter mitochondria and forms aggregates that emit at 595 nm (red-orange range). If the mitochondrial potential is reduced, JC-1 changes to monomers that emit fluorescence at 535 nm (green). The ratio between the red and green signals indicates the mitochondrial potential. Levels of emission were measured by a fluorometer (SPEX Company).

3. Measurements of Apoptosis

Apoptosis (programmed cell death) was measured by Annexin V FITC Kit (Inmunotech Coulter Company). In the early phase of apoptosis, the integrity of the cell membrane is maintained, but the cells lose the asymmetry of their membrane phospholipids. Phosphatidylserine (PS), the negatively charged phospholipid in the inner leaflet of the plasma membrane, becomes exposed at the cell surface. Annexin V binds preferentially with high affinity to PS. Apoptotic cells are detected by emission of bounded Annexin V. The signal from Annexin V was detected by the FITC signal detector of a flow-cytometer. Dead cells were separated by staining with propidium iodide.

4. Cell Differentiation

Treatment of leukemia cells with TPA (12-O–tetradecanoylphorbol-13-acetate) may induce differentiation of a number of leukemia cells. The effect of cell differentiation by TPA is associated with the activation of the stress-activated protein kinase, the release of cytochrome C, activation of caspases and other molecules.16

For differentiation, HL-60 cells were exposed to 32 to 64 nM of TPA. The time of the cell exposure was 24 hours. Differentiation by TPA inhibited cell growth and changed cell morphology. The most evident was an increase in cytoplasm to nucleus ratio. Immuno-fluorescence analysis demonstrated that before differentiation cells were promyelocytes and according to measurements, 90% of cells expressed surface markers of promyelocytes (CD33). After differentiation cells had characteristics of terminally differentiated cells and expressed markers of polymorphonuclear leukocytes (CD3, CD22, CD15 and CD66b).

Results

1. The Effect of Lipoic Acid on Transformed and Differentiated HL-60 Cells

Differentiated and transformed cells were analyzed for levels of ATP, for mitochondrial potential, and mitochondrial mass. Levels of mitochondrial potential and ATP production were compared for TPA treated and untreated cells, which demonstrated increased levels of mitochondrial potential after cell differentiation (25% average difference) and decreased levels of ATP production (28% average difference). Mitochondrial mass for cells after differentiation was measured by flow-cytometer by staining cells with the dye 10-N-nonyl acridine orange (NAO).17 This dye binds to the cardiolipin of mitochondria and the levels of uptake of this dye do not depend on
the mitochondrial potential. Emission was measured by flow-cytometer (excitation 495 nm, emission 525 nm). The data demonstrated lower values of mass for differentiated cells in comparison with the transformed cells (an average 16% difference).

To compare the effect of LA on the level of ATP in differentiated and transformed cells, cells were washed and resuspended at a concentration of 0.5 million cells per mL in Iscove’s medium (ATCC). LA was prepared before use in dimethyl sulfoxide (DMSO). The solution was standardized at 333 nm (e = 150 M⁻¹ cm⁻¹) and was added to the medium with cells in a concentration of 100 to 800 µM. Cells were incubated in an atmosphere with 5% CO₂, 37 °C, and 98% humidity for 24 hours. After incubation the cells were washed by phosphate buffered saline (PBS), counted, and the level of ATP was measured for two different populations. Results of the experiments are presented in Figure 1, (below).

We found that LA had different effects on the level of metabolic activity of transformed and differentiated cells. Supplementation by LA caused inhibition of ATP production in transformed cells. As it is shown in Figure 1, concentration of lipoic acid equal to 800 µM inhibited viability of leukemia cells two times. However, the viability of normal differentiated cells was not changed. That effect was not due to the solvent DMSO, as it was shown by the addition of DMSO without LA. Levels of DMSO in medium were less than 0.5%.

The explanation of the difference in the effect of LA on transformed and differentiated cells might be based on the assumption that LA may up-regulate caspase activity and apoptosis in transformed cells by creating a reducing environment.¹⁸

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**Figure 1.** Effect of lipoic acid on the levels of ATP in differentiated and transformed HL-60 Cells (mean ± SD).
2. The Effect Of Lipoic Acid on Leukemia T Cells and Healthy T Cells and Potentiation of Inhibition of Energy Metabolism in Leukemia Cells by Lipoic Acid

We compared the effect of LA on healthy lymphocytes and T cells and acute pro-myelocytic leukemia cells, chronic myelogenic leukemia, and acute lymphoblastic leukemia T cells. Healthy T cells were separated by the RosetteSep procedure (Stem cell technology) from peripheral blood. The main principle of separation is that blood was mixed with RosetteSep antibody cocktail and unwanted cells were cross-linked to red blood cells (rosetted) with tetrameric antibody complexes. Centrifugation with Ficoll-Pague allowed separation of enriched cells.

In order to determine the potential effect of LA on the level of metabolism of normal and transformed cells, cells were treated with different concentrations of LA. Cells (HL-60- acute pro-myelocytic leukemia, K-562- chronic myelogenic leukemia, Molt-3-acute lymphoblastic leukemia T cells, and healthy T cells) were seeded in 24-well plates with concentrations of 0.5 million cells per mL. Cells were treated by concentrations of LA 100 to 800 µM for 24 hours.

After exposure, ATP concentrations in the treated cells were compared with control non-treated cells (Figure 2, below).

The data presented in Figure 2 are average values of 5 to 8 experiments. According to these data, treatment of leukemia cells by LA resulted in an inhibition of metabolic activity and ATP concentration in transformed cells. The most pronounced effect was measured for HL-60 cells. The same concentrations of LA did not inhibit ATP production in normal T cells.

Under the same experimental con-

Figure 2. Effect of lipoic acid on the levels of ATP concentrations in healthy and leukemia T cells (means ± SD).
ditions, we measured the levels of apoptotic cells. For HL-60 cells, the percentage of apoptotic cells was 5%-10% after exposure to 200 µM of LA and increased to 15%-20% after exposure to 800 uM LA. For T cells, the percentage of apoptotic cells was in the range of 1%-4% for a concentration of LA of 100 to 800 µM.

Results of our analysis demonstrated the cytotoxicity of LA to leukemic cells in comparison with healthy T cells. These results may be explained by a previous study of the mechanism of apoptosis. A reduced environment inside the cells is necessary for caspase activity during apoptosis. LA is a redox active chemical, intracellularly reduces to a potent dihydrolipoic acid, and creates a reduced environment in the cells. It potentiates apoptosis of tumor cells or affects the level of energy metabolism of tumor cells.

### 3. The Effect of Lipoic Acid on Cells Under Oxidative Stress

For many years, LA has been recognized as an antioxidant. Alpha-lipoic acid, or its reduced form, dehydrolipoate, reacts with reactive oxygen species. In this study, we examined whether in vitro supplementation of cells with LA can protect mitochondrial potential and the level of ATP production against oxidative stress. Enhancement of cellular antioxidant status was performed by preincubation of the cells with LA, which was reduced intracellularly to dihydrolipoic acid. The time of exposure to LA was 4 to 6 hours. After incubation with LA, cells were washed and resuspended in fresh medium. Hydrogen peroxide was added at concentrations of 50 to 200 µM. The concentration of H$_2$O$_2$ was standardized at 240 nm (ε=43.6 M$^{-}$.1cm$^{-1}$). After 30 min of exposure, cells were washed and analyzed at the level of ATP and mitochondrial potential. According to our results, the addition of 50 to 200 µM of hydrogen peroxide to the medium with cells resulted in oxidative stress and apoptosis in cells. Addition of 50-200 µM of H$_2$O$_2$ decreased the ratio of intensities of emission at 595 nm to 535 nm 1.2 to 3 times in comparison with controls. Examples of the fluorescence emission curves of mitochondrial potential for control cells and cells under oxidative stress are presented in Figure 3, (p.88).

Our results proved that free LA, when provided exogenously protects the mitochondrial potential against oxidative stress. For example, data showed that the mitochondrial potential was reduced by 34% to 61% in cells under oxidative stress induced by 100 µM of H$_2$O$_2$. After pretreatment of cells by LA before exposure to hydrogen peroxide, the level of mitochondrial potential was 7% to 29% higher compared with non-treated cells. The level of protection depended on the concentration of LA added in the medium for treatment (Figure 4, p.88).

The antioxidant protection by LA before induction of oxidative stress improved levels of ATP production in cells. Lipoic acid supplementation with a concentration of 100uM resulted in increased ATP production on average in 10%-20% in all experiments.

### Conclusion

These findings suggest that LA has different effects on metabolic activity of normal and transformed cells. Treatment of leukemia cells with 100 to 800 µM of LA affected the level of ATP production and mediated apoptosis in leukemia cells. The same treatment of normal T cells did not affect the level of metabolic activity of these cells.

Incubation of blood lymphocytes and leukemic cells with a concentration of 100–800 µM LA has been shown to potentiate apoptosis in the leukemia cells but not in the healthy lymphocytes.

According to these data, LA is pref-
Figure 3. Emission curves for mitochondrial potential for control cells, cells under oxidative stress and cells pretreated by lipoic acid.

Figure 4. Improvement of mitochondrial potential of cells under oxidative stress treated by lipoic acid.
sentially cytotoxic to the leukemic cell lines. These findings suggest that lipoic acid may be considered for the treatment of leukemia.

In addition, we showed that free LA, when provided exogenously, protects mitochondrial potential against oxidative stress. After pre-treatment of cells with 50–400 µM of LA before exposure to 100 µM of hydrogen peroxide, the level of mitochondrial potential was on 7% to 30% higher in comparison with non-treated cells. The level of protection depended on the concentration of LA added in the medium for treatment. The level of ATP production was also improved in 10% to 20% for cells treated by LA before oxidative stress.

Acknowledgement

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References

In his seminal book, Good Calories, Bad Calories, Gary Taubes quotes Hilde Bruch, who wrote: “The literature on obesity is not only voluminous, it is also full of conflicting and confusing reports and opinions. One might well add to this the words of Artemus Ward: “The researches of so many eminent scientific men have thrown so much darkness on the subject that if they continue these researches we shall soon know nothing.”

Determining the causes of the hundreds of psychiatric disorders and their treatment has almost reached that state of total darkness. Dr. Campbell-McBride, in her book Gut and Psychology Syndrome, blows away some of the fog and shows us where to look. After I read it, I wrote to the author: “Had I read your excellent book forty years ago I would have thought you were nuts. Thirty years ago I would have seen some merit and in the last years what I have learned has confirmed what you have written. It is a very good book. Isn’t it a shame that psychiatric illnesses are fueled by foods and the way we deal with them. Ironically, psychiatry may never accept this idea, as it has become the unpaid servant of the drug industry. Many thanks for sending it to me.”

To learn more, please read the book by Dr. Natasha Campbell-McBride, Gut and Psychology Syndrome: Natural Treatment for Autism, ADHD/ADD, Dyslexia, Dyspraxia, Depression, Schizophrenia.

–Abram Hoffer, MD, PhD

We live in the world of unfolding epidemics. Autistic Spectrum Disorders, Attention Deficit Hyperactivity Disorder (ADHD/ADD), schizophrenia, dyslexia, dyspraxia, depression, obsessive-compulsive disorder, bipolar disorder and other neuro-psychological and psychiatric problems in children and adults are becoming more and more common.

In clinical practice these conditions overlap with each other. A patient with autism often is hyperactive and dyspraxic. There is about 50% overlap between dyslexia and dyspraxia and 25-50% overlap between ADHD/ADD and dyslexia and dyspraxia. Children with these conditions are often diagnosed as being depressed, and as they grow up they are more prone to drug abuse or alcoholism than their typically developing peers. A young person diagnosed with schizophrenia often suffered from dyslexia, dyspraxia or and ADHD/ADD in childhood. When we start examining the patients with these so-called mental conditions, we find that they are also physically ill. Digestive problems, allergies, eczema, asthma, various food intolerances and immune system abnormalities are universally present amongst them. We have created different diagnostic boxes for these patients, but a modern patient does not fit into any one of them neatly. The modern patient in most cases fits into a rather lumpy picture of overlapping neurological and psychiatric conditions.

Why are all these conditions related? What underlying problem are we missing?

To answer all these questions we have to look at one factor, which unites all these patients in a clinical setting. This factor is the state of their digestive system. I have yet to meet a child or an adult with autism, ADHD/ADD, dyslexia, dyspraxia, schizophrenia, bipolar disorder, depression or obsessive-compulsive disorder who does not have digestive abnormalities. In many cases they are severe enough for the patients or their parents to start talking about them first. In some cases the parents may not mention their child’s digestive system, yet when asked direct

*GAP Syndrome or GAPS™
questions, would describe a plethora of gut problems. So, what have digestive abnormalities got to do with these so-called mental problems? According to recent research and clinical experience – a lot! In fact it appears that the patient’s digestive system holds the key to the patient’s mental state.

What is a typical scenario we see in clinical practice? Before examining the patient it is very important to look at the health history of the parents. Whenever the parents are mentioned people immediately think about genetics. However, apart from genetics there is something very important the parents, mother in particular, pass to their child: their unique gut micro-flora. Not many people know that an adult on average carries 2 kg of bacteria in the gut. There are more cells in that microbial mass than there are cells in an entire human body. It is a highly organized micro-world, where certain species of bacteria have to predominate to keep us healthy physically and mentally. Their role in our health is so monumental, that we simply cannot afford to ignore them. We will talk in detail about the child’s gut flora later. Now let us come back to the source of the child’s gut flora – the parents.

After studying hundreds of cases of neurological and psychiatric conditions in children and adults, a typical health picture of these children’s mums has emerged: due to various modern factors a modern mum has seriously compromised gut flora by the time she is ready to have children. Indeed, clinical signs of gut dysbiosis (abnormal gut flora) are present in almost 100% of mothers of children with neurological and psychiatric conditions.

A baby is born with a sterile gut. In the first 20 or so days of life the baby’s virgin gut surface is populated by a mixture of microbes. This is the child’s gut flora, which will have a tremendous effect on this child’s health for the rest of his/her life. Where does this gut flora come from? Mainly from the mother at the time of birth. Whatever microbial flora the mother has, she passes to her newborn child. Fathers with abnormal gut flora contribute to the bodily flora of the mother and through her to the gut flora of the child.

The Role and Importance of the Gut Flora

Gut flora is something we do not think much about. And yet the number of functions the gut flora fulfils is so vital for us that if some day our digestive tracts were sterilised we probably would not survive.

The first and very important function is appropriate digestion and absorption of food. If a child does not acquire normal balanced gut flora, then the child will not digest and absorb foods properly, developing multiple nutritional deficiencies. And that is what we commonly see in children and adults with learning disabilities, psychiatric problems and allergies. Many of these patients are malnourished. Even in the cases where the child may grow well, testing reveals some typical nutritional deficiencies in many important minerals, vitamins, essential fats, many amino acids and other nutrients.

Apart from normal digestion and absorption of food, healthy gut flora actively synthesizes various nutrients: vitamin K, pantothenic acid, folic acid, thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), pyridoxine (vitamin B6), cyanocobalamin (vitamin B12), various amino-acids and proteins. Indeed, when tested, people with gut dysbiosis present with deficiencies of these nutrients. Clinical experience shows that restoring the beneficial bacteria in their gut is the best way to deal with these deficiencies.

Apart from taking a vital part in nourishing the body, beneficial bacteria in the gut act as the housekeepers for the digestive tract. They coat the entire
surface of the gut protecting it from invaders and toxins by providing a natural barrier and producing anti-bacterial, anti-viral and anti-fungal substances. At the same time they provide the gut lining with nourishment. Beneficial bacteria normally control various opportunistic and pathogenic microbes in the gut. Lack of beneficial bacteria would allow disease-causing microbes to grow and occupy large parts of the digestive system causing damage and inflammation in the gut wall. So, it is no surprise when the gut flora is abnormal, the digestive tract itself cannot be healthy. Indeed most patients with learning disabilities, psychiatric disorders and allergies present with digestive problems: constipation and diarrhoea, infantile colic and abdominal pain, bloating and flatulence, reflux and indigestion. Examination by gastroenterologists commonly reveals inflammatory process in the gut and many of these patients are diagnosed with coeliac disease. Housing a mass of pathogenic microbes the gut cannot be healthy. Indeed, long before these patients develop so-called mental symptoms they usually suffer from digestive problems: constipation and diarrhoea, infantile colic and abdominal pain, bloating and flatulence, reflux and indigestion.

The Role and Importance of the Immune System

A baby is born with an immature immune system. Establishment of healthy balanced gut flora in the first few days of life plays a crucial role in appropriate maturation of the immune system. If the baby acquires compromised gut flora from the mother then the baby is left immune compromised. The result is lots of infections followed by lots of courses of antibiotics, which damage the child’s gut flora and immune system even further.

The beneficial bacteria in the gut ensure appropriate production of different immune cells, immunoglobulins, keeping immunity in the right balance. Damage inflicted upon the gut flora typically leads to an imbalance between major parts of immunity, resulting in allergies, asthma and eczema – symptoms, which children and adults with neurological and psychiatric conditions commonly suffer from.

There has been a considerable amount of research published into the state of the immune system in patients with learning disabilities and psychiatric problems. The research shows deep abnormalities in all major cell groups and immunoglobulins. The most common autoantibodies found are to myelin basic protein (MBP) and neuron-axon filament protein (NAFP). These antibodies specifically attack the person’s brain and the rest of the nervous system.

To summarize: A child born from parents with abnormal gut flora did not acquire normal gut flora from the start. The flora may have been damaged further by repeated courses of antibiotics and vaccinations. As a result, these children commonly suffer from digestive problems, allergies, asthma and eczema. However, in children and adults who go on to develop neurological and psychiatric problems, something even worse happens. Without control of the beneficial bacteria, different opportunistic and pathogenic bacteria, viruses and fungi have a good chance to occupy large territories in the digestive tract and grow large colonies. Two particular groups, which are most commonly found on testing, are yeasts (including Candida species) and the Clostridia family. These pathogenic microbes start digesting food in their own way producing large amounts of various toxic substances, which are absorbed into the blood stream, carried to the brain and cross the blood–brain barrier. The number and mixture of toxins can be very individual, causing different neurological and psychiatric symptoms. Due to the absence or greatly reduced numbers of beneficial bacteria in the
gut flora, the person’s digestive system instead of being a source of nourishment becomes a major source of toxicity in the body.

The mixture of toxicity in each child or adult can be quite individual and different. But what they all have in common is gut dysbiosis (abnormal gut flora). The toxicity, which is produced by the abnormal microbial mass in these patients, establishes a link between the gut and the brain. That is why it is logical to group these disorders under one name: the Gut and Psychology Syndrome (GAPS). The GAPS children and adults can present with symptoms of autism, ADHD, ADD, OCD, dyslexia, dyspraxia, schizophrenia, depression, bipolar disorder, sleep disorders, allergies, asthma and eczema in any possible combination. These are the patients who fall through the gap in our medical knowledge. Any child or adult with a learning disability, neurological or psychological problems and allergies should be thoroughly examined for gut dysbiosis. Re-establishing normal gut flora and treating the digestive system of the person has to be the number one treatment for these disorders, before considering any other treatments with drugs or otherwise.

Gut and Psychology Syndrome (GAP Syndrome or GAPS) establishes the connection between the state of the patient’s gut and the functioning of the brain. This connection has been known by medics for a very long time. The father of modern psychiatry French psychiatrist Phillipe Pinel (1745–1828), after working with mental patients for many years, concluded in 1807: “The primary seat of insanity generally is in the region of the stomach and intestines.” Long before him Hippocrates (460-370 BC), the father of modern medicine has said: “All diseases begin in the gut!” The more we learn with our modern scientific tools, the more we realize just how right they were.

References


Orthomolecular Treatment For Schizophrenia: A Review (Part Two)

Raymond J. Pataracchia, B.Sc., N.D.¹

Introduction

This two-part review on schizophrenia describes various segments of the schizophrenic population that fall into subgroups of distinct biochemical imbalance. To recap, these subgroups include essential fatty acid deficiency, inadequate nutriture, dysglycemia, food intolerance, digestive compromise, malabsorption, under-methylation, vitamin B₁ deficiency, B₆ deficiency, vitamin C deficiency, zinc deficiency, heavy metal toxicity, brain hypothyroidism, and hypoadrenia. Complementary alternative medicine (CAM) has a key role in the treatment of schizophrenia. In Part Two of this review, we discuss heavy metal toxicity, B₆ deficiency, zinc deficiency, brain hypothyroidism, and hypoadrenia.

Heavy Metal Toxicity in Schizophrenia

Most heavy metals are free radicals that induce oxidative stress (lipid peroxidation) and have an affinity for brain tissue.¹² Free radical-mediated neurotoxicity and oxidative stress are implicated as a causative factor in schizophrenia.³,⁴ These free-radicals have the ability to compromise and/or destroy brain tissue and, in so doing, decrease the availability of viable brain tissue. Note that other mechanisms of brain tissue compromise are involved in schizophrenia, so the added burden of toxic metals is to be avoided.

Elevated heavy metal levels are associated with schizophrenic pathology.⁴⁻⁸ It is not uncommon to see toxic levels of copper, lead, mercury, aluminum, arsenic and cadmium in schizophrenics. We find some of the most advanced schizophrenic cases having three or more heavy metals. Heavy metal toxicity is also associated with ADHD, anxiety, OCD, depression, bipolar disorder and dementia.

Heavy metals are excreted by using the body’s metal-removing protein, metallothionein.²⁹ In the process of rid-ding the body of heavy metals, this protein loses zinc.¹⁰ Zinc loss in schizophrenia in turn compromises the ability to transcribe proteins and make neurotransmitters. Investigators recognize compromised brain protein transcription pathways in schizophrenia.¹,¹¹ Zinc deficiency is associated with schizophrenia and other psychiatric pathologies including mood dysfunction and dementia.⁹

Lead disrupts mental function.¹² Toxic lead levels are associated with psychosis.¹³ Lead toxicity is also associated with behaviour disturbance, mood disorder, learning disabilities, insomnia, immune compromise, brain damage and delayed infant development. Lead has been found to disrupt the carriage of thyroid hormone (T₄) into the brain.¹⁴,¹⁵ If you are a city dweller, you are exposed to lead and the risk of lead toxicity rises with age. With widespread pesticide use, lead accumulates in the food chain. Lead is found in paints, print colour, glass, batteries, rust protectants, alloys and old water pipes and bathtubs.¹⁶

Mercury is toxic and has no therapeutic use; in fact, it disrupts dopamine and norepinephrine metabolism.¹⁷ It is not uncommon to find elevated mercury in patients with schizophrenia. Mercury is found in fluorescent lights, vaccines, thermometers, and fish, animals, and plants exposed to toxic environments. Dental fillings contain on average about 40% mercury which has the potential to leach with electrolytic decay. Mercury
often causes headaches, nervous irritability, memory decline, depression, rapid fatigue, nausea, stomach aches and allergic susceptibilities.\textsuperscript{16} Mercury has a strong affinity for the brain but also sequesters in the liver, kidney, and spleen. Aluminum can be toxic in patients with schizophrenia, mood disorders, Alzheimer’s Disease and digestive system pathologies. Aluminum disrupts enzyme function and is well-documented to disrupt cognition, learning and memory. Environmental sources of aluminum include aluminum cookware (especially from heating and deglazing with an acid such as vinegar or wine), drinking boxes, processed cheese, deodorants, and drinking water (aluminum is more soluble in our acidic magnesium deficient drinking water).\textsuperscript{18}

In excessive concentrations, copper has a toxic effect and, in schizophrenia, contributes to excess catecholamine oxidation, the end products of which are unstable toxic hallucinogens.\textsuperscript{6,19} We have found copper toxicity to be the most common heavy metal pattern in schizophrenia. It is also associated with ADHD, autism, depression, anxiety, bipolar disorder and paranoia. With copper toxicity we see clinical zinc deficiency.\textsuperscript{20} Copper is abundant in food and water as it is found in soil, pesticides and animal feed. Since World War II we have been exposed to greater levels of copper due to copper piping in modern homes and the widespread use of birth control pills (estrogen based). Estrogen dominance is associated with higher circulating copper levels and copper is thought to transfer via placenta from generation to generation.\textsuperscript{20} Other copper sources include copper tea pots, copper sulfate treated Jacuzzis or swimming pools, drinking water, dental fillings, prenatal vitamins, and copper IUD’s. Neuroleptics, antibiotics, antacids, cortisone, Tagamet, Zantac, and diuretics often encourage copper dominant biochemistry.

The liver produces the copper regulating proteins metallothionein and ceruloplasmin and, with low thyroid function, their hepatic protein synthesis is diminished. The body attempts to remove excess copper by excreting it out of the liver via gall bladder excretion to the bowel. Vitamin B\textsubscript{6}, vitamin C, and zinc are helpful clinically because of their physiological antagonism to copper.

Schizophrenics relapse when thyroid function is low.\textsuperscript{21} Poor thyroid function encourages heavy metal retention. Conversely, heavy metals seem to play a major role in blocking peripheral enzyme conversion of T4 to T3.\textsuperscript{22-25} Heavy metal removal involves mobilizing and eliminating the metal and this is often best done after thyroid function has been optimized. The organs involved in the elimination of the metal tend to function more efficiently when thyroid metabolism is intact. It is also essential to avoid environmental exposures to heavy metals.

**Zinc and B\textsubscript{6} Deficiency in Schizophrenia**

Zinc and iron are the most concentrated metals in the human brain. Zinc is important to several biochemical pathways as over 200 enzymes are zinc dependent. Zinc deficiency is very common in schizophrenia.\textsuperscript{7-9} Insufficient levels of zinc are also associated with depression, dementia, mental retardation, learning disability, lethargy and apathy.\textsuperscript{26} Zinc is essential for the synthesis of serotonin and melatonin.\textsuperscript{20} It is crucial to brain development because it plays a major role in protein synthesis.\textsuperscript{20,26} In the brain, zinc lowers excitability by moderating NMDA receptor release of excitatory glutamate. Zinc is involved in the synthesis of inhibitory GABA by the modulation of glutamate decarboxylase activity. Among the zinc-dependant proteins are metallothionein which is essential for heavy metal regulation and zinc bioavailability. The
synthesis of Zn-thionein and CuZnSOD are essential in preventing oxidative damage. Zinc protects against fatty-acid peroxidation which destroys neuron structure and function. Zinc is involved in neuronal plasma membrane structure and functioning and, may play a key role in blood-brain-barrier integrity. Zinc is involved in storing biogenic amines in synaptic vesicles and, in axonal transport. The biogenic amine histamine regulates nucleus accumbens activity, which is responsible for filtering sensory information and communicating with the amygdala, ventral tegmentum, and hypothalamus. In the limbic system, zinc is involved in the metabolism of emotional regulation. In the hypophysis and hypothalamus, zinc is involved in hormonal metabolism.

Vitamin B$_6$ (pyridoxine) is involved in the decarboxylation of tyrosine, tryptophan, and histidine into the neurotransmitters norepinephrine, serotonin, and histamine respectively. B$_6$ deficiencies are associated with schizophrenia, depression and behaviour disorders. It is a cofactor in homocysteine re-methylation, with just a 20mg dose. It has demonstrated usefulness in controlling neuroleptic-induced akathisia and drug-induced movement disorders. B$_6$ is essential for the synthesis of antioxidants such as metallothionein, glutathione, and CoQ$_{10}$ which help prevent neuronal oxidative stress. B$_6$ (and zinc) are involved in the synthesis of glutamic acid decarboxylase (GAD) which blocks excitotoxicity with eventual secondary oxidative damage. B$_6$ is also essential for glutathione peroxidase and glutathione reductase which are helpful in preventing mitochondrial decay.

The major neurotransmitters of the brain are derived from protein building-blocks and precisely assembled according to messenger RNA (mRNA) transcription of neuronal DNA templates. Brain tissue samples of schizophrenics have been assessed with high-dimensional biology and found to be compromised in basic mRNA transcription and protein synthesis. These perturbations influence an array of neuronal changes in the schizophrenic brain among which are neurotransmitter synthesis and mitochondrial functioning. Oxidative stress can cause these perturbations and the ensuing changes in neuronal structure and function may be integral in understanding schizophrenic pathophysiology.

It is interesting to note here that zinc and vitamin B$_6$ together are needed by the body as co-factors for neurotransmitter synthesis; zinc is needed for transcription and B$_6$ is needed for transamination. Previous investigators have described B$_6$ and zinc depletion in the context of pyrolluria. In this metabolic syndrome, B$_6$ and zinc interact with 2,4-dimethyl-3-ethylpyrrole and are readily excreted.

**Hypoadrenia in Schizophrenia**

Thyroid and adrenal function are compromised in many schizophrenics. Thyroid and adrenal function are pivotal endocrine glands. Many symptoms common to adrenal dysfunction are seen in thyroid dysfunction and vice versa. The adrenal works in concert with the thyroid gland and often both glands need to be supported together.

Hypothalamic-Pituitary-Adrenal axis dysregulation is integrally associated with schizophrenia. The adrenal glands are involved in stress response, sugar metabolism, electrolyte balance, peripheral epinephrine synthesis, blood pressure regulation, and sex hormone metabolism. Many schizophrenics who are heavy coffee drinkers have low adrenal function. Low adrenal symptoms include sluggishness on waking, stress intolerance, lack of enjoyment, post-traumatic stress, addiction, dizziness, low blood pressure, fluctuant body temperature, insomnia at 4am, immune compromise, hypoglycemia,
dermatitis, PMS, phobia and poor libido. Schizophrenics can be warm at times and at other times cold with trouble adapting to daily temperature extremes. Fluctuant body temperatures and heat intolerance are a sign of low adrenal function which often accompanies low thyroid function. Adrenal symptoms are a good indicator of adrenal status. In some cases, saliva testing is useful to assess the adrenal hormones DHEA and cortisol. Cortisol is part of the stress response but elevated cortisol disturbs mental function. Cortisol levels are commonly elevated in schizophrenics and depressives. Adaptogens and supplements can be used effectively to support adrenal function without elevating cortisol.

Hypothyroidism in Schizophrenia

Active thyroid hormones are responsible for enabling cells, at the DNA level, to maintain their metabolic rate. Thyroid hormones also maintain oxygen availability in the brain and elsewhere. With healthy thyroid hormone function, our cells produce energy and complete their tasks efficiently. When tissue cells including neurons have energy, they work efficiently. When thyroid function is low, cells remain in a state of hypofunction. Hypofunctioning cells work slowly and produce minimal energy. Consequently, fewer enzymatic reactions occur, cells don’t give off heat and core body temperature decreases. Intolerance to cold is a typical complaint in low thyroid function. When body temperature is insufficient, enzymatic reactions do not occur as readily, yet these reactions are needed throughout the body for, among other things, neurotransmitter synthesis. It is not uncommon to have schizophrenics report that they feel warm despite having low average body temperature.

Low thyroid symptoms are seen often in psychosis. In treatment-refractory depression, psychiatric ‘thyroid augmentation’ treatment is frequently applied. The most obvious low thyroid symptoms include impaired cognition, easy weight gain, fatigue, pain, headache, irritability, anxiety, panic, PMS, depression, poor memory, poor concentration, insomnia, constipation, indigestion, hair loss, high cholesterol and frequent infection. The digestive tract of a low thyroid patient has poor motility and slow stool transit which results in constipation and inefficient nutrient absorption. In low thyroid patients, core body temperatures are often so low that digestive enzymes do not reach their reaction threshold. Patients with varied non-specific complaints often have low thyroid function.

Classical hypothyroidism, occurring in a small percentage of schizophrenics, is a problem with the inability to produce adequate thyroid hormone. In classical “conventional” hypothyroidism, blood tests show low output of thyroid hormone T4 with elevated thyroid stimulating hormone (TSH) levels. Immune involvement as in Hashimoto’s thyroiditis is usually seen in 80% of classic hypothyroid cases. Othman et al. assessed a sample of 249 chronic schizophrenics and reported a prevalence of thyroid antibodies in 20% of cases. Many blood thyroid imbalances are found to correlate with the degree of symptom presentation, as for example, in acute psychotic episodes.

The reliance on thyroid blood tests in schizophrenia leads practitioners astray because a large portion of schizophrenics are euthyroid with “normal” blood test measures but, paradoxically, have a low core body temperature and low thyroid symptoms (fatigue, psychosis, depression, etc). There is no accepted diagnostic agreement on this physiological state, however Wilson’s Temperature Syndrome (WTS) has emerged as a condition that meets this criteria. WTS factors in the possibility of inefficient peripheral conversion of T4 to active T3 despite
having adequate circulating thyroid hormone T4. In classic hypothyroidism and WTS, we can implement desiccated thyroid, sustained release T3 (T3-SR) and botanical medicine.

**Brain Hypothyroidism**

The brain is highly dependent on thyroid hormone for the regulation of dopamine, norepinephrine, and serotonin pathways. Brain hypothyroidism has been described by Hatterer et al. as a state that occurs when systemic T4 does not readily cross into the brain. Active thyroid hormone T3 is synthesized in the brain by brain type II 5'-deiodinase conversion of T4 to T3. Brain neurons therefore depend on a ready supply of T4. The choroid plexus of the brain produces transthyretin (TTR), a transport protein that binds T4 and transports it across the blood-cerebral spinal fluid barrier to the brain. Transthyretin is significantly downregulated in the cerebral spinal fluid (CSF) of schizophrenics versus healthy controls. This suggests that schizophrenics lack adequate amounts of T4 in the brain. Without adequate T4, brain cells remain hypo-metabolic and this may, among other things, reduce neurotransmitter synthesis and disrupt the regulation of dopamine, norepinephrine, and serotonin.

Huang et al. suggest that low CSF transthyretin may prove useful as a biomarker for early diagnosis of schizophrenia. Also of interest is the fact that lead has been linked to the reduction of CSF transthyretin in humans. Reduced CSF transthyretin is also seen in depression and suicidal propensity. Many schizophrenics and depressives relapse when thyroid function drops.

Peripheral blood thyroid levels can be normal in the context of brain hypothyroidism. T4 to T3 conversion by brain type II 5'-deiodinase can be inhibited by cortisol. This is important because cortisol levels are commonly elevated in schizophrenics, especially during stress. Cortisol is an adrenal stress hormone and, during stressful periods, we tend to conserve energy by shutting down thyroid hormone production.

**Anti-thyroidal Adrenochrome**

Adrenochrome is a quinone and many molecules in this class are anti-thyroidal. In schizophrenia, a ready supply of oxidized adrenaline may account for thyroid compromise. Adrenochrome has the ability to induce oxidative stress and functional changes in thyroid tissue and peripheral metabolism. It is not known to what degree adrenochrome damages the thyroid gland. Skoliarova suggests that functional changes can be inferred from the structural “deterioration” of the thyroid and hypophysis of chronic schizophrenics autopsied 20 minutes to five hours post-mortem.

**Thyroid Treatment**

There are some remarkable studies reporting the outstanding efficacy of thyroid therapy in acute and chronic schizophrenia. A study by Danziger reported in 1958, showed that 100 days of optimally dosed desiccated thyroid or thyroxine with B-complex lead to the full recovery of 54 (45%) of 80 schizophrenics. Twenty of the 80 patients were given thyroid therapy alone while 60 of the 80 patients were given thyroid plus ECT therapy. Fifteen (75%) of the 20 patients given thyroid therapy recovered fully and, 39 (65%) of the 60 patients given thyroid therapy plus ECT recovered fully. Of the 15; two were sick for 60 or more months, two were sick 24-59.9 months, three were sick 12-23.9 months, two were sick 12-23.9 months, and six were sick less than 6 months. Of the 39; six were sick for 60 or more months, five were sick 24-59.9 months, five were sick 12-23.9 months, six were sick 12-23.9 months, and 17 were
sick less than six months. After discharge, the incidence of relapse was very small with a maintenance treatment that kept the basal metabolic rate (BMR) in check. Full recovery was defined appropriately; that is, being “symptom-free, returning to a former place in society/occupation and accepted as well by family, friends and co-workers.” The prognosis of the 80 patients at the onset of the study was “generally unpromising” as they were treatment refractory to ECT, psychoanalysis, and psychotherapy (all were neuroleptic naïve).

Many of the 80 schizophrenic patients reported by Danziger required high doses of desiccated thyroid (128–1280 mg) or racemic thyroxine (1–9 mg). Of the 54 patients that recovered with thyroid therapy or thyroid plus ECT, only four required 640 mg or more of desiccated thyroid and, only two required up to 4mg of thyroxine. Such doses were probably required to combat adrenochrome’s anti-thyroid effects and, to make up for the lack of T4 transport from the CSF to the brain (“brain hypothyroidism”). Hoskins and others report on the tolerance of schizophrenics for even higher doses of desiccated thyroid than those used by Danziger.81,82 To enable good treatment outcome, the BMR is raised to a level that likely improves the function and production of respiratory enzymes in the cerebrum.83 In Danziger’s study, first-episode cases had the best response however, one third of the chronic cases (five plus years post-onset) experienced full recovery as well.

A double-blind efficacy study reported by Lochner et al. in 1963 used T3 (L-triiodothyronine) treatment in a six-week trial on 30 chronic male schizophrenics eight plus years post-onset.84 Typical tranquilizers prescribed at the time were discontinued in a wash-out period several weeks prior to treatment. Patients were included if they tolerated withdrawal without exhibiting aggressive behaviour. 15 subjects were randomly assigned to the thyroid group and another 15 subjects to the placebo control group. Red blood cell uptake of I$^{131}$-T3 was normal for all subjects at baseline; they were euthyroid according to blood tests. The treatment group received 50 mcg of T3 b.i.d. for one week, then 100 mcg b.i.d. (200 mcg per day) for six weeks.

In this short treatment period, seven of the 15 patients treated with T3 responded very well. They had improved motor activity, work performance, spontaneity, sociability and logical/relevant thinking. Some reported they were “more lively” and could “think better.” Mood improved and they showed interest in their environment. They showed improvements in executive functioning; some voiced “plans for the future” and wanted to visit relatives, return to work and resume family relationships outside of the hospital. Five of the 15 patients had some worsening. Two of these five patients were responsive and cooperative with generally better mood but, exhibited hallucinations and delusions that had been repressed and were tense, restless, and loquacious. Another two of these five patients became non-conversive and tense with masked facies and motor retardation. The last of these five patients became incoherent, irritable, and explosive with increased hallucinations, delusions, and activity. The remaining three of the 15 experienced no change. All schizophrenics returned to their previous state shortly after discontinuation of treatment. Lochner’s study was reproduced by Scheuing and Flach with the same cohort and, a consensus of results was determined.85 The results with T3 are impressive when you consider the short treatment duration, the chronicity of the cohort and, the failure to implement optimal dosing strategy. Doses of 200 mcg of T3 may have been too high for those...
patients that aggravated in the given six-week time-frame of the study. Conversely, 200 mcg may not have been a high enough dose for those schizophrenics that did not respond. To this author’s knowledge, the use of T3 in first-episode schizophrenia has not been fully investigated.

Hoffer also reports on 12 schizophrenic patients treated on nicotinic acid and optimally dosed desiccated thyroid. Of the 11 patients that completed the treatment, nine had benefited. Six of the nine were moving toward rapid recovery and had very much improved. The remaining three were improving consistent with increasing doses of desiccated thyroid. The average maintenance dose of desiccated thyroid was 300 mg per day.

As adrenochrome reducing nutrients, vitamin B₃ and C play a key role in reducing the oxidative stress on the thyroid gland. This thyroid link may explain in part, why vitamin B₃ and C yield such good success in treatment. As a final note on thyroid function, blood testing can help rule out the hyper-functioning state typical of Grave’s Disease. Grave’s, in its active phase, is a state of thyroid hyperfunction and botanicals are very useful in calming thyroid function and preventing surgery and irradiation. In low thyroid states, botanical interventions are very useful to help support and restore the thyroid gland and peripheral conversion.

**Overview**

Figure 1 (below) is a schematic of the key causative factors of schizophrenia. Modern research continually confirms that these factors are important to schizophrenic pathophysiology. This is why, in

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**Figure 1. Schizophrenia: Summary of Causative Factors.**
support of Dr. Hoffer’s original work, we now see down-regulated niacin receptors in the anterior cingulate cortex of schizophrenics.\textsuperscript{86} The list of assessments and treatments described herein are not exhaustive but represent the core considerations of optimal complementary treatment for schizophrenia. Orthomolecular treatment can be implemented safely as an adjunct to conventional psychiatric therapy. Schizophrenics treated with orthomolecular medicine experience positive changes. Response is based on the degree of severity and the duration of illness. We see schizophrenics who have been sick for a year or two who start responding within weeks. Schizophrenics sick over five years are less responsive initially but, improve with long term care. The pathological deterioration of brain tissue in schizophrenia should impel us to use orthomolecular treatment to keep oxidative stress at bay. The necessity of early screening and early intervention is important for both orthomolecular and conventional psychiatric treatment. In first-episode cases, a cocktail of desiccated thyroid (or T3-SR), vitamin B\textsubscript{3}, and vitamin C may the best early detection-intervention program ever developed. Complementary treatments for schizophrenia have been in the workings since the 1930s. A large outcome study is needed to compare the efficacy of orthomolecular treatment versus psychiatric medication. Orthomolecular treatment should play a key role in mainstream mental health care and schizophrenic patients/families constantly express their desire to see that happen.\textsuperscript{87,88} Conventional mental health costs are exorbitant in comparison to orthomolecular treatment costs and the potential for improved quality of life should empower practitioners to be steadfast in addressing core underlying biochemistry.\textsuperscript{89}

References
Orthomolecular Treatment For Schizophrenia: A Review (Part Two)


45. Candina R, Giustina G: Addison’s disease and...
68. Hidal JT, Kaplan MM: Inhibition of thyroxine 5'-deiodination type II in cultured human placental cells by cortisol, insulin, 3',5'-cyclic adenosine monophosphate, and butyrate. Metabolism, 1988; 37(7): 664-668.
73. Nauman A, Kamin´ski T, Herbaczyn´ska-Cedro K: In vivo and in vitro effects of adrenaline
on conversion of thyroxine to triiodothyronine and to reverse-triiodothyronine in dog liver and heart. Eur J Clin Invest, 1980(Jun); 10(3): 189-192.


79. Skoliarova NA: Morphology of the endocrine system in schizophrenia according to early autopsy findings (the hypophyseal-thyroid system). Zh Nevropatol Psikhiatr Im S S Kor-sakova, 1975; 75(7): 1045-53. (abstract only)


Lime sherbet makes me crazy. That is not a figure of speech, merely implying that I really like eating it. Rather, it means that eating it literally makes me nuts. I still recall, as a young man, having a double cone of the chartreuse-green stuff. About 30 minutes later, I was, to use my grandmother’s expression, fit to be tied: I was agitated, irritable, angry. I could barely control my behavior, and certainly could not control how I felt. When the haze cleared, I wondered what the heck happened.

It finally dawned on me that it might be my reaction to the load of sugar and artificial color that I had just ingested. As Dr. Lendon Smith said, if you crave a food, it is probably bad for you. To this day, I am cautious about consuming sugar, and I do not eat artificially colored foods of any kind.

It isn’t just me, and it isn’t just anecdotal. Long dismissed by medical authorities, sugar, food colorings, and other all-too-common food additives do indeed adversely affect mood. In June 2004, Archives of Disease in Childhood reported a study, involving 277 preschool children conducted by the UK’s Southampton General Hospital. The findings? Artificial food colorings and other additives increased hyperactive behavior. Said commentator Will Boggs, M.D., “Children’s hyperactivity fell after withdrawal of food additives from the children’s diets (and) there was an increase in hyperactivity when food additives were re-introduced.” If you have ever taught school the day after Halloween, as I have, you already know this.

There is not a teacher, a parent, or for that matter, a human being that would not benefit from reading Jack Challem’s The Food-Mood Solution. As the title promises, the book explains exactly how moods go so swiftly south when sugar intake is high, and nutrient intake is low. With personal-use checklists, succinct case stories, plain language, clear organization, and an exceptionally reader-friendly writing style, Challem presents a plan that anyone can follow, and perhaps everyone should. “The world is a meaner, angrier, and more anxious place than it was just a few years ago,” he writes. And without blaming all societal ills on malnutrition, Challem offers real help for real people: keep your blood sugar from crashing by avoiding simple carbs, taking your vitamins, and eating whole foods.

By Chapter Three, Challem is discussing neurotransmitters and the “neuronutrients” that make them work, and in Chapter Four he presents and lists nutritional supplements as the “first step” to improved mood. Orthomolecular quantities are recommended, along with the author’s welcome candor about prevailing anti-vitamin mythology: “Ignore statements warning that the body cannot use more than 200 mg of vitamin C a daily,” he writes, correctly terming that a “paltry recommendation.”

Then, Challem says, there are three further steps: Eat good-mood foods; exercise; and make tactical lifestyle changes to reduce stress. Good, practical, worth-the-cost-of-the-book-and-then-some advice. And there is still more to follow. Chapter Eight addresses anger, aggressiveness and violence, and Chapter Nine is on anxiety, panic attacks and obsessive compulsive behavior. The next chapters discuss ADHD, overweight, depression, bipolar disorder, and alcohol and drug abuse. To bring all these topics in at under 300 pages requires expert writing, something we have come to expect from this author.
This book does not disappoint. *The Food-Mood Solution* contains numerous “Quick Tip” boxes and some helpful diagrams. Additional visuals would be a welcome addition, particularly the inclusion of main-point summary tables. Meal plans, recipes, supporting references, a list of available resources, and a thorough index are provided.

Lendon Smith often said that if your children are cranky, give them something to eat. Extending this point, comedian and natural health advocate Dick Gregory asked, “Are you going to have food, or just something to eat?” Big difference. *The Food-Mood Solution* proves the point brilliantly.

—Reviewed by Andrew W. Saul

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**Obesity: Why Are Men Getting Pregnant?**

by Alexander G. Schauss

Basic Health Publications, 2006

Paperback, 254 pages.

As a boy, my vision of the year 2008 was of personal jets, light-speed rocket ships and Star-Trek transporters. Surely the new millennium would be a magically mobile world evolved far, far beyond the rubber-footed, gasoline-slurping automotive dinosaurs which still dominate our paved landscape. I also remember wondering if, like the intergalactic astronauts of my daydreams, we would do away with eating altogether and live entirely on efficient supplement tablets: a diet of just the best, the essential nutrients. Predictably, my parents chuckled at that, while giving my brothers and me a multivitamin every day.

So here we are today, doing exactly the opposite. As a population, we are eating pretty much everything except nutrients. But who would want to give up eating junk food? Problem is, eating fats and carbos is so enjoyable on so many levels that it is sure to be with us long after all petrol has perished. Eating right remains our civilization’s great unattainable health goal. Should we eat right? Certainly. Do we know what that means? Of course we do. We know which foods are healthy as well as we know the names of our children.

But we aren’t doing it. People are fatter than ever, and, as Alexander Schauss’ book says, “That potbelly can kill you.” It’s true, and right out the door in his introductory chapter, Schauss shows you why fat men are in real trouble. Chapters One and Two discuss the causes and risks of obesity. The good news begins in Chapter Three, a practical guide to dietary change, which includes a comparison of popular weight-loss approaches. The more technical Chapter Four discusses fat distribution, hormones, neuropeptides, lipogenesis and insulin resistance. Various drug and surgical interventions are summarized in Chapter Five.

Perhaps it is in Chapters Six and Seven, on the safety and effectiveness of dietary supplements for weight loss, that the author makes some of his most intriguing points. “Not a single medical school teaches a course on dietary supplements,” Schauss writes. “I am dismayed by how many practitioners base what they know on what they have read in a newspaper, saw on television, or heard on the radio.” After first discussing safety (a good idea), he highlights seven weight-loss supplements as particularly beneficial: chitosan, chromium, DHEA, digestive enzymes, *Garcinia cambogia*, green tea, and melatonin. Chapter Eight presents many more, including vitamins, that may probably or possibly be useful. Chapter Nine covers supplements for depression.

Lest people presume that pill-popping prevents potbellies, Chapter Ten is a really fine exercise guide. Did you know that hiking downhill lowers blood sugar, and hiking uphill lowers cholesterol?
That people who fidget a lot weigh less than those who don’t? Strengthening the *transversus abdominus* muscles, the author writes, “can serve as a natural corset to hold in your gut.” Odd the way words work sometimes: you can get rid of a beer-gut with a six-pack.

Chapters 11 and 12 offer steps to reduce stress, and how to get started losing weight right away. The book’s graphic illustrations are well done, and still more visuals would be a welcome addition. There is a very good index, and over 25 pages of scientific references.

Almost all of *Obesity: Why Are Men Getting Pregnant?* is applicable to both sexes, yet I value its premise that men need to get their body-shape act together. Truth to be told, I watch my weight at least as much due to vanity as I do for health. Hardly a surprise. After all, women, it has been said, are in a beauty contest from the day they are born. But the stakes are considerably higher for us guys: men die sooner than women do from cardiovascular disease. In fact, men die sooner than women. Overweight is not the only reason, but it is a major one. And, it is a factor we have the power to do something about starting today. Now I am going for a walk.

—Reviewed by Andrew W. Saul
The 2008 Orthomolecular Medicine Hall of Fame

The following is excerpted from the introduction to the presentations by Andrew W. Saul, Master of Ceremonies. For full text please see www.doctoryourself.com/2008HOF.html

Many years back, my 6th grade teacher taught me to debate fairly, by the rules and by the book. The facts were the issue, she said, and they would speak for themselves; whether or not people liked your position wasn’t crucial.

On this, she is wrong. Facts simply do not speak for themselves. As Dr. Abram Hoffer has said, “No amount of evidence can persuade someone who is not listening.” Dr. Hoffer has also frequently stated that we need a new paradigm of nutrition, one where “nutrition as treatment” replaces the old “nutrition as prevention” paradigm.

Ignoring therapeutic nutrition carries a high price: The United States now spends over two trillion ($2,000,000,000,000;) per year on disease care, and yet has well over a million people die annually just from cardiovascular disease and cancer.

Now, however, the public and the professions are hearing a lot more about orthomolecular medicine. Google Scholar indexes the *Journal of Orthomolecular Medicine*. Indeed, any Internet search engine can find the new, free, online JOM archives at orthomolecular.org/library/jom.


But not the U.S. National Library of Medicine (MEDLINE). In May 2007, NLM wrote, “While we hold the Journal of Orthomolecular Medicine in our print collection here at NLM, it is not currently indexed for MEDLINE/PubMed.” One might well wonder why NLM, a taxpayer-supported public library, physically archives a journal, and yet refuses to index it. JOM Associate Editor Harold Foster has wryly observed that “Medline treats the Journal like a dirty magazine: to be read privately, but the fact kept hidden from the public.

The Orthomolecular Medicine News Service has been very active since 2005 in increasing public awareness. OMNS has now issued a total of 39 press releases emphasizing the positive side, the safety and effectiveness of nutritional medicine.

All this must be done, and can be done, due to the very important contributions by the scientists whose work we are pleased to honor tonight.

**Inductees for 2008**

**Joseph Goldberger, MD (1874–1929)**

Joseph Goldberger was born in 1874 and studied medicine at Bellevue Hospital Medical School in New York, graduating with honors in 1895. After an internship at Bellevue Hospital College, he engaged in private practice for two years and then joined the Public Health Service Corps in 1899. During routine work as a quarantine officer on Ellis Island, Goldberger rapidly acquired a reputation for outstanding investigative studies of various infectious
diseases, including yellow fever, dengue fever, and typhus. Goldberger devoted the latter part of his career to studying pellagra. After quickly contradicting the contemporary general belief that pellagra was an infectious disease, he spent the last 15 years of his life trying to prove that its cause was a dietary deficiency. During the first half of the 20th century, an epidemic of pellagra produced roughly 3 million cases in the United States, about 100,000 of which were fatal. (From: Elmore JG, Feinstein AR. Joseph Goldberger: an unsung hero of American clinical epidemiology. Ann Intern Med, 1994 Sept 1;121(5): 372-5.)

Abram Hoffer adds: “In the early 1940s, the United States government mandated the addition of niacinamide to flour. This eradicated the terrible pandemic of pellagra in just two years, and ought to be recognized as the most successful public health measure for the elimination of a major disease in psychiatry, the pellagra psychoses. The reaction of contemporary physicians was predictable. Indeed, at the time, Canada rejected the idea and declared the addition of vitamins to flour to be an adulteration. The United States has long been the leading nation in nutrition research.”

Knowledge comes at a cost: Goldberger had yellow fever, dengue, and very nearly died of typhus. The US National Institutes of Health says he “stepped on Southern pride when he linked the poverty of Southern sharecroppers, tenant farmers, and mill workers to the deficient diet that caused pellagra.” (http://history.nih.gov/exhibits/goldberger/index.html)

In the end, Goldberger was nominated for the Nobel Prize. Had he not died earlier in the year, he might well have shared it in 1929 with vitamin researchers Christiaan Eijkman and Frederick G. Hopkins.


Adelle Davis, MSc (1904–1974)

Adelle Davis, one of America’s best known nutritionists, was born Daisie Adelle Davis and raised on a farm in Lizton, Indiana. She attended Purdue University from 1923 to 1925, and received her bachelor’s degree in dietetics from the University of California at Berkeley in 1927. Trained in hospital dietetics at Bellevue and Fordham Hospitals in New York City, Davis served as a nutritionist for the New York City public schools until 1931. After several years of private practice as a consulting nutritionist, she earned her M.S. in biochemistry from the University of Southern California in 1939. She continued to see patients in southern California, many thousands of which were referred to her by physicians.
The Adelle Davis Foundation (adelle-davis.org) comments that “she repeatedly stated that the body does best when provided with all of the known nutrients, as well as fresh food sources for obtaining nutrients yet to be discovered by science. Knowing the amounts of nutrients that the body requires under given conditions, one can make educated decisions...Without knowing the research, one cannot judge what amounts are necessary to avoid vitamin deficiencies. Deficiencies in vitamins, minerals, and other nutrients can cause illness that is reversed when the nutrients are added to the diet.”

Adelle Davis wrote four bestselling books, starting with Let’s Cook It Right in 1947. Let’s Have Healthy Children (1951), Let’s Eat Right to Keep Fit (1954), and Let’s Get Well (1965) would follow, each later revised and updated. She was a popular speaker and frequent guest on television, beginning in 1947 and continuing for over 25 years, including a number of appearances on the Tonight Show with Johnny Carson.

Linus Pauling considered Adelle Davis to be “a pioneer in the health movement. She was essentially correct in almost everything she said.” In 1990, Natural Food and Farming magazine wrote, “Today’s research shows that she was indeed ahead of her time.”

Carlton Fredericks, PhD (1910–1987)

Carlton Fredericks, born Harold Carlton Caplan, grew up in the Flatbush section of Brooklyn. He earned his bachelor’s degree at the University of Alabama in 1931, and received a master’s degree in 1949 and a PhD in 1955, both in Public Health Education, and both from New York University. He wrote over twenty books, lectured widely, and was associate professor of public health at Fairleigh Dickinson University.

Fredericks became famous, and in some circles infamous, for his pioneering use of the media to educate people about vitamin and nutrition therapy. On the radio for nearly half a century, his most famous thirty years began in 1957 at New York City station WOR. Fredericks' call-in “Design for Living” program, broadcast six days a week and syndicated nationally, resulted in literally millions of letters to a man whom many considered to be “America’s Foremost Nutritionist.” KABC Los Angeles presented his program “Living Should Be Fun” saying that “Dr. Fredericks presents interviews with doctors and nutritionists (and) examines the fact or superstition in certain nutrition beliefs.” In one such 1978 interview, he interviewed orthomolecular niacinamide pioneer Dr. William Kaufman.

Dr. Fredericks, a colleague of Drs. Robert Atkins and Linus Pauling, was heavily
Robert Cathcart III, MD (1932–2007)

Robert Cathcart’s observations on clinical use of ascorbic acid drew worldwide renown, along with the respect of Linus Pauling. A native of Texas, Bob came to Northern California as a child and spent most of his life in the Bay Area. He earned his medical degree from the University of California in San Francisco in 1961, then completed his internship and residency at Stanford Hospital. Bob was an instructor in orthopedic surgery at Stanford after his residency. The “Cathcart Prosthesis” has been implanted in over 100,000 hips.

Bob became interested in vitamin C when he read Linus Pauling’s Vitamin C and the Common Cold, and he began using it for his own allergies and his patients’ viral infections. He thought about a common side effect of high-dose ascorbate, namely diarrhea, in a new way. He observed that a person’s tolerance for the vitamin increased considerably in the presence of viral illness, seemingly in proportion to the severity of the illness. A person who ordinarily develops diarrhea from, say, a 12-gram dose of ascorbate, might be able to tolerate upwards of 100 grams when ill with a cold or flu. Bob found that titration of vitamin C dosage to bowel tolerance permitted quicker resolution of an illness.

Bob treated tens of thousands of patients with vitamin C megadoses. He was a popular lecturer at medical meetings, where he freely shared his findings with his colleagues. However, he was not well published. Like Linus Pauling himself, Cathcart encountered rejection and even scorn at the hands of scientific and medical journal editors. JOM is proud to be one of the few platforms to have brought Bob’s work to the attention of the world’s healing professions.

Bob Cathcart received the Linus Pauling Award from the Society for Orthomolecular Health Medicine in 2002. He leaves a reminder for all who would do science: progress and success rest more on dispassionate observation and creative thinking than on all the gee-whiz technology mankind has ever come up with. (From Richard Huemer’s article, “In Memoriam: Robert Fulton Cathcart III, M.D.” JOM, 2007, 22:4).

Richard Kunin, MD (b. 1932)

Educated at the University of Minnesota, Dr. Kunin received his MD degree in 1955. Following psychiatric residency training at New York Hospital, which he completed in 1959, he served for two years in the United States Army Medical Corps. Dr. Kunin has been in private practice since 1963, now in San Francisco.

Inspired by Dr. Linus Pauling’s work with vitamin C and antioxidants in orthomolecular medicine, his 1973 discovery of manganese as a cure for drug-induced dyskinesia (muscle-movement disorder caused by drug therapy) was the first orthomolecular research to verify the efficacy of mineral therapy for a disease (other than simple deficiency). His studies on the effects of niacin (1975) were the first to identify prostaglandins in the niacin flush and aspirin as an antidote.

He co-founded the Orthomolecular
Medical Society with Dr. Michael Lesser and Dr. Linus Pauling in 1976, and served as its President from 1980-82. Dr. Kunin’s clinical research led to the “Orthocarbohydrate Diet”, the first diet plan based on individualized carbohydrate-protein-fat effects on mood, energy, and weight. The “Listen To Your Body Diet,” popularized in his best-selling books Mega Nutrition (1980) and Mega Nutrition for Women (1983) remains one of the most user friendly, safe and effective diet-energy plans.

In 1986, Dr. Kunin began a 12-year stint as a columnist for the San Francisco New Fillmore. His column, “Putting Nutrition First,” was a big hit with its readers.

He achieved the first measurement of EPA in snake oil in 1989, substantiating its anti-inflammatory benefits (published in JOM, 1989, Vol 4, no 3). Dr. Kunin demonstrated that snake oil is not quackery after all!

In 1994, he founded the Society for Orthomolecular Health Medicine (OHM) in San Francisco, and has organized its annual scientific meetings for 14 years. In the same year, Dr. Kunin became the first Interim President of the International Society for Orthomolecular Medicine. Dr. Kunin is also director of research of Ola Loa Products, leaders in powdered nutrition supplements.

Dr. Kunin also serves on the Board of Governors of the National Health Federation and has been on the Editorial Review Board of the Journal of Orthomolecular Medicine, since 1982.

Michael Lesser, MD (b. 1939)

Michael Lesser received his MD from Cornell University in 1964 and has maintained a private practice since 1971 in Berkeley, California. He became a member of the Academy of Orthomolecular Psychiatry in 1972 and served as Vice President from 1976-1986. During the same period he served on the Board of Trustees for the Huxley Institute for Biomedical Research.

On numerous occasions since 1972, Dr. Lesser has served as an expert witness in Psychiatry and Orthomolecular Medicine in criminal and civil cases before municipal, state and federal courts in California and Arizona.

Along with ten other doctors, Dr. Lesser founded the Orthomolecular Medical Society in San Diego, CA, in 1975. He served as its first President (1975-1979), with Linus Pauling, PhD, as Honorary President; Richard Kunin, MD, Vice President.

Dr. Lesser gave testimony before California State Legislature leading to passage of Orthomolecular Medicine Bills in 1976 and 1977. He also gave testimony before United States Select Senate Committee on Nutrition and Human Needs, “Diet Related To Killer Diseases, V: Nutrition and Mental Health,” in Washington DC, June 22, 1977. An excerpt of his testimony was broadcast on CBS and NBC News that night and he appeared as a guest on ABC’s Good Morning America, June 23, 1977.

In 1997 he founded Nutritional Medicine, a communications company that sponsors conferences on nutrition and vitamin therapy. With Dr. Kaneko of Japan he organized the OrthoMolecular Nutrition Laboratory Symposium in New York, October 1997.

Dr. Lesser’s books include Nutrition and Vitamin Therapy (1980) which sold 350,000 copies; Fat and The Killer Diseases (1991); and The Brain Chemistry Diet (2002) in which he identifies six primary psychological types—each type evinces certain strengths when health is optimal, and suffers from specific psychiatric vulnerabilities when imbalances occur. His dietary and supplement recommendations are predicated on these differences.

He has published over 50 papers and lectures on orthomolecular medicine and psychiatry and has served on the Editorial Review board for the Journal of Orthomolecular Medicine.
2008 Orthomolecular Doctor of the Year
James A. Jackson, Ph.D.

Dr. James A. Jackson received his Ph.D. from Auburn University School of Veterinary Medicine in Physiology, Pharmacology and Biochemistry. His career includes academia, industry and clinical research. He taught at the University of Kentucky and served as a Department Chair and Associate Dean of the Graduate School, Wichita State University. He was in training and product development for the Ames Division, Miles Laboratories.

He made 13 trips to China as a consultant for modernizing clinical laboratories. Dr. Jackson worked on the initial research of intravenous vitamin C and cancer with Dr. Hugh Riordan. He has authored or co-authored 130 publications and is the Laboratory Director and Senior Research Consultant of the Bio-Center Laboratory. Over 50 “Cases for the Centre” have been published in the Journal since 1992, under lead author, Jim Jackson.

The Linus Pauling Event was organized in Schloss Anholt in Germany, April 19 and 20, exactly 40 years after the publication of "Orthomolecular Psychiatry" by Linus Pauling, in Science, introducing and defining the term “orthomolecular.” The event was sponsored by the Ortho Fund, a Dutch non-profit foundation, founded by Elsieden de Groot and Gert Schuitemaker.

From seven countries, a select group of 16 scientists and doctors who are dedicated to Linus Pauling, attended. The participants agreed upon the following objective: To get orthomolecular medicine widely accepted in society. For the complete report please see: www.orthomed.org/news/news.html
ISOM Meeting Report: Vancouver, May 2, 2008

For full report see www.orthomed.org/news/news.html

During the 37th Orthomolecular Medicine Today Conference, a meeting of the International Society for Orthomolecular Medicine was organized. About 60 persons were present from 13 countries around the world.

The meeting opened with a welcome from the President of ISOM, Gert Schuitemaker, followed by a short archival video featuring Linus Pauling, recorded in October 1993 during a satellite connection between the Linus Pauling Institute in Palo Alto and the conference room in the Dutch city, Utrecht. Schuitemaker outlined that the main activity of the ISOM is enhancing mutual communication. For this purpose the forum website www.isom.eu is functioning with more than 150 participants. Besides sharing clinical information, the forum “alert wire” functions to warn each other regarding negative scientific studies, so the individual participants are aware of such a study and can react adequately in his own country, e.g. to the press. A more tight organization on an international level is quite difficult, since there have to be checks and controls and these are hardly possible on a worldwide basis, i.e. for the quality of practice or for the kind of license (MD, practitioner, scientist).

After this introduction, the representatives from the different countries gave brief presentations about the acceptance of orthomolecular medicine and availability of supplements in their country:

The Netherlands – Dr. G. Schuitemaker
Finland – Dr. K. Munsterhjelm.
Sweden – Prof. K. Cederwal
New Zealand – Dr. D. Proverbs
Canada – Steven Carter, Dr. Jon Prousky
Switzerland – Dr. Catherine Gontard
Korea – Dr. Sung Ho Park
Japan – Dr. O. Misakami, Ken Kitahara
Mexico – Dr. Roberto Ortiz Gonzalez
Spain – Dr. Marja van Engelen
United Kingdom – Dr. Damien Downing
Philippines – Dr. Jaime C. Cua
USA – Richard Kunin

Legal Affairs Around the World

Damien Downing (UK) gave a presentation about legal affairs around the world with the emphasis on the role of the Codex Alimentarius. Established in 1963 by FAO and WHO, Codex’s stated purpose is to protect the health of consumers, ensure fair trade practices in the food trade and to promote coordination of all food standards work undertaken by international governmental and non-governmental organizations. It is comprised of many committees, including a committee on Nutrition and Foods for Special Dietary Uses. There are eight steps involved in the lengthy Codex process, which moves so slowly that people are generally not aware of what’s going on. Examples are the introduction of genetically modified foods, terminator seeds, and genetically modified food animals on the way. The EU to date refuses GM foods and has to pay $150 million per year for their refusal. Through Codex organic foods have been debased, food and dietary supplements limited to very low maximum permitted levels on the basis of scientifically flawed risk assessment methods; vitamins above determined doses will be classified as drugs. The Food Supplements Directive is providing the template for supplements for the world, but these directives are set by Codex. Unless people take political incentive, the trend will continue; with the one country/one vote Codex voting system, the EU could outvote the rest of the world.

In Canada Bill C-51 opens the door to allowing Codex regulations to deny access
to supplements. To read the letter sent to health minister Tony Clement, Canada’s Health Minister, see www.orthomed.org/news/news.html

In Europe the Alliance for Natural Health challenged the food supplement directive. This organization stresses the need to be aware, think free, spread the word, lobby, for dialogue not polarization, to contribute money, and to participate in the political process.

Evidence Based Medicine

Gert Schuitemaker indicates that many discussions about the value of orthomolecular medicine are stopped by the argument that this type of medicine is not evidence based (EBM). There is a big misunderstanding about EBM. The term was coined in 1992 by prof. David Sackett, father of clinical epidemiology. According to Sackett, EBM requires the integration of the best research evidence with our clinical expertise and our patient’s unique values and circumstances. However, EBM is usually considered to be solely the first point instead of the integration of these four points:

1. By best research evidence we mean valid and clinically relevant research, often from the basic sciences of medicine, but especially from patient-centered clinical research into the accuracy of diagnostic tests (including the clinical examination), the power of prognostic markers, and the efficacy and safety of therapeutic, rehabilitative, and preventive regimens. New evidence from clinical research both invalidates previously accepted diagnostic tests and treatments and replaces them with new ones that are more accurate, more efficacious, and safer.

2. By clinical expertise we mean the ability to use our clinical skills and past experience to rapidly identify each patient’s unique health state and diagnosis, their individual risks and benefits of potential interventions, and their personal circumstances and expectations.

3. By patient values we mean the unique preferences, concerns and expectations each patient brings to a clinical encounter and which must be integrated into clinical decisions if they are to serve the patient.

4. By patient circumstances we mean their individual clinical and the clinical setting.

The next ISOM meeting will be May 1, 2009, in Montreal, Canada.

–Gert Schuitemaker
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1. Evidence Based Medicine (3rd Edition) by SE Straus, WS Richardson, P Glasziou, R Brian Haynes (Turtleback April 29, 2005)
Correspondence

Why Put the Mentally Ill in Jail?

In 1970 less than 200,000 mentally ill patients wound up in prison in the United States. In 2002 about 1.3 million were incarcerated. A great many unfortunate citizens are getting a one way ticket to jail instead of being treated for their mental illness in hospitals.

In late 2006 a shortage of facilities for care of mental patients created a crisis which required the State of Florida to budget over $70 million for an expansion program. The State is spending $250 million yearly to provide 1,700 beds for inmates with mental illness according to a Florida Supreme Court sponsored study. According to Dr. Katharine Lyon, Director of Florida’s Mental Health Program Office, there is now secure capacity for 1,232 individuals and a forensic step-down capacity for 517 individuals. The National Alliance on Mental Health suggests that this money would be better spent on keeping the mentally ill out of jail rather than maintaining them in jail.

A couple of centuries ago it was not uncommon in the Western World for the mentally ill to be chained in dungeons and treated like wild animals. Since that time their treatment has had a tendency to be more humane and enlightened. However there does not seem to have been much consistency from one generation to the next. In America, treatments have varied from state to state as well as from time to time. Early last century most of our mental patients were housed in hospitals. Today a great many find themselves in jail.

The transition from hospital to jail started about the middle of last century after Thorazine was developed. This neuroleptic drug appeared to be a perfect solution to a difficult problem. It quickly turned even extremely violent patients into unresisting cooperators. It was welcomed with open arms by psychiatrists, hospital personnel and politicians. They were led to believe that housing the insane was no longer a problem. Mental patients were discharged from the hospitals. Many hospitals went out of business. Unfortunately the closed doors that had been opened turned into revolving doors. The supposedly cured patients did not do well. Many returned again and again for rehospitalization. One psychosis changed into another. Furthermore, the neuroleptic drugs caused nervous system changes and about 36% of patients who were given Thorazine developed Parkinson’s disease. There were lots of laws to break and soon more than 10% of the inhabitants of jails were mental patients.

Therapies included in “The Standards of Care for Psychiatrists” have been turning most of their patients into dependent wards of the state. Only about 10% of American psychiatric patients become fully effective taxpaying citizens. This is not acceptable. Something better is needed. Fortunately something better is available.

About 50 years ago, Abram Hoffer, Ph.D., M.D., the father of orthomolecular psychiatry, and Dr. Humphrey Osmond demonstrated, with a double blind study and long term follow up, that schizophrenic patients could be turned into Canadian taxpayers. They did this with conventional psychiatric treatment while changing the chemistry of their patient’s brains with orthomolecular therapy. Their hypothesis was that an abnormal conversion of adrenalin into adrenochrome caused mental illness. Dr. Hoffer’s training in biochemistry led him to conclude that vitamin B₃ might prevent this conversion. His years of successful experience with this protocol indicates that 75 to 85% cure rates are possible, with lowered requirements for hospitalization. Large doses of vitamin B₃ have helped his insane patients become sane–worked miracles beyond the range of psychiatric drugs. But if this is so good, why isn’t every psychiatrist using it?
In 1973 the American Psychiatric Association published a report which is said to have used lies and innuendos to discredit the Hoffer-Osmond experimental work and publications. It was very effective. Psychiatrists didn’t bother to investigate the original work or read the publications on orthomolecular medicine. As a result they have failed to take advantage of a remarkable advancement in the state of the medical arts which could have benefited millions of people and saved billions of dollars.

It should be noted that there is a precedent for using niacin and niacinamide, vitamin B₃, to cure mental patients. In the early 1900s about 10% of patients in some insane asylums were there because they had a disease called Pellagra. When they received 14 milligrams of niacin daily, they recovered their mental capabilities and were discharged as cured. Niacin added to flour and bread has kept many people out of mental hospitals since then (see Orthomolecular Medicine Hall of Fame inductee, Joseph Goldberger, p 109).

Considering the large potential savings, which appears to be achievable by inexpensive niacin supplementation, wouldn’t it be insane not to give it a try? Is it possible that our psychiatrists need to be reconditioned with education in nutrition in order to improve their effectiveness? Something needs to be done to improve their performance. It has been far from satisfactory over the last 50 years. In addition our politicians might want to consider mandating the addition of more niacin in bread. It is the basic food of the poor who are most subject to malnutrition. Dr. Hoffer believes that this would keep more people sane and effective and reduce the need for hospital beds.

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