

Orthomolecular medicine – History

Orthomolecular medicine and *Optimum nutrition* are nutritional health and medical approaches that are based upon the premise that many diseases and abnormalities result from varying biochemical and/or chemical needs specific to each individual. It holds that they can be prevented, treated, or sometimes cured by achieving optimum levels for that individual's body of various biochemicals which are natural to the body, either through diet or metabolism. It normally employs doses of vitamins, minerals, amino acids, trace elements, and essential fatty acids.

Orthomolecular medicine is practiced by few conventional medical practitioners. Orthomolecular treatments are instead more common in complementary and alternative medicine fields, increasingly being integrated into over the counter retail products, naturopathic medical textbooks and mainstream pharmaceuticals. The controversial field of orthomolecular psychiatry deals with the use of orthomolecular medicine to treat psychiatric problems.

The orthomolecular field is based on research in biochemistry, nutrition, medicine, and pharmaceuticals, which is interpreted in the light of the clinical experience of its practitioners. Orthomolecular medicine and optimum nutrition are based on the idea of individual variation in humans, with individual nutrient requirements varying widely with health, genetic and environmental influences. Aspects of orthomolecular therapy remain controversial among mainstream medical organizations and physicians, who consider many aspects to be lacking sufficient RCT based evidence. In contrast, orthomolecular proponents argue that many mainstream nutritional studies, both recent and historical, provide investigational and clinical support for their treatments and recommendations. They also argue that orthomolecular therapies are intrinsically less likely to cause dangerous side-effects or harm, since they utilize only chemicals that are normally present in the body.

Orthomolecular treatments typically have been experimentally or empirically introduced by physicians or researchers when conventional

medical treatments offered neither solution nor hope. Orthomolecular psychiatry began to be developed in the early 1950s by a group of biochemists and psychiatrists who identified a number of biochemical abnormalities that they thought were associated with mental illness and treated a number of mental disorders using high dosages of certain vitamins. Orthomolecular megavitamin therapies, such as with tocopherols and ascorbates, date back to the 1930s.

Frederick Klenner, (1907 – 1984) was an American medical researcher and doctor in general practice in Reidsville, North Carolina. From the 1940s on he experimented with the use of vitamin C mega dosage as a therapy for a wide range of illnesses, most notably polio. He authored 28 research papers during his career. He is considered one of the originators of orthomolecular medicine, but his work remains largely unacknowledged by established medicine.

In the late 1950's, Irwin Stone published his belief that scurvy was not a dietary disturbance, but a potentially fatal problem that had been misunderstood by nutritionists. Ascorbate was not a trace vitamin but was required in humans in large daily amounts. He produced four papers, between 1965 and 1967, describing the human requirement for ascorbate as genetic defect which he named hypoascorbemia.

The term 'orthomolecular' was first used by Linus Pauling in 1968 to express the "*idea of the right molecules in the right amounts*" within the context of psychiatry. Pauling subsequently defined '*orthomolecular medicine*' as "*the treatment of disease by the provision of the optimum molecular environment, especially the optimum concentrations of substances normally present in the human body*" or as "*the preservation of good health and the treatment of disease by varying the concentrations in the human body of substances that are normally present in the body and are required for health.*"

Since 1968 the orthomolecular field has diversified, but the term is still often closely associated with Pauling's advocacy of multi-gram doses of vitamin C for optimal health. Partly for this reason, detractors of orthomolecular ideas have described them entirely in terms of mega

dose nutrient therapy. Cassileth, a widely quoted critic of Pauling's ideas, asserts: "In 1968, the Nobel-prize-winning scientist Linus Pauling coined the term 'orthomolecular' to describe the treatment of disease with large quantities of nutrients." In this way, criticism of orthomolecular medicine has, to a large extent, been confused with much older medical traditions of high-dose vitamin therapies, such as earlier 'megadose' usages of retinol and ergocalciferol or synthetic pharmaceutical analogues, such as menadione. However, such definitions of orthomolecular therapy are not synonymous with Pauling's definition.

The orthomolecular field remains controversial among mainstream medical organizations, including the American Cancer Society, the American Psychiatric Association, the National Institute of Mental Health, the American Academy of Pediatrics, CHAMPUS, and the Canadian Paediatric Society. A number of individuals and organizations contest the claims, benefits, degree of evidence and toxicity. Based on testing with dosages well below orthomolecular recommendations, Linus Pauling has been criticized for making overbroad claims for the efficacy of vitamin C but Pauling's claims have received some support from tests closer to the orthomolecular recommendations during the last few years.

The relationship of mainstream medicine to orthomolecular proponents has often been adversarial; orthomolecular proponents argue that mainstream medical claimants confuse orthomolecular medicine with other, less science based modalities.

The American Academy of Pediatrics labelled orthomolecular medicine a 'cult' in 1976, in response to claims that orthomolecular medicine could cure childhood psychoses and learning disorders.

Conventional health professionals see orthomolecular medicine as encouraging individuals to dose themselves with large amounts of vitamins and other nutrients without conventional supervision, which they worry might be damaging to health. Rare risks of *non-orthomolecular*

‘mega’ dosages of vitamin relatives, which frequently involved pharmaceutical analogues such as synthetic menadione, unsupervised misuse, deliberate abuse and earlier medical treatments, may include increased risk of coronary heart disease, hypertension, thrombophlebitis, peripheral neuropathy, ataxia, neurological effects, liver toxicity, congenital abnormalities, spontaneous abortion, gouty arthritis, jaundice, kidney stones, and diarrhea.

Megavitamin proponents point to an almost zero level of deaths caused by vitamins, even with large overdoses, compared to the significant numbers from pharmaceuticals, including a number of over-the-counter items.

The accumulated evidence of randomized clinical trials with conventional, chemically-modified alpha tocopheryl esters, containing only one kind of natural vitamin E (of eight vitamers) in the stabilized (chemically inactivated) ester form (usually acetate) have been controverted. Initial hopes for alpha tocopheryl esters (usually acetate) were based on suppositional grounds and epidemiological data that often involved the natural, full spectrum dietary forms of vitamin E (mixed R, R,R *tocopherols* - alpha- beta- gamma-, delta- isomers).

Meta analysis of several randomized clinical trials of manufactured antioxidants, including alpha tocopheryl esters (acetate, succinate) not in an antioxidant form, have not shown any benefit to alpha tocopheryl ester supplementation for preventing coronary heart disease.

Orthomolecular recommendations for the full vitamin E complex typically include an additional 25% to 200% w/w of beta-, gamma-, and delta-*tocopherols*. Recent scientific and medical research shows gamma-tocopherol, the most common vitamer of natural vitamin E, has unique beneficial functions and “gamma tocopherol is considered an integral component of the nutrient-based recommendations in many EU member countries.”

A controversial meta-analysis published in 2005 claimed that ‘high dose’ alpha tocopheryl esters (≥ 400 units/day) were associated with an all-

cause mortality risk difference of 39 per 10,000 persons. Furthermore, a significant relationship was claimed between dose and all-cause mortality, with increased risk with doses exceeding 150 I.U. per day. This meta-analysis, however, was criticized on a number of grounds. One of several criticisms which the authors did not rebut was that the mortality effect was a confounder resulting entirely from excess mortality in a few studies of combined alpha-tocopheryl ester and synthetic beta carotene in heavy smokers. Known for decades, that “the antagonisms that exist between...carotene and vitamin E are complicated”, this supplement and smoking exposure combination once had some academic support but synthetic “beta carotene...has previously been shown to be harmful” in smokers, a subpopulation with high oxidative stress. Long commercialized, multiple antioxidant megavitamin combinations, such as ‘ACES’, that also include antioxidants vitamin C and selenium to recycle the first two antioxidants and aid liver peroxide detoxification, were not tested or measured.

The orthomolecularly-preferred ‘vitamin E’, mixed (natural) R, R,R tocopherols, available for two-thirds of a century, remain to be authoritatively evaluated in tests controlled for bile, pancreatic function, certain specific heart problems and risk factors, blood levels and cofactors (vitamins C, D₃, K₁, K₂, selenium, co-enzyme Q10, etc.) in the common orthomolecular range, 600 - 3200 IU alpha tocopherol *plus* 25%-200% by weight of other R, R,R tocopherols. With the exception of controlling for standard co-morbidities such as heart disease, controlling for pancreatic function, various vitamin cofactors, etc. has not been felt by conventional medicine to be neither clinically relevant nor routinely done in clinical trials. However, naturopathic medicine texts and naturopathic physicians routinely recommend such laboratory tests of biliary and pancreatic functions in their orthomolecular-related modalities.

Conventional physicians express concern that megavitamin and orthomolecular therapies used solely as alternative treatments by other practitioners, if not successful, may create dangerous delays in obtaining conventional treatments, such as radiation and chemotherapy for cancer.

For example, in a highly publicized Canadian case, the chemotherapy and orthomolecular treatments of a 13-year-old cancer patient, Tyrell Dueck, were delayed, possibly fatally, due to his parents' religious beliefs, interest in alternative treatments, and lengthy legal battles. Orthomolecular medical practitioners and orthomolecular oriented naturopaths have long expressed similar concerns about conventional medicine, particularly with gut related and chronic diseases as well as viral diseases. The use of conventional medical treatments, if not successful, may create dangerous delays in people obtaining orthomolecular treatments.

Several orthomolecular related AIDS approaches such as multivitamins, selenium and amino acids are used with reported improvements in patients. High dose vitamin C treatments have long been used clinically by some orthomolecular practitioners to treat AIDS patients; a minor 1994 *in vitro* laboratory study raised questions that sustained megadoses of vitamin C might inhibit some immune cells. In these situations, mainstream medical criticism arises when orthomolecular approaches are advocated as *substitutes for*, rather than complements to, current medical treatments.

Some orthomolecular proponents claim partisan politics, pharmaceutical industry influence, and competitive considerations to be significant factors. Some prominent orthomolecular proponents sell lines of orthomolecular products and accept some tests questioned about their benefit that vary by medical affiliation. The Linus Pauling Institute's funding comes mostly from National Institutes of Health. Several orthomolecular therapies have been officially sanctioned within Europe and Japan.

