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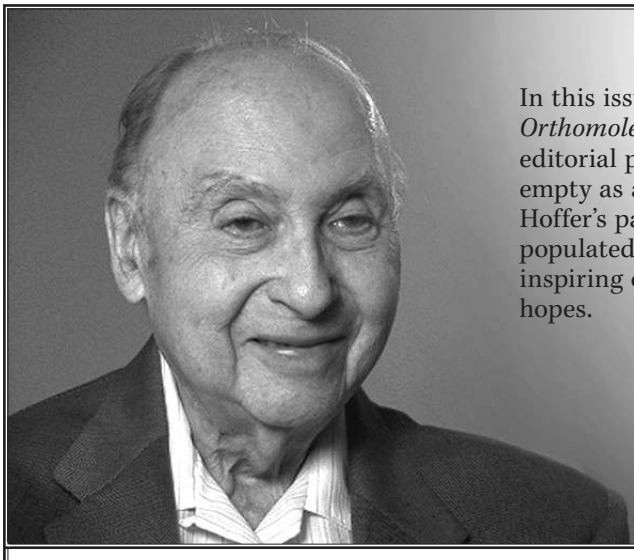
Editorial



In this issue of the *Journal of Orthomolecular Medicine,* the editorial pages have been left empty as a symbol of Dr. Abram Hoffer's passing. For 40 years he populated these pages with his inspiring opinions, ideas and hopes.

Editorial

My Paranoid Patients Are Now My Friends

Abram Hoffer, M.D., Ph.D; Frances Fuller, RNCP (Cand)[1]

Introduction

Just before Christmas in 1960, I received a handwritten two-page letter from Dr. Ted Robie of New Jersey. Ted had been practising psychiatry for about forty years. He was compelled to write to me because, for first time in his career, his paranoid patients had become his friends. I think that in this very brief statement he demonstrated the fundamental difference between standard psychiatry as practised then and even now, and orthomolecular medicine, practised by a few.

You have to understand paranoid patients to grasp what Ted wrote. Paranoid patients are fearful because of their delusional beliefs and they do not trust very many people. Even patients who have had loving relationships with their partners for many years will doubt them and, in the past, it was not unusual for paranoid patients to believe their mates were poisoning their food. Since most paranoid patients do not believe they are sick and it's the rest of the world that is out of order, it becomes very difficult to treat them. They have had to be forced or committed into hospital, where treatment was forced upon them, and since most of them did not recover, they never had a chance to establish positive relationships with their doctors.

A paranoid patient in one of Ontario's mental hospitals refused to accept treatment. He said that he preferred to deal with his ideas free of the drugs with their terrible side effects. This issue was taken to the Supreme Court of Canada, which found that forcing anyone to submit to treatment against his or her will was against Canada's constitution. Of course, governments have immense power to have their own way. He was therefore kept in hospital under a Provincial Act. In Ontario it is against the law to force medication. Not so in the rest of Canada.

What is Paranoia?

Paranoid ideas are delusions that are held firmly against known facts. It is therefore a value judgement that has to balance the probability that the facts used by the paranoid patient to support his delusion are real. There is no doubt that many paranoids are not really paranoid but are responding to their altered perceptions, as Dr. John Conolly pointed out many years ago. A common example was the belief that one's spouse was putting poison into one's food. However, this could be traced to the bitter taste that food may develop when patients are deficient in zinc. When I explained to some of these patients that the bitter taste arose from a deficiency of zinc, they were no longer paranoid.

There is no limit to the number of paranoid delusions patients will develop. Here is an example of a paranoid delusion that forced a prisoner from Prince Albert prison to flee and kidnap several police in their car. After being returned to prison he told me he had to escape in order to save his life. He was convinced that poison gas was being piped into his cell. His evidence was that he could smell it coming from the vents. He tried to stop this by plugging the air vents. (Kahan, 1973).

In her second report, Kahan described the history of a young man who killed almost the entire Hoffman family in northern Saskatchewan because he had been ordered to do so by the Devil, and this command was not countered by the usual advice he would get from his guardian angel not to do so. He died psychotic in a mental hospital.

Recently in Canada, another schizophrenic patient was found not guilty by

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reason of insanity because he too believed he was ordered by God to kill a fellow bus passenger, which he did by cutting off his head.

Conolly described a woman in his hospital who was very depressed because she knew her husband was dead. She could see his ghost perched in a tree outside her window. Her doctor told her husband about this delusion, but would not let him go into the room lest it frighten her too much. However, when no one was looking, he went in anyway. She looked at him, fainted, and when she came to said, "Let's go home, John." Confronted with reality she no longer believed that her hallucination was his ghost.

An example of the tenacity with which patients can hold onto their delusions was the patient who had concluded he was dead, and could not be argued out of this. When his doctor asked him, "Do dead men bleed?" He replied, "Of course not! What a ridiculous question." The doctor followed up, "Will you allow me to prick your finger to see if you bleed?" "Of course," he replied and held up his forefinger. The doctor pricked the finger and it bled. The patient was astounded. He exclaimed, "I did not realize dead men could bleed." This delusion reminds me of the delusions held by modern psychiatry that their toxic, poisonous drugs are more helpful than harmful to patients.

Paranoid ideas are not always injurious. For some occupations, being paranoid can be very useful. I think being paranoid is very helpful for police officers, for detectives, for the military, as this will prolong their lives. I think paranoia is advantageous evolutionally if it is not excessive, or else it would have disappeared long ago. The Trojan horse tactic succeeded because of insufficient paranoia. Even for many business affairs it may be very helpful. Had the government controllers of the world's banking system displayed a little more paranoia, perhaps we would not be in our present financial situation. I think also it can be helpful to believe when driving that other drivers may actually want to hurt you, as long as you know this is seldom true. Interestingly, paranoid patients, no matter how delusional and paranoid they can be, are gullible when it comes to other ideas, like falling for the billion dollar scams that flood the Internet.

Why So Few Paranoid Patients Become Friendly With Their Psychiatrists

The main reason is that most of these patients do not recognize they are sick, and therefore cannot be persuaded that treatment will do any good. *'In vino veritas'* refers to men or women who, under the influence of alcohol, will blurt out paranoid and other socially unacceptable ideas. The alcohol reduced some of their social controls. Paranoid patients are very pleased when they are no longer bothered by these repetitive intrusive ideas, and the odds they will become friendly with the doctors who treated them increased. Otherwise, they cannot be persuaded that to get well they need correct treatment, nor that it would be smarter on their part not to talk about their paranoid ideas.

In Hoffer reported by Challem (2007), I summarized the major change that has occurred from psychiatry of 1950 and orthomolecular psychiatry today. In June, 2007, a forty-year-old man came to see me, accompanied by his sister. He had been a very busy and skilful artisan. He told me that he had suffered from anxiety and depression most of his life, and latterly from what he described as a delusional disorder, meaning he became extremely suspicious of any girlfriend, believing she is unfaithful. This always broke up the relationship. Five years ago he had been diagnosed schizophrenia, but more recently had been given a more esoteric diagnosis, "Othello's Syndrome", by his current psychiatrist. For this he

was prescribed Risperidone, 3 mg per day. Risperidone made him more anxious, and he was depressed most of the time. He denied having experienced visions or voices. He had been in a psychiatric ward twice, the last time for five days at the end of April, 2007. He had been abstinent from pot and cigarettes for two months prior to seeing me.

There was clear evidence that he was allergic to dairy products. He was advised to follow the following nutrient program: niacin 1 gram TID, ascorbic acid 1 g TID, B-complex 100 mg OD, pyridoxine 250 mg OD, vitamin D 6000 IU during winter, 4000 IU in summer, zinc citrate 50 mg OD, salmon oil 1 g TID, selenium 200 mcg OD, and apple cider vinegar 1-2 tbsp with meals.

Two months later he was normal. "Othello" had vanished, driven away by a few simple vitamins. Had he gone for help in 1950 he would have been offered deep psychotherapy, preferably psychoanalysis, and if he could afford it, weekly sessions or more often for up to ten years, because it was believed that paranoid ideas arose from unexpressed homosexuality. At one of our conferences the presenting psychiatrist described a similar case and then told us he was homosexual. I asked what the evidence was. Had he, in fact, ever been or even expressed any interest in men? The doctor replied that of course he was homosexual, since Freud had shown this in a book he had written about one paranoid psychotic judge. He was paranoid and that was enough to prove to this doctor he was a latent homosexual. The odds are that this patient would eventually have wound up in some chronic mental hospital ward and later, if he survived, he would have been driven into the streets, as is the case with so many of these patients today,

This recovery from "Othello's syndrome" shows that in this man no psychological complexes were involved; he did not need psychotherapy. He was given the information doctors must give to their patients. He did not have "Othello's syndrome", whatever that is. It is another example of psychiatrists attempting to develop fancy diagnoses by describing the symptoms of the illness in more and more detail, and by attaching a name to it that gives it more cachet. This man was another example of a pellagra psychosis, the vitamin B_3 dependency, which can take almost any clinical form. When modern psychiatry becomes better informed, it will depend upon simple laboratory tests and the response to vitamins to make the diagnosis. No one diagnoses syphilis anymore by describing the clinical symptoms. It is diagnosed by laboratory tests. In brief, in 1950 there was no treatment; today there is. What a difference!

The schizophrenic psychosis characteristic of late stage pellagra cannot be distinguished from schizophrenia unless the typical nutritional history associated with it is present. The discovery that niacin and niacinamide cured pellagra made it possible to use a very simple diagnostic test that in my opinion turned out to harmful to schizophrenics. In the 1930s pellagra psychotics were distinguished by giving them the vitamin. If they recovered quickly, in a matter of weeks, they were called pellagra, but if they did not they were allowed to remain schizophrenic. The gross error in this reasoning was that it did not take into account the fact that individuals' needs do differ, and optimum doses are not invariant. As has been pointed out repeatedly, whether the deficiency is low dose or high dose, the condition is the same except that high doses were not continued long enough to make any difference. Paranoid ideas were common amongst pellagrins; not surprisingly, they vanished when patients were given the correct doses of vitamin. This is recently referred to by Prakash, Gandotra, Singh et al (2008).

Brief Case History of a Very Sick Paranoid Schizophrenic Patient Who is on the Road to Recovery

Several decades ago a young man was referred to me. After having seen more than five thousand schizophrenic patients over fifty years, I think I have seen nearly every form it can manifest. He was the only one who made me fearful by his manner, which sizzled with the intensity of his anger at the whole world, and by the tenacity with which he adhered to his fantastic delusional ideas. He frightened his social workers, who refused to see him alone, and also alienated most of the doctors at the clinic he attended. He never threatened my staff, or me, nor was he paranoid about us.

I never argue with paranoid patients, nor do I try to convince them they are wrong. After each visit he may have felt better, but I felt very much worse, tired from listening to all those psychotic ideas pouring out of him. I immediately started him on niacin, 1 gram after each of three meals, plus 5 mg of Haldol, one of the safest antipsychotics, until its patent ran out, when it suddenly became very dangerous, especially as the new 'atypicals' were developed.

His visits went on year after year. I measured the degree of improvement by the amount of time he gave to his paranoid ideas compared to the time given to reality-based problems. After I changed my status from psychiatrist to consultant, there was a subtle shift. Over the past year, almost 90 percent of the content of his conversation was reality based. We speak about vitamins, whether he needs any more, and so on. He is no longer frighteningly hostile and, amazingly, he now has a job. The last interview he told me how much he liked me, and that I was the best doctor he had ever had; this, from an originally very hostile paranoid patient.

What Helped Him Become So Much Better?

Fortunately, he was always able to find living quarters with which he was able to cope. Physically he was well; he did not show the typical appearance of a chronic tranquilized patient. My office always treated him with respect and consideration, and when he was abused by the system I became his advocate, writing letters and making calls on his behalf. And of course, he never stopped taking niacin every day, 1 gram after each of three meals. I did not treat his paranoid ideas. I did not try to persuade him they were wrong, and no matter how bizarre they were, I still listened. He would have made an excellent science fiction writer on the morbid side. His paranoid delusions are playing a much lesser role because his schizophrenia is coming under control. One does not treat the paranoid delusions; one treats the basic disease present in the human being.

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Antioxidant Vitamins Reduce the Risk for Cancer: Part Two

Michael J. Glade, Ph.D., FACN, CNS[1]

Part One (JOM 24.1) presented the evidence for vitamin C in reducing cancer risk.

Vitamin E Reduces the Risk for Breast Cancer

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for breast cancer. The results of several retrospective observational studies support the conclusion that increased consumption of vitamin E reduces the risk for breast cancer.[10,11,16-18,21,37-39,43,98] In a case-control study conducted in New York state, the multivariate-adjusted odds of developing breast cancer were reduced significantly among premenopausal women by any daily intakes of a-tocopherol equal to or greater than 2/3 of the RDA (OR, daily vitamin E intakes > 10 mg vs < 7 mg: 0.55; 95% C.I.: 0.34, 0.88; adjusted for age, education, age at first birth, age at menarche, history of first-degree relatives with breast cancer, personal history of benign breast disease, BMI and total daily energy intake).[10] This significant reduction in risk was independent of the intakes of other dietary antioxidants and did not require but was not attenuated by dietary supplementation with vitamin E, although it became less important with increasing consumption of vegetables. In a case-control study of women conducted in western New York state, the multivariate-adjusted odds of developing breast cancer were reduced significantly in both premenopausal and postmenopausal women without a family history of breast cancer and who consumed the most a-tocopherol, despite the almost universal prevalence of vitamin E deficiency among these women (OR, premenopausal women with daily a-tocopherol intake > 10.4 mg vs < 6.4 mg: 0.5; 95% C.I.: 0.2, 1.0; OR, postmenopausal women with daily a-tocopherol intake > 10.4 mg vs < 6.4 mg: 0.5; 95% C.I.: 0.3, 1.0; both adjusted for age, education, age at menarche, age at first pregnancy and BMI).11 These protective effects was not enjoyed by similar premenopausal women who had a positive family history of breast cancer, indicating that chronic vitamin E deficiency cannot overcome factors that predispose a woman of any age to breast cancer.[11]

In a case-control study conducted in China (the Shanghai Breast Cancer Study), the odds of women developing breast cancer were reduced significantly among women who consumed more than the RDA for vitamin E, compared to vitamin E deficient women (OR, vitamin E intake > 19.9 mg/day vs < 9.4 mg/day: 0.72; 95% C.I.: 0.54, 0.96).37 In an extension of this study, the multivariate-adjusted odds of developing breast cancer were reduced significantly among women with diets deficient in vitamin E and who consumed dietary supplements of vitamin E (OR, vitamin E deficient diet plus vitamin E supplement vs vitamin E deficient diet alone: 0.8; 95% C.I.: 0.6, 1.0; adjusted for age, education, age at menarche, parity, BMI, menopausal status, level of recreational exercise, history of fibroadenoma, history of breast cancer in first-degree relatives and phase of study).[38] In addition, in a case-control study nested within the Danish Diet, Cancer and Health Study of postmenopausal women, the odds of developing breast cancer were reduced significantly by the daily consumption of at least 25 mg of vitamin E, compared to the odds associated with the daily consumption of 10 to 15 mg (Incidence Rate Ratio: 0.59; 95% C.I.:

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0.37, 0.95; adjusted for vitamin C intake, vitamin A intake, number of childbirths, age at first childbirth, history of surgery for benign breast disease, education, years of hormone replacement therapy, alcohol consumption and BMI).[43]

From the data obtained in a case-control study conducted in Italy it was determined that 8.6% of the risk of developing breast cancer is attributable to daily vitamin E intake less than 8.5 mg.[98] The impact of poor vitamin E nutrition on risk for breast cancer was confirmed further by the results of another case-control study conducted in Italy, in which the energy-adjusted odds of developing breast cancer were reduced significantly by increased vitamin E consumption (OR, 5th quintile of daily vitamin E intake vs 1st quintile: 0.75; $p < 0.05$)[39] and in another, the odds of developing breast cancer were inversely correlated with daily intakes of vitamin E.[21] Furthermore, in a case-control study conducted in Uruguay, the multivariate-adjusted odds of developing breast cancer were reduced significantly by even moderately increased daily vitamin E intakes (OR, 2nd quartile of vitamin E intake vs 1st quartile: 0.53; 95% C.I.: 0.35, 0.83; adjusted for adjusted for age, residence, urban or rural status, family history of breast cancer in a first-degree relative, BMI, age at menarche, parity, menopausal status and total energy intake)[17] and in a more recent case-control study conducted in Uruguay, the likelihood of breast cancer in premenopausal women was inversely correlated with vitamin E intake.[18] In addition, in a case-control study of women conducted in western India, the odds of developing breast cancer were significantly lower among women with the highest plasma a-tocopherol concentrations, compared to the odds among women with the lowest (OR: 0.37; 95% C.I.: 0.21, 0.67).[16] (Circulating concentrations of vitamin E can be used as biomarkers of exposure to dietary vitamin E; for example, for every doubling of a-tocopherol intake, plasma a-tocopherol concentration increases 10%).[23,99]

In contrast to this large body of evidence demonstrating that increased consumption of vitamin E reduces the risk for breast cancer, the prospective observational data collected during the 8-year prospective observational Nurses' Health Study II of 90,655 premenopausal women aged 26 to 46 years indicated that the multivariate-adjusted risk of developing breast cancer was not affected by differences in the daily intakes of vitamin E from foods or from foods plus supplements (adjusted for age, smoking status, height, parity, age at first full-term birth, BMI, age at menarche, family history of breast cancer, personal history of benign breast disease, oral contraceptive use, menopausal status, alcohol consumption, daily energy intake and daily intake of animal fat).[27] Similarly, in the 14-year prospective Nurses' Health Study of 83,234 women in the US, the multivariate-adjusted risk of developing breast cancer was not affected by differences in daily intakes of vitamin E from foods alone or from foods and dietary supplements (adjusted for age, length of follow-up, daily energy intake, parity, age at first birth, age at menarche, history of breast cancer in a mother or sister, history of benign breast disease, alcohol consumption, BMI at age 18 years, change in body weight since age 18 years, height, age at menopause and postmenopausal hormone therapy).[28] The results of a prospective observational study of 34,387 postmenopausal women in the state of Iowa in the US (the Iowa Women's Health Study) also indicated that the multivariate-adjusted risk of developing breast cancer was not affected by differences in vitamin E intakes (adjusted for age, daily energy intake, age at menarche, age at menopause, age at first live birth, parity, BMI at entry into study, BMI at age 18 years, family history of breast cancer, personal history of benign breast disease, alcohol consumption and education).[29]

Three other prospective observational studies also failed to reveal a relationship between vitamin C consumption and the incidence of breast cancer.[9,30,31] For example, data obtained from 4,697 women, initially cancer-free and aged 15 years or older, after 25 years of observation failed to reveal a significant relationship between differences in daily vitamin E intakes and the occurrence of breast cancer.[30] After the first 4.3 years of the prospective observational study of 62,573 women aged 55 to 69 years (the Netherlands Cohort Study), the risk of developing breast cancer was not affected by differences in vitamin E intakes.[31] Interestingly the results of an 8-year prospective observational study of 59,036 women aged 40 to 76 years in Sweden (the Swedish Mammography Cohort), among women with BMI >25, differences in vitamin E intakes were unable to overcome the established procarcinogenic influence of excess body weight on the risk of developing breast cancer.[9]

The results of retrospective observational studies conducted in the US[32,33,100-103] also failed to demonstrate the protective effect of increased vitamin C consumption against breast cancer. In a case-control study conducted in western New York state, the odds of developing breast cancer were not affected by differences in vitamin E intakes[33] and in a more recent case-control study of women conducted in North Carolina, the multivariate-adjusted odds of developing breast cancer were not affected by dietary supplementation with any amount of vitamin E (adjusted for age, age at menarche, age at first full-term pregnancy, menopausal status, lactation history, family history, BMI, waist-to-hip circumference ratio, education, alcohol consumption, smoking history and daily intakes of fruits and vegetables).[32] In case-control studies nested within prospective studies conducted in Missouri,[100] Washington County, MD,[101,102] and within the prospective Nurses' Health Study in the US,[103] the odds of developing breast cancer were not affected by differences in serum a-tocopherol concentrations.

Similarly, in a case-control study nested within the Canadian National Breast Screening Study of 56,837 women, the multivariate-adjusted odds of developing breast cancer were not affected by differences in the daily intakes of vitamin E or a-tocopherol from either foods or dietary supplements (adjusted for adjusted for age, daily energy intake, age at menarche, surgical menopause, age at first live birth, education, family history of breast cancer, and personal history of benign breast disease).[34] In case-control studies conducted in China (the Shanghai Nutrition and Breast Disease Study,[35] the Shanghai Breast Cancer Study[36] and studies conducted in Shanghai and Tianjin[20]), differences in vitamin E intakes had no effects on the age-adjusted odds of developing nonproliferative benign breast disease, proliferative benign breast disease without atypia or proliferative benign breast disease with atypical hypertrophy. In several European case-control studies conducted in Sweden,[104] Italy,[40] Greece[41] and the UK[105] and in a similar study conducted in western India,[16] the odds of developing breast cancer were not affected by differences in daily intakes of vitamin E.

In case-control studies conducted in Germany[12] and Seoul, Korea,[13] the odds of developing breast cancer were not affected by differences in vitamin E intakes; however, over 80% of the subjects in these studies were chronically vitamin E deficient.

One double-blind, randomized, placebo-controlled clinical trial directly addressed the effects of dietary supplementation with vitamin E in the prevention of breast cancer. In the 10-year Women's Health Study, in which 39,876 apparently healthy women over 45 years old consumed either placebo or 600 IU of vitamin E every other day, this amount and pattern of vitamin E supplementation did not affect the age-adjusted risk for breast cancer (RR,

vitamin E vs placebo: 1.00; 95% C.I.: 0.90, 1.12).[106] However, the extent to which separating episodes of vitamin E consumption by 48 hours prevents the establishment of an elevated steady-state of circulating a-tocopherol concentration is not known; a-tocopherol concentrations were not measured during this study.

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for breast cancer. The evidence documented by 11 retrospective observational studies[10,11,16-18,21,37-39,43,98] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for breast cancer. In addition, the results of two studies[12,13] confirm that vitamin E deficiency does not protect against breast cancer.

Vitamin E Reduces the Risk for Colon Cancer

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for colon cancer. The results of a prospective observational study of 35,215 women aged 50 to 69 years in Iowa (the Iowa Women's Health Study), largely as a result of the protective effect of supplemental vitamin E intakes greater than 30 mg/day (age-adjusted RR, supplemental vitamin E intake > 30 mg/day vs none: 0.44; 95% C.I.: 0.28, 0.71), women consuming the most vitamin E experienced significantly less risk for colon cancer (age-adjusted RR, total vitamin E intake > 35 mg/day vs < 6 mg/day: 0.32; 95% C.I.: 0.19, 0.54).[107] These protective effects remained significant after further adjustment of the calculated risk ratios for age, daily total energy intake, height, parity, vitamin A supplementation and daily intakes of seafood and skinless chicken (multivariate-adjusted RR, supplemental vitamin E intake > 30 mg/day vs none: 0.50; 95% C.I.: 0.28, 0.87; multivariate-adjusted RR, total vitamin E intake > 35 mg/day vs < 6 mg/day: 0.42; 95% C.I.: 0.22, 0.78).[107]

In addition, the results of retrospective observational studies support the conclusion that increased consumption of vitamin E reduces the risk for colon cancer.[99,108-113] In the case-control North Carolina Colon Cancer Study, a group of African-American men and women with "high" vitamin E intakes (median: 140 mg/day) experienced significantly less risk for colon cancer than was experienced by another otherwise similar group of African-American men and women with "low" vitamin E intakes (median: 6 mg/day; OR: 0.3; 95% C.I.: 0.1, 0.6).[108] In contrast, the odds of developing colon cancer were not affected by differences in vitamin E intakes among white men and women, over half of whom were vitamin E deficient.[108] On average, individuals with colon cancer consumed significantly less vitamin E but vitamin intakes appeared to have no effect on the relative incidence of microsatellite instability (a biomarker for risk for colon cancer).[109]

In a case-control study conducted in the Seattle, Washington area, the age- and sex-adjusted odds of developing colon cancer were reduced significantly in men and women who supplemented their diets with vitamin E (OR, daily supplemental vitamin E intake > 15 mg vs none: 0.61; 95% C.I.: 0.42, 0.87)[110] and in a case-control study conducted in Montreal, Quebec, Canada, the multivariate-adjusted odds of developing colon carcinoma were reduced significantly by increased consumption of vitamin E (OR, 2nd quartile of vitamin E intake vs 1st quartile: 0.54; 95% C.I.: 0.37, 0.80; adjusted for sex, age, marital status, history of colon carcinoma in first-degree relatives and total daily energy intake).[111] In a case-control study conducted in Shanghai, China, the odds of men developing colon cancer were reduced significantly by greater daily intake of vitamin E (OR, vitamin E intake > 32 mg/day vs < 26 mg/day: 0.6; 95% C.I.: 0.4, 0.9), although the odds of women developing colon cancer

were not affected by differences in vitamin E intakes.[99]

In a case-control study conducted in New York City, NY, the odds of adenomatous polyp recurrence were reduced significantly among patients who supplemented their diets with vitamin E (OR, vitamin E supplementation vs none: 0.62; 95 % C.I.: 0.39, 0.98).[112] Similarly, in Denmark, the odds of adenomatous polyp recurrence were inversely correlated with daily intakes of vitamin E.[113]

In contrast to these reports, when the data from 87,998 women in the prospective Nurses' Health Study were combined with the data from 47,344 men in the prospective Health Professionals Follow-Up Study, the risk for developing colon cancer was found to be unaffected by differences in vitamin E consumption.[114] In addition, in a case-control study conducted in Salt Lake City, Utah, the odds of developing colon cancer did not reflect differences in daily intakes of a-tocopherol.[115] In a 17-year prospective study of 2,974 men in Basel, Switzerland,[86,87] and in a case-control study nested within a prospective study in Washington County, MD,[101] differences in serum vitamin E concentrations had no effect on the risks of developing colon cancer.

One double-blind, randomized, placebo-controlled clinical trial directly addressed the effects of dietary supplementation with vitamin E in the prevention of colon cancer. In the 10-year Women's Health Study, in which 39,876 apparently healthy women over 45 years old consumed either placebo or 600 IU of vitamin E every other day, this amount and pattern of vitamin E supplementation did not affect the age-adjusted risk for colon cancer (RR, vitamin E vs placebo: 1.00; 95% C.I.: 0.77, 1.31).[106] However, the extent to which separating episodes of vitamin E consumption by 48 hours prevents the establishment of an elevated steady-state of circulating a-tocopherol concentration is not known; a-tocopherol concentrations were not measured during this study.

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for colon cancer. The evidence documented by a prospective observational study[107] and 7 retrospective observational studies[99,108-113] supports this conclusion and there is no evidence hat increased consumption of vitamin E may increase the risk for colon cancer.

Vitamin E Reduces the Risk for Colorectal Cancer

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for colorectal cancer. The results of several retrospective observational studies support the conclusion that increased consumption of vitamin E reduces the risk for colorectal cancer.[53,55,63] In a case-control study conducted in North Carolina, the multivariate-adjusted odds of developing colorectal adenoma were reduced significantly in men by intakes of vitamin E greater than the RDA (OR, vitamin E intake > 15.3 mg vs < 0.3 mg: 0.22; 95% C.I.: 0.07, 0.77; adjusted for age, BMI, daily energy intake, smoking status, use of dietary supplements, family history of colon cancer and daily intakes of fat, dietary fiber and alcohol).[63] In a case-control study conducted in Italy, the multivariate-adjusted odds of developing colorectal cancer were reduced significantly by increased vitamin E intakes (OR, vitamin E intake > 12.3 mg/day vs < 12.3 mg/day: 0.72; 95% C.I.: 0.6, 0.9; adjusted for age, study center, sex, education, level of physical activity and daily intakes of energy and dietary fiber).[53] In another case-control study conducted in northern Italy, the odds of developing colorectal cancer were reduced significantly by vitamin E consumption (OR, 5th quintile of daily vitamin E intake vs 1st quintile: 0.60; $p < 0.05$).[55]

In contrast, the results of several other retrospective observational studies failed to reveal a relationship between increased

consumption of vitamin E and reduced risk for colorectal cancer.[52,63,116] In a case-control study conducted in North Carolina, the multivariate-adjusted odds of developing colorectal adenoma were not affected by differences in vitamin E intakes in women (adjusted for age, BMI, daily energy intake, smoking status, use of dietary supplements, family history of colon cancer and daily intakes of fat, dietary fiber and alcohol).[63] In a case-control cross-sectional observational study of men and women in California, differences in vitamin E intakes, with or without supplements, had no effect on the odds of developing colorectal adenomatous polyps.[116] In a case-control study conducted in France, the multivariate-adjusted odds of developing colorectal adenoma were not affected by differences in the consumption of vitamin E.[52]

In a case-control study conducted in Los Angeles, CA, the multivariate-adjusted odds of developing colorectal adenoma were not affected by differences in vitamin E intakes from foods or from supplements among a study population that was almost entirely vitamin E deficient, even with vitamin E supplementation (adjusted for daily intakes of calories, saturated fat, folate and fiber, alcohol consumption, current smoking status, BMI, race, level; of daily physical activity and use of nonsteroidal anti-inflammatory drugs).[62] In this study, varying the degree of vitamin E deficiency did not reduce the risk for colorectal adenoma. Similarly, in a case-control study conducted in the Canton of Vaud, Switzerland, the multivariate-adjusted odds of developing colorectal cancer were not affected by differences in daily intakes of vitamin E in another population that was largely vitamin E deficient (adjusted for age, sex, education, smoking status, alcohol consumption, BMI, level of physical activity and daily intakes of energy and dietary fiber).[54]

In a case-control study conducted in Los Angeles, CA, the multivariate-adjusted odds of developing colorectal adenoma were not affected by differences in plasma a-tocopherol concentration (adjusted for location, sex, age, date examined, ethnicity, serum total cholesterol concentration, serum triglyceride concentration, BMI, exercise, smoking, alcohol consumption, daily caloric intake, daily intakes of saturated fat, fruits, vegetables, folate and calcium, use of nonsteroidal anti-inflammatory drugs and plasma Ferritin concentration).[117] Similarly, in three case-control studies conducted in Japan, no relationship was observed between colorectal adenoma or cancer and circulating vitamin E concentrations.[118-120]

The results of a double-blind, randomized placebo-controlled clinical trial in which men and women supplemented their diets with either placebo, β-carotene (25 mg/day), vitamin C (1000 mg/day) plus vitamin E (400 mg/day) or all three antioxidants for 4 years indicated that combined dietary supplementation with this amount of vitamin E did not affect the incidence of colorectal adenoma (RR: 1.08; 95% C.I.: 0.91, 1.29; adjusted for age, sex, number of prior adenomas, actual length of time between clinical evaluations and study center).[58] This finding was confirmed in another 2-year double-blind, randomized, placebo-controlled human clinical trial, patients who were thought to be free of colorectal polyps after polyp removal and who added either placebo or a supplement containing 400 mg of vitamin C and 400 mg of vitamin E to their diets exhibited no difference in the multivariate-adjusted risk of developing new polyps (adjusted for age and the usual frequency of consumption of meats and fish).[59] However, the placebo-controlled trials were of inadequate duration to measure accurately the incidence of new polyps or tumors; even in patients who have undergone polypectomy, the minimum time before re-examination recommended by the 2006 Consensus Update on Guidelines for Colonoscopy

after Polypectomy of the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society is 5 years.[61]

The results of secondary endpoint analyses of the data obtained during the prospective, double-blind, randomized and placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of -carotene or placebo for 5 to 8 years indicated that supplementation with 50 mg of vitamin E was associated with a significant increase in the incidence of colorectal polyps,[121] although the incidence of colorectal cancer was not affected.[60,122] This report is hardly credible; the incidence of new colorectal adenoma reported in the subjects who did not receive supplemental vitamin E was over 10 times the projected incidence of such cancers among the general US male population in 2008123 and an additional 2- to 10-fold increase would be expected to dominate the findings of every clinical trial that employed at least 50 mg of vitamin E. This has not happened.[3,106,124-127]

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for colorectal cancer. The evidence documented by three retrospective observational studies[53,55,63] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for colorectal cancer.

Vitamin E Reduces the Risk for Adenocarcinoma of the Esophagus

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for adenocarcinoma of the esophagus. The results of several retrospective observational studies[70,128,129] support the conclusion that the consumption of increased amounts of vitamin E reduces the risk for adenocarcinoma of the esophagus. In a case-control study conducted in Germany, the multivariate-adjusted odds of developing adenocarcinoma of the esophagus were reduced significantly in men who consumed more than 13 mg of vitamin E daily (RR, adenocarcinoma, daily vitamin E intake > 13 mg vs < 13 mg: 0.13; 95% C.I.: 0.09, 0.54; adjusted for unspecified "known risk factors").[70] In a case-control study in Uruguay, the multivariate-adjusted odds of developing esophageal cancer were reduced significantly by daily vitamin E intakes greater than the lowest quartile of intake (OR: 0.41; 95% C.I.: 0.22, 0.76; adjusted for age, gender, residence, urban or rural status, education, BMI, smoking status, alcohol consumption, total energy intake and daily intakes of β-carotene, -carotene , lutein, lycopene, β-cryptoxanthin, vitamin E, glutathione, quercetin, kaempferol, total flavonoids, β-sitosterol, campesterol and stigmasterol).[128] In a case-control study conducted in China (the General Population Trial in Linxian, China), although the mean serum concentration of a-tocopherol did not differ between men and women with esophageal cancer and cancer-free men and women, for every 25% increase in serum a-tocopherol concentration above the mean, the risk for esophageal cancer decreased significantly by 10%.[129]

On the other hand, a secondary endpoint analysis of the data obtained during the prospective, double-blind, randomized, placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of -carotene or placebo for 5 to 8 years, determined that 5 to 8 years of daily supplementation with 50 mg of vitamin E was unable to overcome the procarcinogenic effects of lifelong cigarette smoking on the incidence of esophageal cancer.[130] However, the results of this epidemiologic analysis is relevant only to populations that match the parent experiment's subjects – middle-aged male life-long cigarette smokers.

The results of three retrospective observational studies[71,73,131] failed to reveal a protective effect of increased vitamin E intakes against adenocarcinoma of the esophagus. In a case-control study conducted in New York state, the odds of developing adenocarcinoma of the esophagus were not affected by differences in vitamin E intakes.[71] In a case-control study of the impact of vitamin E deficiency on adenocarcinoma of the esophagus conducted in Sweden, the multivariate-adjusted odds of developing squamous cell carcinoma of the esophagus were not affected by differences in vitamin E intakes in a vitamin E deficient population (adjusted for age, sex, BMI and smoking status).[73] In a case-control study conducted in the state of Hawaii, mean serum a-tocopherol concentrations of subjects with and without esophageal cancer were not different.[131]

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for adenocarcinoma of the esophagus. The evidence documented by three retrospective observational studies[70,128,129] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for adenocarcinoma of the esophagus.

Vitamin E Reduces the Risk for Squamous Cell Carcinoma of the Esophagus

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for squamous cell carcinoma of the esophagus. The results of several retrospective observational studies[69,70,128,129,132] support the conclusion that the consumption of increased amounts of vitamin E reduces the risk for squamous cell carcinoma of the esophagus. In a case-control study conducted in the US, compared to men and women with daily vitamin E intakes less than the 25th percentile, men and women with daily vitamin E intakes greater than the 75th percentile exhibited significantly reduced odds of developing esophageal squamous cell carcinoma (OR: 0.37; 95% C.I.: 0.27, 0.60; adjusted for sex, state of residence, age, race, income bracket, education, BMI, cigarette smoking, alcoholic beverage consumption and total daily energy intake).[69] Similarly, in a case-control study conducted in France, the multivariate-adjusted odds of developing squamous cell carcinoma of the esophagus were reduced significantly by less-deficient intakes of vitamin E (OR, daily vitamin E intake > 7 mg vs < 7: 0.49; 95% C.I.: 0.28, 0.87; adjusted for interviewer, age smoking status and daily consumption of beer aniseed aperitives, hot Cakvados, whisky, total alcohol and total energy).[132] This protection was strongest among the heaviest consumers of alcoholic beverages. In a case-control study conducted in Germany, the multivariate-adjusted odds of developing squamous cell carcinoma of the esophagus were reduced significantly in men who consumed more than 13 mg of vitamin E daily (RR, daily vitamin E intake > 13 mg vs < 13 mg: 0.17; 95% C.I.: 0.09, 0.48; adjusted for unspecified "known risk factors").[70]

In a case-control study in Uruguay, the multivariate-adjusted odds of developing esophageal cancer were reduced significantly by daily vitamin E intakes greater than the lowest quartile of intake (OR: 0.41; 95% C.I.: 0.22, 0.76; adjusted for age, gender, residence, urban or rural status, education, BMI, smoking status, alcohol consumption, total energy intake and daily intakes of β-carotene , lutein, lycopene, β-cryptoxanthin, vitamin E, glutathione, quercetin, kaempferol, total flavonoids, β-sitosterol, campesterol and stigmasterol).[128] In a case-control study conducted in China (the General Population Trial in Linxian, China), although the mean serum concentration of a-tocopherol did not differ between men and women with esophageal cancer and cancer-free men and women, for every 25% increase in serum a-tocopherol concentration above

the mean, the risk for esophageal cancer decreased significantly by 10%.[129]

In contrast, a secondary end-point analysis of the data obtained during the prospective, double-blind, randomized, placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of β-carotene or placebo for 5 to 8 years, determined that 5 to 8 years of daily supplementation with 50 mg of vitamin E was unable to overcome the procarcinogenic effects of lifelong cigarette smoking on the incidence of esophageal cancer.[130] However, the results of this epidemiologic analysis is relevant only to populations that match the parent experiment's subjects – middle-aged male life-long cigarette smokers.

Data obtained during four retrospective observational studies[73,82,131,133] failed to reveal a protective effect of increased vitamin E intakes against squamous cell carcinoma of the esophagus. In two case-control studies conducted in Uruguay, the multivariate-adjusted odds of developing squamous cell carcinoma of the esophagus were not affected by differences in vitamin E intakes (adjusted for age, sex, residence, urban or rural status, birthplace, education, BMI, smoking status, years since quit smoking, number of cigarettes smoked per day, alcohol consumption, mate tea consumption and total daily energy intake;[133] adjusted for age, residence, urban or rural status, education, family history of prostate cancer, BMI and total daily energy intake).[82] In a case-control study of the impact of vitamin E deficiency on squamous cell carcinoma of the esophagus conducted in Sweden, the multivariate-adjusted odds of developing squamous cell carcinoma of the esophagus were not affected by differences in vitamin E intakes in a vitamin E deficient population (adjusted for age, sex, BMI and smoking status).[73] In a case-control study conducted in the state of Hawaii, mean serum a-tocopherol concentrations of subjects with and without esophageal cancer were not different.[131]

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for squamous cell carcinoma of the esophagus. The evidence documented by five retrospective observational studies[69,70,128,129,132] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for squamous cell carcinoma of the esophagus. In addition, the evidence documented by a retrospective observational study[73] demonstrates that squamous cell carcinoma of the esophagus is not prevented by vitamin E deficiency.

Vitamin E may Reduce the Risk for Laryngeal Cancer

The scientific evidence suggests that increased consumption of vitamin E may reduce the risk for laryngeal cancer. The results of a retrospective observational study[134] support the conclusion that the consumption of increased amounts of vitamin E reduces the risk for laryngeal cancer. In a case-control study conducted in Uruguay, the multivariate-adjusted odds of developing laryngeal cancer were inversely correlated with vitamin E intake (adjusted for age, sex, residence, urban or rural status, education, BMI, smoking status, years since quit smoking, number of cigarettes smoked per day by current smokers, age at start of smoking and total daily energy intake).[134] Increased vitamin E intake was most effective in the prevention of cancer of the superglottis and less effective in the prevention of cancer of the glottis. Risk reduction was weakened by continuation of cigarette smoking.

In contrast, a post hoc secondary end-point analysis of the data obtained during the prospective, double-blind, randomized, placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers

in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of -carotene or placebo for 5 to 8 years, determined that 5 to 8 years of daily supplementation with 50 mg of vitamin E was unable to overcome the procarcinogenic effects of lifelong cigarette smoking on the incidence of laryngeal cancer.[130] However, the results of this epidemiologic analysis is relevant only to populations that match the parent experiment's subjects – middle-aged male life-long cigarette smokers.

On the other hand, the results of two retrospective observational studies[131,135] failed to reveal a protective effect of increased vitamin E intakes against laryngeal cancer. In a case-control study conducted in Japan, the multivariate-adjusted odds of developing laryngeal cancer were not affected by differences in vitamin E intakes (adjusted for age, sex, smoking status, alcohol consumption, use of multivitamin supplements, total daily energy intake, dental hygiene and year of first hospital visit)[135] and in a case-control study conducted in the state of Hawaii, mean serum a-tocopherol concentrations of subjects with and without laryngeal cancer were not different.[131]

The scientific evidence suggests that increased consumption of vitamin E may reduce the risk for laryngeal cancer. The evidence documented by a retrospective observational study[134] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for laryngeal cancer.

Vitamin E Reduces the Risk for Melanoma

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for melanoma. The results of a case-control study conducted in Washington County, MD, indicated that the odds of developing malignant melanoma were inversely correlated with age, education, and energy intake-adjusted vitamin E intakes.[136] Although the odds of men in the US developing malignant melanoma were not affected by differences in the intakes of vitamin E from foods and supplements, the odds of women developing malignant melanoma were halved when daily total vitamin E intakes from foods and supplements exceeded the RDA (OR: 0.41; 95% C.I.: 0.21, 0.81).[137] Consistent with these reports, the results of observing the 39,268 male and female participants in the Finnish Social Insurance Institution's Mobile Clinic Health Survey, aged 15-99 and initially free from cancer, prospectively for 8 years indicated that serum a-tocopherol concentrations were inversely correlated with the risk of developing melanoma.[138]

In contrast, the results of combining the data obtained from 73,525 female participants in the prospective observational Nurses' Health Study and from 88,553 prospective observational Nurses' Health Study II indicated that the multivariate-adjusted risk of developing melanoma was not affected by differences in vitamin E intakes from foods or dietary supplements (adjusted for age, skin reaction after 2 hours of sun exposure during childhood, number of sunburns over lifetime, number of sunburns during adolescence, number of moles on left arm, number of moles on lower legs, hair color, family history of melanoma, state of residence, menopausal status, use of oral contraceptives, use of postmenopausal hormone therapies, parity, height and BMI).[139] In a case-control study conducted in Boston, MA, the multivariate-adjusted odds of developing malignant melanoma were not affected by differences in plasma a-tocopherol concentrations or vitamin E intakes (adjusted for age, sex, plasma lipid concentrations, hair color and the ability to suntan).[140] In a series of case-control studies nested within a prospective study in Washington County, MD, prediagnostic serum vitamin E concentrations were not associated with the odds of developing melanoma.[101,141]

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for melanoma. The evidence documented by a prospective observational study[138] and 2 retrospective observational studies[136,137] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for melanoma.

Vitamin E Reduces the Risk for Cancer of the Oral Cavity

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for cancer of the oral cavity. The results of four retrospective observational studies[135,142-144] support the conclusion that increased consumption of vitamin E reduces the risk for cancer of the oral cavity. In a case-control study conducted in New York City, the odds of developing cancer of the oral cavity were inversely correlated with dietary supplementation with vitamin E.[142] In another case-control study conducted in the US, the odds of developing cancer of the oral cavity were inversely correlated with vitamin E supplementation (OR, supplementation vs none: 0.5; 95% C.I.: 0.4, 0.6).[143] In a case-control study conducted in Japan, the multivariate-adjusted odds of developing cancer of the oral cavity were reduced significantly in men and women by greater intakes of vitamin E (OR, daily vitamin E intake > 7.7 mg vs < 4.0 mg: 0.54; 95% C.I.: 0.33, 0.88; adjusted for age, sex, smoking status, alcohol consumption, use of multivitamin supplements, total daily energy intake, dental hygiene and year of first hospital visit).[135] In a case-control study conducted in Italy and Switzerland, the multivariate-adjusted odds of developing either pharyngeal cancer or cancer of the oral cavity were reduced significantly by increased intake of vitamin E (OR: 0.74; $p < 0.05$; adjusted for age, sex, center, education, occupation, body mass index, smoking and drinking habits and non-alcohol energy intake).[144]

However, the results of four retrospective observational studies[131,145-147] failed to document a relationship between vitamin E and cancer of the oral cavity. For example, in a case-control study conducted in Melbourne, Australia, the odds of developing squamous cell cancer of the oral cavity were not affected by differences in dietary vitamin E intakes.[145] In a case-control study conducted in Japan, the odds of developing oral leukoplakia, a precursor of cancer of the oral cavity, were not affected by differences in serum a-tocopherol concentrations.[146] In a case-control study conducted in the state of Hawaii, mean serum a-tocopherol concentrations of subjects with and without any upper aerodigestive tract cancer were not different.[131] In a case-control study conducted in Washington County, MD, the odds of developing cancer of the oral cavity were not affected by prediagnostic serum a-tocopherol concentration.[147]

In addition, in the prospective, double-blind, randomized and placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of -carotene or placebo for 5 to 8 years, supplementation with 50 mg of vitamin E daily did not appear to affect the prevalence of either oral leukoplakia or dysplastic lesions of the buccal epithelium or the incidence of upper aerodigestive tract cancers (cancers of the oral cavity, pharynx, esophagus or larynx).[130,148]

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for cancer of the oral cavity. The evidence documented by four retrospective observational studies[135,142-144] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for cancer of the oral cavity.

Vitamin E Reduces the Risk for Ovarian Cancer

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for ovarian cancer. The results of retrospective observational studies support the conclusion that increased consumption of vitamin E reduces the risk for ovarian cancer.[74,79,149] In a case-control study of women conducted in North Carolina, total daily intakes of vitamin E in excess of 75 mg reduced significantly the odds of developing epithelial ovarian cancer (OR: 0.44; 95% C.I.: 0.21, 0.94) and dietary supplementation with any amount of vitamin E also reduced significantly the odds of developing epithelial ovarian cancer (OR: 0.33; 95% C.I.: 0.18, 0.60).[74] Consistent with this report, in a case-control study conducted in Canada, any amount of supplementation with vitamin E for more than 10 years halved the adjusted odds of developing ovarian cancer (OR: 0.49; 95% C.I.: 0.30, 0.81; adjusted for age, residence, education, alcohol consumption, cigarette smoking, BMI, daily energy intake, recreational physical activity, parity, years of menstruation and menopausal status).[79] In a case-control study conducted in Italy, the risk of developing epithelial ovarian cancer was reduced significantly among women who regularly consumed more than the median amount of vitamin E daily, compared to the risk of women who regularly consumed less than the median amount of vitamin E daily (RR: 0.6; 95% C.I.: 0.4. 0.7; adjusted for age, study center, year of entry into study, BMI, parity, use of oral contraceptives, occupational physical activity and daily energy intake).[149]

In contrast, the results two prospective[75,77] and three retrospective observational studies[78,80,150] failed to discern a relationship between vitamin C and ovarian cancer. Among 97,275 initially cancer-free women participating in the 8-year prospective California Teachers Study of women,[77] and among 80,326 initially cancer-free women participating in the 16-year prospective Nurses' Health Study,[75] the risks of developing ovarian cancer were not affected by differences in vitamin E intakes. In a case-control study conducted in Hawaii and Los Angeles, CA, differences in vitamin E intakes did not affect the odds of premenopausal or postmenopausal women developing ovarian cancer.[78] In a case-control study nested within a prospective study conducted in Washington County, MD, the odds of developing ovarian cancer were not affected by differences in cholesterol-adjusted serum a-tocopherol concentrations.[150] In a case-control study conducted in New Hampshire and eastern Massachusetts, differences in daily intakes of vitamin E had no effect on the odds of premenopausal or postmenopausal women developing ovarian cancer.[80]

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for ovarian cancer. The evidence documented by three retrospective observational studies[74,79,149] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for ovarian cancer.

Vitamin E Reduces the Risk for Pancreatic Cancer

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for pancreatic cancer. The results of retrospective observational studies conducted in Shanghai, China, support the conclusion that increased consumption of vitamin C reduces the risk for pancreatic cancer.[151,152] In one study, the multivariate-adjusted odds of developing pancreatic cancer were reduced significantly in men (but not women) consuming "high" amounts of vitamin E (OR, daily vitamin E consumption > 41 mg vs < 26 mg: 0.57; 95% C.I.: 0.35, 0.93; adjusted for age, income, smoking, green tea drinking and daily caloric intake).[151] In the other,

the multivariate-adjusted odds of developing pancreatic cancer were reduced significantly in both men and women consuming "high" amounts of vitamin E (OR, men, 4th quartile of daily vitamin E consumption vs 1st quartile: 0.5; 95% C.I.: 0.3, 0.7; women, 4th quartile of daily vitamin E consumption vs 1st quartile: 0.5; 95% C.I.: 0.3, 0.8; both adjusted for age, income, smoking, green tea drinking and daily caloric intake).[152]

However, in a case-control study nested within a prospective study in Washington County, MD, prediagnostic serum vitamin E concentrations were not associated with the odds of developing pancreatic cancer.[101] In addition, the results of a secondary endpoint analysis of the data obtained in the prospective, double-blind, randomized and placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of β-carotene or placebo for 5 to 8 years indicated that supplementation with 50 mg of vitamin E daily had no effect on the incidence of pancreatic carcinoma.[153] In addition, an epidemiologic analysis of that data indicated that the risk of developing pancreatic cancer was not affected by differences in the intake of vitamin E.[154] Similarly, the results of observing a cohort of 13,979 initially cancer-free residents of a retirement community for 9 years indicated that the risk of developing pancreatic cancer was not affected by differences in the daily consumption of vitamin E.[155]

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for pancreatic cancer. The evidence documented by two retrospective observational studies[151,152] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for pancreatic cancer.

Vitamin E Reduces the Risk for Pharyngeal Cancer

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for pharyngeal cancer. The results of a case-control study conducted in Italy and Switzerland indicated that the multivariate-adjusted odds of developing either cancer of the oral cavity or pharyngeal cancer were reduced significantly by increased intake of vitamin E (OR: 0.74; $p < 0.05$; adjusted for age, sex, center, education, occupation, body mass index, smoking and drinking habits and non-alcohol energy intake).[144]

However, in the prospective, double-blind, randomized and placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of β-carotene or placebo for 5 to 8 years, supplementation with 50 mg of vitamin E daily had no effect on the incidence of upper aerodigestive tract cancers (cancers of the oral cavity, pharynx, esophagus or larynx).[130] Consistent with this report, in a case-control study conducted in Japan, the multivariate-adjusted odds of developing pharyngeal cancer were not affected by differences in vitamin E intakes (adjusted for age, sex, smoking status, alcohol consumption, use of multivitamin supplements, total daily energy intake, dental hygiene and year of first hospital visit).[135] Similarly, in a case-control study conducted in Melbourne, Australia, the odds of developing either squamous cell cancer of the oral cavity or pharyngeal cancer were not affected by differences in dietary vitamin E intakes.[145] In addition, the results of a case-control study conducted in the state of Hawaii indicated that the mean serum a-tocopherol concentrations of subjects with and without upper aerodigestive tract cancer were not different.[131]

The scientific evidence indicates that

increased consumption of vitamin E reduces the risk for pharyngeal cancer. The evidence documented by a retrospective observational study[144] supports this conclusion and there is no evidence that increased consumption of vitamin E may increase the risk for pharyngeal cancer.

Vitamin E Reduces the Risk for Prostate Cancer

The scientific evidence suggests that the consumption of increased amounts of vitamin E reduces the risk for prostate cancer. In a secondary endpoint analysis of the data obtained during the prospective, double-blind, randomized and placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of β-carotene or placebo, it was determined that 5 to 8 years of daily dietary supplementation with 50 mg of vitamin E produced a significant decrease in the incidence of new prostate cancer (RR: 0.52; 95% C.I.: 0.29, 0.95; adjusted for age, presence of benign prostatic hyperplasia, living in an urban area, presence or absence of concurrent dietary supplementation with β-carotene and serum total cholesterol concentration).[122,156-158] Consistent with this result, two groups of analysts performing systematic reviews of human clinical trials concluded that daily supplementation with 50 mg of vitamin E significantly reduces the risk for developing prostate cancer.[159,160]

In addition, an analysis of the effects of prestudy serum a-tocopherol concentrations on the development of prostate cancer 19 years later in participants in the prospective, double-blind, randomized and placebo-controlled Alpha-Tocopherol, Beta-Carotene Cancer Prevention study of 29,133 middle-aged male cigarette smokers in Finland who supplemented their diets with 50 mg of vitamin E, 20 mg of -carotene or placebo for 5 to 8 years found that even though differences in serum a-tocopherol concentrations had no effect on the odds of developing prostate cancer during the study,[161] 19 years later the risks for any prostate cancer and for advanced prostate cancer were inversely correlated with prestudy serum a-tocopherol concentrations (risk estimates were adjusted for age at blood sample collection, trial intervention arm, serum total cholesterol concentration, body weight, urban residence and education).[162] These findings are even more remarkable given the continued cigarette smoking by the subjects during and after the study and the data from a 20-year prospective observational study of 17,633 white males aged 35 years and older (the Lutheran Brotherhood Cohort Study) that confirm that the use of tobacco products increases the risk of developing prostate cancer.[163]

The results of prospective observational studies also support the conclusion that increased consumption of vitamin E reduces the risk for prostate cancer.[86-88,164,165] For example, although the results of an 8-year prospective observational study (the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial) suggest that among all men, differences in vitamin E or a-tocopherol intakes from foods or dietary supplements do not affect the multivariate-adjusted risk of developing prostate cancer (adjusted for age, daily energy intake, race, study center, family history of prostate cancer, BMI, smoking status, physical activity, daily consumption of fats and red meats, history of diabetes and aspirin use) among current smokers and nonsmokers who had quit smoking within 10 years, daily dietary supplementation with more than 400 IU of vitamin E reduces significantly the risk of developing advanced prostate cancer (OR, daily dietary supplementation with more than 400 IU of vitamin E vs none: 0.29; 95% C.I.: 0.12, 0.68; adjusted for age, daily energy intake, race, study center, family history of prostate cancer, BMI, smoking

status, physical activity, daily consumption of fats and red meats, history of diabetes and aspirin use).[88] Similarly, among current smokers and nonsmokers who had quit smoking within 10 years and who had consumed any amount of supplemental vitamin E for at least 10 years, daily dietary supplementation with vitamin E reduces significantly the risk of developing advanced prostate cancer (OR, supplementation with any amount of vitamin E for at least 10 years vs none: 0.30; 95% C.I.: 0.09, 0.96; adjusted for age, daily energy intake, race, study center, family history of prostate cancer, BMI, smoking status, physical activity, daily consumption of fats and red meats, history of diabetes and aspirin use). Consistent with this report, in a 17-year prospective study of 2,974 men in Basel, Switzerland, serum vitamin E concentrations < 30.02 uM increased significantly the risk of developing prostate cancer among cigarette smokers (RR: 19.89; 95% C.I.: 3.60, 109.80).[86,87] On the other hand, the results of the double-blind, randomized placebo-controlled Prevention Research Veteran Affairs E-vitamin Nutrition Trial indicated that daily supplementation with 400 IU of vitamin E produced a significant increase in mean serum a-tocopherol concentration without affecting mean serum prostate specific antigen concentration[164] and the results of a 10-year prospective observational study of 35,242 men conducted in Washington State indicated that the risk for advanced (regionally invasive or distant metastatic) prostate cancer was reduced significantly by daily supplementation with at least 400 IU of vitamin E (HR: 0.43; 95% C.I.: 0.19, 1.0; adjusted for age, family history of prostate cancer, history of benign prostatic hyperplasia, income, use of multivitamins and serum prostate specific antigen concentration).[165]

The results of retrospective observational studies also support the conclusion that increased consumption of vitamin E reduces the risk for prostate cancer.[95,166-168] In a case-control study conducted in Serbia, the odds of developing prostate cancer were reduced significantly by greater daily intakes of a-tocopherol (OR: 0.15, 95% C.I.: 0.05, 0.53)95 and in a case-control study conducted in Athens, Greece, the odds of developing prostate cancer were inversely correlated with vitamin E intakes.[166]

In a case-control study nested within a prospective study conducted in Washington County, MD, the multivariate-adjusted odds of developing prostate cancer were reduced significantly when serum a-tocopherol concentration was greater than 1.31 mg/dl, serum gamma-tocopherol concentration was greater than 0.28 mg/dl and serum selenium concentrations was either less than 0.79 ppm (OR: 0.34; 95% C.I.: 0.12, 0.99; adjusted for age, education and hours since last meal when blood was obtained) or greater than 0.79 ppm (OR: 0.27; 95% C.I.: 0.10, 0.72; adjusted for age, education and hours since last meal when blood was obtained).167 Consistent with this report, in a case-control study conducted in India, mean erythrocyte ascorbic acid content and mean plasma vitamin E concentration were significantly lower among patients with prostate cancer.[168]

In contrast to this body of supportive evidence, the results of prospective[85,89,169,170] and retrospective[91,94,96,97,101,171-174] observational studies did not provide support for the conclusion that increased consumption of vitamin C reduces the risk for prostate cancer. After 10 years of observation, those among the 47,780 men participating in the prospective US Health Professionals Follow-Up Study who consumed dietary supplements containing vitamin E exhibited no change in their multivariate-adjusted risk of developing prostate cancer (adjusted for period of study, age, family history of prostate cancer, vasectomy status, smoking status, current BMI, BMI at age 21 years, physical activity level at entry into study, daily energy intake and daily intakes of calcium, lycopene,

fructose and total fat).[169] Similarly, among the 72,704 men of the American Cancer Society Cancer Prevention Study II Nutrition Cohort, the risk of developing prostate cancer was not affected by the intakes of vitamin E from either foods or supplements,[170] among the 475,726 men participating in the 18-year prospective observational American Cancer Society Cancer Prevention Study II, daily dietary supplementation with vitamin E did not affect the multivariate-adjusted rate of death from prostate cancer (adjusted for age, race, education, smoking status, family history or prostate cancer, exercise, BMI, alcohol consumption, vegetable consumption and dietary supplementation with multivitamins, vitamin A and vitamin C)[85] and the results of a 6.3-year prospective observational study of 58,279 men aged 55 to 69 years (the Netherlands Cohort Study) indicated that the age- and sex-adjusted risk of developing prostate cancer was not affected by differences in vitamin E intakes in that study population.[89]

In case-control studies conducted in Sweden[94] and Montreal, Quebec, Canada,[96] the odds of developing either any form of prostate cancer or advanced prostate cancer were not affected by differences in daily intakes of vitamin E (adjusted for age and daily energy intake). In a case-control study conducted in the state of Washington in the US, the multivariate-adjusted odds of developing prostate cancer were not affected by the use of any dietary supplements of vitamin E (adjusted for dietary intakes of fat and total energy, race, age, family history of prostate cancer, BMI, serum prostate specific antigen concentration and education).[91]

In a case-control study nested within the prospective Beta-Carotene and Retinol Efficacy Trial (CARET) of dietary supplementation of 18,314 high-risk subjects (heavy smokers and workers exposed to asbestos) with placebo, beta-carotene or retinyl palmitate, the multivariate-adjusted odds of developing prostate cancer were not affected by differences in prestudy serum a-tocopherol concentrations (adjusted for study center, asbestos exposure, age, sex, smoking status during study, year of entry into study and cigarette smoking history prior to the study).[171] Similarly, in a case-control study nested within the 8-country European Prospective Investigation into Cancer and Nutrition (EPIC), the multivariate-adjusted odds of developing prostate cancer were not affected by differences in prestudy plasma a-tocopherol concentrations (adjusted for BMI, smoking status, alcohol consumption, level of physical activity, marital status and education).[172] In individual case-control studies nested within a prospective study in Washington County, MD, prediagnostic serum vitamin E concentrations were not associated with the odds of developing prostate cancer[101,173] and when the data from 2 case-control studies conducted in Washington County, MD were combined, the odds of developing prostate cancer were found to be unaffected by differences in serum concentrations of a-tocopherol.[97] In a case-control study conducted in Hawaii, the multivariate-adjusted odds of developing prostate cancer were not affected by differences in serum a-tocopherol concentrations.[174]

The scientific evidence indicates that increased consumption of vitamin E reduces the risk for prostate cancer. The evidence documented by a secondary endpoint analysis of the data obtained during a prospective trial,[122,156-158] the results of two systematic reviews,[159,160] 6 prospective observational studies[86-88,163,165,166] and 4 retrospective observational studies[95,166-168] supports this conclusion and there is no evidence that increased consumption of vitamin E increases the risk for prostate cancer.

Conclusions

The foregoing credible scientific evidence establishes that adequate intakes of vitamin C and vitamin E safely reduce the

risk for cancer in general. Individually, vitamin C reduces the risk for bladder cancer, breast cancer, cervical cancer, colon cancer, colorectal cancer, endometrial cancer, adenocarcinoma of the esophagus, squamous cell carcinoma of the esophagus, gastric carcinoma, lung cancer, cancer of the oral cavity, ovarian cancer, pancreatic cancer, pharyngeal cancer, prostate cancer, renal cell cancer, and cancer of the salivary glands. Vitamin C also may reduce the risk of laryngeal cancer. Individually, vitamin E reduces the risk for bladder cancer, brain cancer, breast cancer, cervical cancer, colon cancer, colorectal cancer, adenocarcinoma of the esophagus, squamous cell carcinoma of the esophagus, gastric carcinoma, lung cancer, melanoma, cancer of the oral cavity, ovarian cancer, pancreatic cancer, pharyngeal cancer, prostate cancer, and renal cell cancer. Vitamin E also may reduce the risk of laryngeal cancer and rectal cancer.

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Vitamin D (25-OH-D3) Status of 200 Chronically Ill Outpatients Treated at The Center

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There have been many studies recently concerning the proper amount of Vitamin D (25-OH-D3) that is necessary to combat the many diseases that are now being associated with vitamin D deficiencies. Two studies examined the vitamin D status of hospitalized patients, general population and those admitted to a rehabilitation hospital.[1,2] The study of hospitalized patients found the vitamin D status of sub-optimal to overt deficiency levels to be a common finding. The same findings were found in 51 non-hospitalized volunteers. It also found that sub-optimal levels of vitamin D increased the length of stay (LOS) in hospitalized patients.[1]

A study of 100 patients, men and women with various diagnoses (mean age of 70 years) admitted to a rehabilitation hospital found that 11% of the patients to be overtly vitamin D deficient (<8.0 ng/mL) and "ninety-four percent" of the patients had sub-optimal levels (<32 ng/mL) of vitamin D. A simple, inexpensive treatment with vitamin D (25-OH-D3) could improve the patient's functional ability, decrease the LOS and dramatically reduce the cost of health care.[2]

The Center only treats chronically ill patients with various diseases on an outpatient basis. Based on geography, most of our patients come from the mid-West. However, patients have come from every state in the U.S. as well as from over 40 foreign countries. To check the finding of sub-optimal or deficient vitamin D in patients with various illnesses, we examined the vitamin D (25-OH-D3) levels that were ordered on 200 patients seen at The Center over the past four months. The test was performed in our own BioCenter Laboratory (www.biocenterlab.com) using the DiaSorin® R.I.A. method. Reference ranges were established from data collected from our patient population and cross checked with other laboratories.

Table 1 (p.89) shows some of the demographic data and preliminary results. Sixty-six percent of the patients were female and the ages of all patients ranged from 6 to 91 years of age with a mean age of 55 years. Results of the vitamin D tests ranged from 5.0 ng/mL (overt deficiency) to 96 ng/mL. The mean range of the 200 tests was 32.5 ng/mL (sub-optimal). The optimal range of The BioCenter Laboratory is 40 to 80 ng/mL.

Table 2 (p.89) shows the results of patients based on four different classifications. Considering that the minimum optimal range is 40 ng/mL, 152 patients (76%) had less than optimal vitamin D levels. It does appear that the older the patient, the lower the level. One 78-year old female had a value of 5.0 ng/mL; 3 females age 60 and one male age 66 had levels of 6.0 mg/dL. Only 48 patients (24%) had optimal levels of vitamin D.

These data tends to confirm that patients suffering from different disease and older patients have low or sub-optimal levels of vitamin D. It has been shown in many studies that vitamin D deficiency is a contributing factor for hypertension, diabetes, multiple sclerosis, rheumatoid arthritis, insulin-resistance, early age macular degeneration, bone health, depression and cancer.[3,4,5] Most of the patients in this study had one or more of these diseases.

How can this international finding of

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deficient or sub-optimal vitamin D levels be corrected? Plenty of sunshine (UVB) without layers of sunscreen, eating foods high in vitamin D, supplementation with vitamin D, to name a few. The RDA is designed to prevent deficiency diseases such as osteomalacia or rickets, not to maintain good health. The RDA in the U.S. of 400 IU/day is entirely too low to prevent the diseases shown above. The RDA should be at raised to maintain a level of 2000-4000 IU/day.[6,7] This is the amount routinely prescribed by The Center's physicians.

Although the data is too limited to be statistically significant, one other interesting finding in this study is that in some patients with sub-optimal vitamin D levels, Co-Q10 enzyme levels were also in the low range. Not every patient that had vitamin D test ordered had Co-Q10 ordered. The Co-Q10 test was also performed in our laboratory and the reference ranges are 0.3 to 1.5 ug/mL. **Table 3** (below) There were 41 patients in the sub-optimal vitamin D range. The Co-Q10 tests on these patients ranged from 0.1 to 0.6 - very low. We will examine these data on future patients to determine if there is any physiological and/or biochemical connection between the two tests.

Table 1. Data on number, age and vitamin D (25-OH-D3) results on 200 chronically ill out patients.

Number = 200	Age- Years	Results, ng/mL Vitamin D (25-OH-D3)
Females = 132 (66%)	Range = 6 to 91	Range = 5 to 96
Males = 68 (34%)	Mean = 55	Mean = 32.5

Table 2. Vitamin D (ug/dL) ranges based on classification of results and gender on 200 patients.

Deficient	Insufficient	Expected Range	Optimal Range
1 to 5.0 ng/mL	6 to 14 ng/dL	15 to 40 ng/mL	> 40 ng/mL
Male = 1 (0.5%)	Male = 5 (2.5%)	Male = 50 (25%)	Male = 12 (6%)
Female= 0	Female = 10 (5.0%)	Female= 86 (43%)	Females = 36 (18%)
Totals= 1 (0.5%)	15 (7.5%)	136 (68%)	48 (24%)

Table 3. Comparison of limited numbers of Co-Q10 to sub-optimal vitamin D levels.

Number	12	23	6
Vitamin D Range	12-20 ng/mL	21-30 ng/mL	31-40 ng/mL
Range Co-Q10	*0.1-0.8 ug/mL	.1-1.0 ug/mL	0.1-0.6 ug/mL
Mean Co-Q10	0.3 ug/mL	0.4 ug/mL	0.3 ug/mL

*= reference range for Co-Q10 at our laboratory = 0.3 to 1.5 ug/mL

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Oriental Medicine and Orthomolecular Medicine: Six Lyme Disease Cases Examined from Both Perspectives

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Abstract

Interconnection and cross-cultural learning is as important in modern medicine as it is in the rest of contemporary life. This case study documents six chronic Lyme disease cases as observed through both Orthomolecular and Oriental Medicine approaches. These two medical paradigms were cross-referenced and both found disorders of microcirculation with blood coagulopathy. A cross-cultural review demonstrates that Oriental Medicine provides a more specific treatment to address blood coagulopathy than does Orthomolecular Medicine.

Introduction

The Chinese have taken most of the credit for the development of acupuncture and herbal therapies. After the Cultural Revolution in 1959, acupuncture and its related therapies were modernized and named Traditional Chinese Medicine or TCM. Many of the more ancient principles, which were associated with alchemical elements and religious disciplines, were then banned in China, with dire consequences for those who made any attempt to preserve these philosophies. However, in adjacent regions such as the Japan, Korea, India, and Taiwan, acupuncture and its related therapies continued to flourish and were not affected by the restrictive political and intellectual climate of China. Acupuncture and its related therapies in these countries maintained a combination of ancient techniques and modern methods of application. Recognition in these countries outside China of this combination of old and new acupuncture-associated traditions resulted in what is now termed Oriental Medicine (OM).

OM practices date back as far as 2000 B.C., but the West has imported and developed these therapeutic principles and techniques only in the past 30 years. OM is not standardized, either within Asia or the West, and styles of acupuncture and its application vary as much as any other medical specialty.

In the United States, although there are no standardized care protocols, there are national standardized credentialing requirements for licensed acupuncturists. There are 36 accredited educational programs, which demand from 2,500 to 3,000 hours of training, extended over three to four years of full-time study. In California, acupuncturists are required to undergo 3,000 hours of training because they are classified as primary-care providers.

There are approximately 20,000 licensed acupuncturists in the United States with licensure in all but two states.[1] There is a national board exam and Continuing Education Units (CEUs) required biannually to maintain licensure. In certain states, a state board exam is also required. A Doctor of Acupuncture and Oriental Medicine (DAOM) is the highest formal education credential available in the field of acupuncture in the United States. There are currently three nationally-accredited DAOM programs; these require 1,200 hours of graduate didactic and clinical training beyond an existing state acupuncture license.

Additionally, the American Medical Acupuncture Association offers a 300-hour Continuing Medical Education (CME) program offered only to medical

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doctors who are interested in studying acupuncture. This program does not result in a special license or a required board exam. Also, it is not required to accrue ongoing continuing education in order to practice acupuncture. There are approximately 5,000 medical doctors in the U.S. who have completed this program.[2]

Validating OM with Western Measurement

With the growth of acupuncture as an increasingly mainstream medical specialty in the United States it not surprising that the National Institute of Health (NIH) has taken considerable interest in this medical specialty.

As long ago as 1999, the NIH and its Complementary and Alternative Medicine (CAM) division allotted ninety million dollars to perform acupuncture research.[3]

Investigational studies have continued to be funded by the NIH. Billions of dollars have been spent researching OM in an effort to verify that the ancient healing principles of the East have statistical validity. Scientific studies have cross-referenced Western medical findings with those indicated by acupuncture. Functional MRI (fMRI) brain imaging has demonstrated cortical tissue response that maps one medical tradition to the other. The goal of these investigative studies that cross-reference practices of OM with diagnostic imaging is to reveal after thousands of years of clinical use how OM actually works.

The application of state-of-the-art medical technology to the low-tech, millennia-old practice of acupuncture seems at first to represent scientific overkill, but several preliminary explorations in this "West meets East" field of inquiry have yielded extremely promising results. Just as brain imaging is used on acute ischemic stroke patients to assess the need for administering so-called clot busting drugs, research is being conducted to look more closely at how diagnostic imaging can elucidate where acupuncture impacts the brain.

A collaborative study between the University of California-Irvine and university medical centers in Seoul, Korea used fMRI to observe the correlation between traditional acupuncture points for the treatment of eye disorders and the corresponding brain localization for vision. This was a small study of 12 volunteers.[4]

Stimulation of the prescribed acupuncture point activated the occipital lobes seen in the center of this fMRI (**Figure 1**, below). On the left is a depiction of

Figure 1. MRI showing stimulation of prescribed acupuncture point activating the occipital lobes.

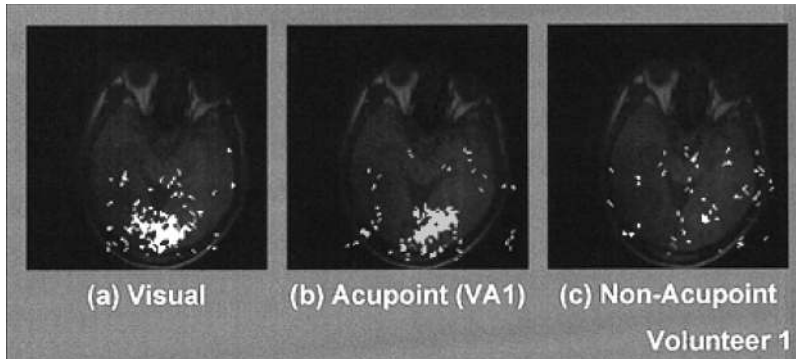
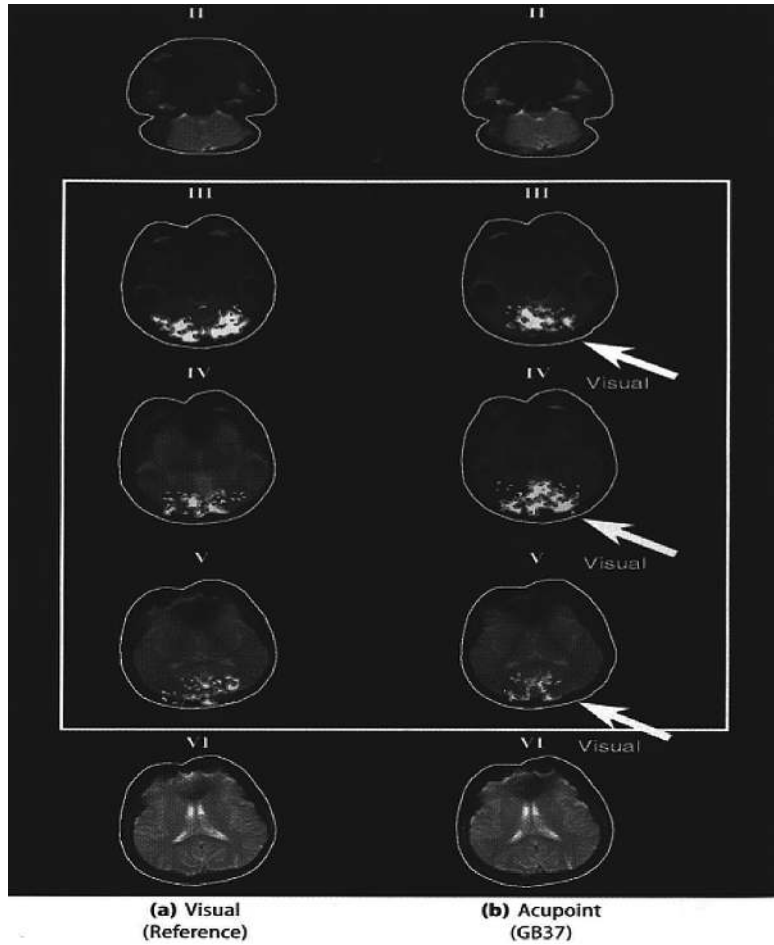


Figure 2. Cortical-activation map shows the result of acupuncture stimulation on another vision-related acupuncture point on the Gall Bladder channel (GB.37).



the occipital lobes when the eye had been stimulated by an eight-Hz flash stimulator. The results showed similar activation in both occipital lobes regardless of the source of stimulation.

As a control, acupuncture points were stimulated 2-5 cm away from the vision-related acupuncture points. These control acupuncture points did not activate the occipital lobes, as shown on the fMRI on the far right; compare to the visual-cortex activation as initiated by the vision-related acupuncture points and the light stimulator.

The acupuncture points used in this study were located on the Urinary Bladder channel. They were named here as VA1 thru VA8. The Urinary Bladder is unique because it is the longest meridian of the body and includes 67 specific points. This meridian follows the vertebral column. There, it connects to each of the intra-thoracic body organs, enters the intrathecal space and brain, then doubles back and

extends more superficially down the leg to the outer foot and 5th toe metatarsal where the points in this study were stimulated.

A separate cortical-activation map (**Figure 2**, p. 93) shows the result of acupuncture stimulation on another vision-related acupuncture point on the Gall Bladder channel (GB.37). The observations from this fMRI showed visual-cortical activation from both direct retinal stimulation from a flashing light (shown in column a) and acupuncture application to another vision-related point GB.37 (shown in column b). Cortical stimulation looks comparatively the same in both groups.

This research shows that physiological effects initiated by the ancient modalities of acupuncture can be documented by modern Western technology. Despite these physiological parallels, the medical terminology used to describe functions within each of these medical paradigms is not so neatly equivalent. The lack of common descriptive terminology prevents cross-referencing of common medical findings and hinders coherent communication between these medical paradigms.

Translating between OM and OMM

Figure 3 (below) shows a correlation of OM therapeutic language with the physiological goals as described by Orthomolecular Medicine (OMM) terminology.

These descriptions demonstrate the distinctly different languages used by the two medical paradigms. Bearing essentially the same message, both medical paradigms support ideal regulatory function or balanced homeodynamic physiology. In OM, this same healing philosophy is articulated as the intent to enhance and maintain uninterrupted Qi flow and promote microcirculation to the central nervous system and all organ tissues.

The best description of Qi (pronounced "chee" by the Chinese, or "key" by the Japanese) is that it is the vital impulse that keeps the heart beating. It might be understood as the life force itself. Similar concepts in other cultures would be "spiritus" in Roman mythology or Christianity, or "mana" in Polynesian mythology. It is measured only in its detriment–otherwise it is taken for granted that it is present in adequate amounts. Put in Western medical terms, the Qi function keeps mitochondria healthy enough to manufacture adequate ATP for life-sustaining activities.

Both OMM and OM see illness as an opportunity to change and improve health. Both emphasize prevention and early intervention.

Treatment Goals in OMM

Improve detoxification pathways
Support the immune function
Reduce inflammation
Balance hormones
Correct nutrition

Figure 3. Oriental Medicine therapeutic language with the physiological goals as described by Orthomolecular Medicine terminology.

OMM deals with the body's regulatory functions	OM deals with the body's innate qi status
Serious illness can be prevented by good regulatory system functioning	Serious illness can be prevented by reinforcing adequate measurements of qi flow
Goal: Sound cellular metabolism and mitochondrial respiration	Goal: Uninterrupted qi and blood flow to all body tissues and organs

Treatment Goals in OM
Regulate and circulate the flow of Qi
Warm and remove cold from the body
Enhance microcirculation
Control the regulation of the interior and exterior

OMM and OM may appear to have different treatment goals, given the differences in language.

In OMM, treatment goals focus on methods of detoxification and, for example, look to the enhancement of methylation, glycation, and glucoronidation pathways.

The treatment goals of OM, however, focus on a process of regulating the flow of vital life force or Qi, removing the constrictive effects of cold, and enhancing effective microcirculation. Controlling both the body's interior and exterior implies the importance of its largest organ, the skin. The skin's multifunctional structures and layers, along with its enormous protective and regulatory function of blood and lymph circulation, is all but ignored in the Western biomedical paradigm but is of paramount importance in OM.

Treatment Modalities of OMM
Laboratory testing
Physical exam
Kinesiology
Nutrient Therapy

Treatment Modalities of OM
Abdominal and body palpation
Pulse analysis
Tongue analysis
Acupuncture techniques
Herbal therapies

Obviously, OMM and OM use dissimilar diagnostic and treatment methods. OMM relies primarily on a reductionist approach that analyzes objective findings and treats with countering replacement nutrients. OM relies on more of a holistic dynamic that simultaneously observes and treats multiple systems and includes herbal therapy as a whole foods approach.

Comparison between OM and OMM in Lyme Disease (Figure 4, p. 96)

Bearing these complementary medical paradigms in mind, I conducted a small retrospective clinical study in my medical practice with six Lyme disease patients.

As a brief review, Lyme disease is known as the fastest-growing vector-borne disease in the United States today. By 2006, the Centers for Disease Control has reported more than 19,000 cases annually.[5] These are primarily acute cases, with vast numbers of chronic disease cases remaining uncounted. Lyme disease is recorded in almost every state, with highest concentrations on the two coasts and in the Great Lakes region.

Although standardized treatment protocols are designed either for prophylaxis or for early recognition of acute Lyme disease, Johns Hopkins University online patient-education pages list Lyme disease in three stages:[6]
Early localized disease: skin inflammation.
Early disseminated disease: heart and nervous system involvement, including palsies and meningitis.
Late disease: motor and sensory nerve damage, brain inflammation and arthritis.

Accumulated resources summarize common symptoms and observations which include:
Erythema migrans–less than 50%
Fever–30-40%
Fatigue–60%
Flu-like symptoms–50%
Headache–40-50%
Stiff neck–30-40%
Myalgias–40-50%
Polyarthralgias–40-50%

Complications in the disease progression include:
Peripheral Neuropathy

Radiculoneuropathy
Atrioventricular nodal block
Pericarditis
Eye symptoms–Optic neuritis
Meningitis
Encephalopathy

Treatment protocols initiated by Lyme experts consist of multiple rotating antibiotics and symptomatic treatment. Periodic laboratory and diagnostic testing monitors the treatment course, which may last from months to years.

OMM strategies target nutritional deficiencies and the disorders of various detoxification pathways that interfere with eradication of the Lyme bacteria and its related pathogens.

OM's holistic approach offers restorative treatments that target the core constitutional imbalance.

Clinical observations of Lyme disease patients in my practice showed three subtypes of symptom complaints. These groups included:

Dizziness and Disequilibrium (D): Symptoms of vertigo, unsteady gait, woozy feeling, depth perception disorder

Arthralgias (A): Large and small joints unilateral or bilateral

Fatigue (F): Leading to cognitive decline and disability

These symptom categories were not mutually exclusive although each symptom category constituted a primary set of complaints.

Biomedical Laboratory Markers

Several laboratory markers were tracked throughout the course of treatment. Most observable were contributable factors to blood coagulopathy or haemorheology. The clinical intent was to monitor coagulation markers and genetic influences that change the course of optimal blood fluidity. Research has shown that changes in the blood and its constituents (for example, blood viscosity, blood viscoelasticity, blood plasma viscosity, erythrocyte and platelet aggregation and adhesion) all play a very important role in the appearance and development of many dangerous and chronic diseases associated with microcirculation.[7] Biomedical conditions such as cardiovascular disease, diabetes, renal failure, and apoplexy are more obvious conditions stemming from coagulopathy. There appears to be a direct connection between the scope of haemorheologic changes and the gravity of most critical conditions and their prognosis.

More recently, evaluation of chronic diseases like Lyme disease, fibromyalgia, and chronic fatigue, have shown evidence

Figure 4. Summary of a retrospective analysis comparing six patients with chronic lyme disease.

Background:
Current treatment protocols of Lyme disease are standardized regardless of each patient's health status

Objective:
Observe for subtypes in symptom patterns
Observe course of illness using OM; Compare biomedical and OM markers

Results and Conclusion:
Integrated medicine shortens the course of treatment and prevents illness progression
Microcirculation disorders are a common finding in both the OM and OMM.

of abnormal blood coagulopathy indicators. In a cohort study of 54 patients with Chronic Fatigue Syndrome and 23 controls, 92% of the patients had a demonstrable hypercoagulable state or low-level activation of coagulation.[8]

In this retrospective study of six Lyme disease patients, the following coagulation markers were measured periodically throughout the course of treatment.

Fibrinogen: Although it is a variable marker, fibrinogen is a major contributor to the accumulation of fibrin by the action and influence of thrombin production. Fibrinogen was repeatedly measured and averaged throughout the course of treatment.

Lipoprotein A (LpA): A highly heritable marker, Lipoprotein A is related to an increase risk of atherosclerosis and thrombosis. Its structure is similar to plasiminogen and tPA (tissue plasminogen activator) and competes for binding sites leading to reduced fibrinolysis.[9] LpA additionally stimulates PAI-1, which is a contributing factor to thrombogenesis.[10,11]

MTHFR (methylenetetrahydrofolate reductase): MTHFR is considered one of the many polymorphisms that can be measured and expressed as a heterozygous or homozygous heritable mutation. This mutation prevents a crucial link in converting homocysteine to methionine. Elevated homocysteine is a leading cause of increased risks of blood clotting and thrombosis.[12]

A model which looks to the influence of coagulation defects in the presence of chronic pathogens predicts that fibrin will be deposited and blood viscosity increased. In this model, chronic disease such as Lyme disease can become exacerbated and resistant to treatment. [13]

Patient Laboratory Results

Over the course of five years, as I treated six patients diagnosed with Lyme disease, I followed their contributory coagulation markers. The results revealed (**Figure 5**, below):

Patients with disequilibrium (D) showed elevated fibrinogen and LpA.

Patients with arthritis (A) showed consistently elevated fibrinogen and a heterozygous MTHFR.

Patients with fatigue and cognitive decline (F) showed less coagulation defects but showed one homozygous positive MTHFR mutation.

Patient summary of coagulation indicators suggest a strong link between hypercoagulopathy and the chronicity of Lyme disease.

OM Diagnosis

In OM, a diagnosis is based upon a combination of physical signs and symptoms unique to its medical methodology. Although each individual's clinical presentation may vary from visit to visit, the core constitutional diagnosis remains the same. This constitutional diagnosis is what long-term treatment is based upon.

The medical term "blood stasis" is

Figure 5. Patient summary of coagulation factors.

	D1	D2	A1	A2	F1	F2
Fibrinogen	High	High	High	High	Low	normal
MTHFR	Negative	+/-	Negative	+/-	Negative	positive
LpA	High	High	High	Normal	Normal	normal

commonly used in OM and implies biomedical pathology described as agglutination of RBCs, increased intracellular viscosity, or decreased plasticity of erythrocytes. In advanced blood stasis there may be increased fibrinogen, thombogenesis, or increased hematocrit.[13] The accumulative effect of these leading pathologies contributes to and results in symptoms of blood stasis.

Notable physical signs related to blood stasis (or, in OMM terms, hypercoagulopathy), include a radial pulse that is considered "choppy" or has a feeling of discontinuity. The pulse may also feel deep or hard as though the blood flow is impeded. The tongue may appear with a darker color or be slightly purple. The abdomen may feel tight and mildly tender, especially in the mid-epigastric area.

The primary and secondary diagnosis pattern for each of the six Lyme disease patients is outlined in **Figure 6** (below).

Based on these OM diagnoses, there is evidence of pathology related to the insufficiency of core organ systems. These core imbalances directly influence blood circulation and regulate its coagulation pathways.

OM and the Use of Chinese Herbs to Treat Blood Stasis

For millennia, Chinese herbs provided the basis for most treatment modalities practiced in China. This held true until Western medicine was introduced. Hundreds of herbs have been observed, researched and studied for every condition imaginable. In the past 25 years, these herbs have been imported into the Western hemisphere, where they have been used according to ancient principles. There are now strict growing and manufacturing processes that make Chinese herbs a safer alternative than in earlier days of their importation. Various sources of organic herbs are now also available. American and European collaborations with the Chinese have been instrumental in ensuring that herb quality now meets standards of good manufacture and processing.

The category of Chinese herbs classified as blood vitalizing or blood circulating herbs are of interest in the treatment of blood hypercoagulopathy.

One of the most commonly-known herbs in this category is Salvia miltorrhizae. The root of this common sage plant by chance is a deep red color. Its primary metabolite is a diterpene, most notably studied in the Pacific yew tree. The yew tree is best known for its extract originally developed by Bristol-Meyers Squibb to manufacture Paclitaxel or taxol. It is used as one of the most commonly prescribed chemotherapy agents in the treatment of breast cancer, classified as an anti-angiogenesis agent.

Additional blood anticoagulants found in Salvia miltorrhizae, also known as *dan shen* in Chinese pinyin terms, is salvianolic acid. In research studies salviol (or salviano-

Figure 6. Oriental Medicine diagnosis based on system patterns.

	Primary Diagnosis	Secondary Diagnosis
D1	Spleen qi deficiency	Damp heat in the gallbladder
D2	Stomach and kidney yin deficiency	Deficient heat rising
A1	Spleen qi deficiency	Damp bi and blood stasis
A2	Spleen qi deficiency	Stomach and gallbladder heat with shen disturbance
F1	Yin and yang deficiency	Damp heat toxin
F2	Spleen and kidney deficiency	Liver qi stagnation with wind symptoms

lic acid) has been demonstrated to inhibit platelet aggregation as a thromboxane inhibitor. Salviol increases cerebral blood flow after ischemia and has shown to increase the production of a potent vasodilator, nitric oxide (NO).[14] Additional chemical constituents such as tanshinones, also derived from *dan shen*, are protective against myocardial ischemia and reperfusion. Tanshinones have been found to increase the proteolysis of fibrinogen to fibrinogen degradation products.[15] There are also anti-inflammatory effects associated with its pharmacological activity.[16]

Numerous clinical trials have been performed in China using the herb *dan shen* orally and intravenously. Although some of these research studies would not match the standards of research methodology in the West, taken as a whole, these multiple clinical trials make compelling evidence of its beneficial effects as an anti-coagulant.

Conclusion

The parallels between different medical paradigms are evidence of conjoined practice principles. While Eastern and Western medical traditions demonstrate disparate cultures, language, and modalities, it is significant that blood stasis or hypercoagulopathy is becoming better known as a condition in the West but is an ancient remedied treatment in the East.

Recognizing subtypes in Lyme disease can help to identify more difficult-to-diagnose cases in the absence of definitive findings. These subtypes may assist in a more precisely guided, quickly implemented treatment protocol.

The evaluation of the pathophysiolgical and therapeutic implications of blood coagulopathy can influence a better prognosis and outcome of chronic disease.

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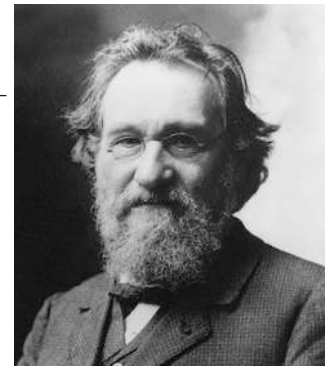
2009 Orthomolecular Medicine Hall of Fame

The following is excerpted from introductory remarks by Andrew Saul. For the full text of his presentation, please visit www.doctoryourself.com/2009HOF.html



Ilya Metchnikov, Ph.D.

T. L. Cleave, M.R.C.P.

"Welcome to the Sixth Annual Orthomolecular Medicine Hall of Fame inductions. I am representative of the malnourished generation. Typically, our mothers consumed too little folic acid while they were carrying us. We were bottle-fed on formula containing no biotin. Vitamin E wasn't even listed as an RDA item until 1968. We chowed down on "Wonder Bread," which supposedly, somehow built strong bodies 12 ways. We ate a lot of frankfurters. For dinner, our mom opened canned vegetables and then cooked them. On the other hand, my mother was at least partly orthomolecular. Having opened the cans, she drank the juice the vegetables were packed in, or put it into homemade soups. We were compelled to eat liver. My brothers and I each had to take a multivitamin every day, long before it was popular. We never had a day without orange juice, nor a day without whole grain cereals at breakfast.

And, we rarely went to the doctor; at five dollars a visit, it was "too damned expensive." When we did go, it usually had to be for a condition serious enough to require a tetanus shot, or an antibiotic.

Speaking of antibiotics, not everyone knows that Alexander Fleming, M.D., wrote, "Penicillin sat on my shelf for 12 years while I was called a quack. I can only think of the thousands who died needlessly because my peers would not use my discovery."

Orthomolecular researchers, educators and practitioners understand this all too well. Acceptance of nutrient-based therapeutics has been decades-long in coming. Tonight's honorees have been criticized, even ridiculed, in their time. These five very important gentlemen are being enrolled in our Hall of Fame not just because they were unappreciated, but because they were right.

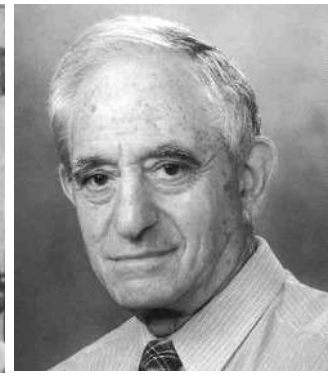
Perhaps we are what we eat after all. Dr. Abram Hoffer and I, in our new book *Orthomolecular Medicine for Everyone,* note that the average age of Orthomolecular Medicine Hall of Fame inductees is about 80 years of age. Nobel Laureate Dr. Albert Schweitzer was right: "Not only is example the best way to teach, it is the only way." Tonight we offer five outstandingly good examples.

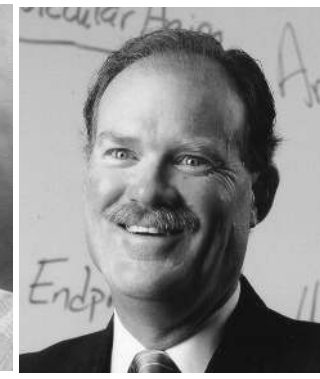
Ilya Metchnikov

"Death begins in the colon."

Born in 1845 in Ukraine, Ilya Metchnikov studied natural sciences at the University of Kharkov and pioneered research in immunology. In 1904, he became the deputy director at the Pasteur Institute laboratory in Paris from where he discovered the process of phagocytosis which demonstrated how specific white blood cells can engulf and destroy harmful bacteria in the body. His theories were radical and the "sophisticated" microbe hunters in the West –Pasteur, Behring and others–scorned the Russian and his humble theory.


Hugh MacDonald Sinclair, Ch.B.


Archie Kalokerinos, M.D.


Jeffrey Bland, Ph.D.

Nevertheless, history vindicated Metchnikov's brilliant theory and he was awarded the Nobel Prize for medicine in 1908. Although references to the nutritional power of fermented foods date back thousands of years, Metchnikov is regarded as the father of modern probiotics. He made a landmark observation that the regular consumption of lactic acid bacteria in fermented dairy products, such as yogurt, was associated with enhanced health and longevity in Bulgarian peasant populations. He linked this to the "Bulgarian bacillus" and he later demonstrated how healthy bacteria in yogurt helped digestion and improved the immune system. The reduction of the harmful bacteria coupled with the increase in good bacteria in the intestines appear to improve the immune system and reduce the burden on the cleansing organs such as the kidneys and liver.

The scientific rationale for the health benefit of lactic acid bacteria was provided in his book *The Prolongation of Life* published in 1907, in which he asserted that some of the bacterial organisms present in the large intestine were a source of toxic substances that contributed to illness and aging. This book also delved into the potential life-lengthening properties of lactic acid bacteria. He suggested that "The dependence of the intestinal microbes on the food makes it possible to adopt measures to modify the flora in our bodies and to replace the harmful microbes by useful microbes." He wrote two more books: *Immunity in Infectious Diseases* (1905) and *The Nature of Man* (1938).

In recognition of Metchnikov's place in the probiotic realm, the International Dairy Federation (IDF) created, in 2007, "The IDF Ilya Metchnikov Prize" to recognize outstanding scientific discoveries in the fields of microbiology, biotechnology, nutrition and health with regard to fermented milk products.

T. L. Cleave

"Cleave saw that many of the diseases of civilization could be explained as the consequences of eating refined carbohydrate, pointing out the crucial fact that refined foods are an artefact of technological civilization."

–Kenneth Heaton

Thomas Latimer Cleave was born in Exeter and entered the Bristol Medical School at the age of sixteen, finished his training at St. Mary's Hospital and went straight into the Royal Navy. There he was a medical specialist in various hospitals at home and abroad, ending up as surgeon captain and director of medical research until he retired in 1962.

After working in obscurity for many years, in the 1970s Cleave received international acclaim as the father of the dietary fibre hypothesis. His great vision was to see

that the human body was maladapted to the refined foods of civilization, primarily carbohydrates, sugar and white flour. He reasoned that if man avoided unnatural foods he would avoid unnatural diseases which were generally absent in wild animals or primitive communities. He spent his life gathering evidence and developing arguments to support this view, which culminated in his grand hypothesis that a range of diseases –from obesity, to diabetes, coronary heart disease, ulcers, dental caries, constipation and appendicitis–were caused by maladaptation to foods containing refined carbohydrates. Since they all had a common cause he viewed them as a single master disease, he called "the saccharine disease." His book of the same name, published in 1974, sold thousands of copies and was written in laymen's language that the public could readily grasp. In 1986, the British Medical Association finally answered Cleave's voice in the wilderness in its report *Food, Nutrition and Health*, which recommended an increase in consumption of fresh food and vegetables and whole grains.

One of Cleave's most effective advocates was Dr. Denis Burkitt, the legendary cancer researcher, and their collaboration was turning point in the fortunes of Cleave's hypothesis. Burkitt's connections with 150 third world hospitals enabled him to confirm many of Cleave's epidemiological observations. Burkitt acknowledged his debt to his friend, stating "Cleave was one of the most revolutionary and far-sighted medical thinkers of the twentieth century, seeing far beyond the small vision of intricate details of individual diseases."

Hugh Macdonald Sinclair

"He may prove to be one of those people whose long term influence is far greater than ever seemed likely while he was alive"

–David Horrobin

Hugh Macdonald Sinclair, was one of the twentieth century's outstanding experts in human nutrition. He was born in Duddington House, Edinburgh, Scotland, and went to Oriel College, Oxford to study Animal Physiology. He was appointed Departmental Demonstrator in Biochemistry, before going on to study Clinical Medicine at University College Hospital Medical School, London. Sinclair spent most of his working life as a Fellow of Magdalen College, Oxford, though he made many forays into a wider world, notably during the Second World War when he was involved in planning how the British could be properly nourished and in famine relief in the Netherlands and Rhineland.

Sinclair is most widely known for claiming that "bad fats" worsened what he called "diseases of civilization", such as coronary heart disease, cancer, diabetes, strokes and skin disease. He believed that diets deficient in essential fatty acids are the cause of most degenerative illnesses. Sinclair's forceful arguments on this matter preceded firm scientific evidence, however. His self-experimentation, including the infamous 100 day seal-meat diet, dramatically demonstrated the importance of long-chain fatty acids of fish oils in decreasing the aggregation of platelets and thus the incidence of thrombosis. Sinclair recognized the central importance of nutrition to human life and, at a time when it had become unfashionable, he constantly emphasized the importance of the right food for proper health. In a famous letter to the *Lancet* in 1956, he made a particular contribution in identifying the crucial role of essential fatty acids in health, which readers classed as either visionary or lunatic, depending on their point of view. His letter foreshadowed half a century of research on a nutritional topic which is steadily increasing in importance.

Sinclair's greatest dream was to establish an international centre for the study of human nutrition. He argued that nutrition is an important area of science in its own right, and that new insights into the relationships between food and human health

should guide developments in medicine, agriculture, and food technology. Many of his ideas have relevance for us today.

Archie Kalokerinos

"Any attempt to adequately write about Archie Kalokerinos would need a thousand pages and would incorporate many such adjectives as: far-sighted, intelligent, sensible, observant, honest, caring, altruistic, congenial, meticulous, brave, dogged, intrepid, and last but not least, the trite, but well-deserved, 'great.' " –Oscar Falconi

Archie Kalokerinos was born in Glenn Innes, Australia, in 1927 and took his MD degree from Sydney University in 1951. He was appointed Medical Superintendent of the hospital at Collarenebri, Australia, where he served until 1975. His practice is based on Linus Pauling's theory that many diseases result from excessive free radicals and can accordingly be prevented or cured by vitamin C.

Kalokerinos is well known worldwide as the doctor who spent much of his time fighting for the well-being of the Aboriginal inhabitants of Australia. He became very concerned about the high death rate of Aboriginal children in New South Wales and came to the conclusion that the infants had symptoms of scurvy, a deficiency of vitamin C. In his ground-breaking book, *Every Second Child,* he discovered that the an acute vitamin C deficiency provoked by the vaccinations was the reason why, at a certain point, up to half of the vaccinated Aboriginal infants died. Instead of being rewarded for this lifesaving observation, Kalokerinos was harassed and his methods were disregarded by the authorities, probably because they were too simple, too cheap and too efficacious to be accepted by the vested interests of modern medicine. Besides, they were meant to protect a population which, in its own native county, is regarded by some as not worth taking the trouble for anyway. Dr. Kalokerinos, thought differently, and the Nobel prize winner Linus Pauling, (who wrote the foreword to *Every Second Child*) endorsed his views.

Kalokerinos is a Life Fellow of the Royal Society for the Promotion of Health, of the International Academy of Preventive Medicine, of the Australasian College of Biomedical Scientists, of the Hong Kong Medical Technology Association, and a Member of the New York Academy of Sciences. In 1978 he was awarded the AMM (Australian Medal of Merit) for outstanding scientific research. He is an author of 28 papers listed in PubMed. He retired from full time practice in 1993 and spends most of his time doing private research.

Jeffrey Bland

"Jeff is the most important innovator and educator in natural medicine in North America." –Abram Hoffer

Jeffrey Bland was born in 1946 in Illinois, and grew up in Southern California, where he graduated from the University of California, Irvine, in 1967 with degrees in biology and chemistry. In 1971, he completed his doctorate degree in synthetic organic chemistry and began his career as a university professor and researcher at the University of Puget Sound with a dual appointment in Chemistry and Environmental Sciences. From 1976-1995, he served as a prominent educator for the natural foods and nutritional supplement industries and was involved in the founding of Bastyr University of Natural Health Sciences in Seattle, the first accredited university of naturopathic medicine in North America. In 1981, Bland was invited by Linus Pauling to become the Director of Nutritional Supplement Analysis at the Linus Pauling Institute in Palo Alto, California.

In 1984, he started HealthComm, a company dedicated to teaching physicians and other licensed health care providers how to successfully implement nutrition intervention into their practices. Since 1978, Dr. Bland has authored four books on

nutrition and health for the general public and six books for health professionals. He is also the principal author of over 100 peer-reviewed research papers on nutritional biochemistry. With his establishment of the Institute for Functional Medicine in 1991, Jeffrey Bland conceptualized functional medicine as a patient-centered systems biology approach to medicine. Utilizing his *Textbook of Functional Medicine,* first published by the Institute in 2005, Dr. Bland introduced the concept of functional medicine to Europe, Asia, Mexico, Brazil, Australia, and New Zealand.

Since 2000, Jeffrey Bland has served as the Chief Science Officer of Metagenics and the President of Metaproteomics, a nutrigenomic research and development company employing more than 40 scientists and physicians at its research centers. Dr. Bland merged his company, HealthComm International, with Metagenics, the combined Metagenics has become the largest global nutraceutical and medical food company serving the fields of functional and integrative medicine. In 2006, Jeffrey Bland established "Synthesis" on his website to serve as a repository for his functional medicine educational materials.

2009 Orthomolecular Doctor of the Year Aileen Burford-Mason, Ph.D.

Aileen Burford-Mason receives the award from 2008 recipient, Jim Jackson, PhD,, the lab director and senior research consultant at the Bio-Center Laboratory, Wichita, KS. The award is inscribed: "For Your Dedication as an Educator, Researcher, Practitioner and Spokesperson in the Advancement of Orthomolecular Medicine"

The recipient of the 2009 Orthomolecular Doctor of the Year Award, Aileen Burford Mason, is a nutritionist and immunologist with a deep interest in the evidence base for orthomolecular medicine. Dr. Burford-Mason has authored articles in many fields including gastroenterology, pathology, cancer, and infectious diseases. She has presented at Orthomolecular Medicine Today Conferences on the orthomolecular approach to candida, insomnia, and addiction. Dr. Burford-Mason maintains a private practice as a biochemical nutrition consultant in Toronto. Her long-time advocacy and tireless promotion of orthomolecular medicine to the public and to practitioners has made her an invaluable leader in our cause.

Jack Challem
Dysglycemia–The Common Factor in Mental Disorders

Jack Challem's talk focused on the dyglycemia, the syndrome of clinical features which often progress to diabetes, heart disease, obesity and negative cognitive effects. Prediabetes is of vital interest because it can be reversed through relatively simple dietary strategies. Prediabetes is intertwined with obesity, and is an often overlooked problem in diet failures

The early signs of prediabetes, according to Jack, are hyperinsulinemia, insulin resistance, reactive hypoglycemia and abdominal obesity. Dietary causes include too many refined carbohydrates, trans fats and junk oils and too many calories-Americans eat 3,900 calories a day, but they only need 2,000 for health maintainence.

Jack cited useful laboratory tests for assessing prediabetes including fasting glucose, fasting insulin and glycated hemoglobin. Interventions include a focus shifting to protein rich Mediterranean and paleo diet models and using the glycemic index. He ended his talk with his own experiences in the grip of prediabetes. After instituting his own recommendations eating fresh, minimally processed foods, smaller and smaller fibre portions he lost 20 pounds and reversed the physiological biomarkers of his own prediabetes.

Doron Gothelf, MD
Pediatric Psychiatry

Doron Gothelf, MD, is a professor of psychiatry at Sackler Faculty of Medicine, Tel Aviv University, director of the Child Psychiatry Outpatient Clinics at Schneider Children's Medical Center of Israel. He has published more than 70 peer-reviewed articles in the field of child psychiatry, psychopharmacology, genetics and neuroscience.

Dr Gothelf outlined two current challenges of psychiatry i.e. current medications do not treat causes or mechanisms of psychiatric disorders, which remain largely unknown, and approved medications are less effective in children but have more serious adverse effects. Dr Gothelf recommended the following:

Personalized medicine includes pharmacogenetics, and medication that targets causes or deficits of disorders This approach, he states, will bring psychiatric treatment out of the '50s to the present time.


Jack Challem


Doron Gothelf, MD


Natash Campbell-McBride, MD


James Greenblatt, MD

Natasha Campbell-McBride, MD
Gut and Psychology Syndrome

Natasha Campbell-McBride, MD, practiced in Russia as a neurologist and a neurosurgeon and then moved to the UK. After her son was diagnosed with autism she developed her theories on the relationship between neurological disorders and nutrition, competing a second degree in Human Nutrition. She opened the Cambridge Nutrition Clinic and has written several books.

Dr Campbell-McBride introduced the Gut and Psychology (GAP) Syndrome, a combination of digestive problems, asthma, eczema, bed wetting, chronic cystitis, allergies, malnutrition and thrush. In children the syndrome is connected to autism, ADHD, dyslexia as well as learning, behavioural and social problems. In adults, it is often present with substance abuse, depression and mental disorders.

Dr. Campbell McBride stressed the critical need to re-establish normal gut-flora in GAP patients. The key supplements are vitamin A, EFAs, mineral amino-acids and digestive enzymes. With these treatment recommendations, a major component of psychological disorders can be addressed.

James Greenblatt, MD
Orthomolecular Treatment for Eating Disorders

James Greenblatt, MD, is the Chief Medical Officer of Walden Behavioral Care in Waltham, Massachusetts. He has been treating patients with complex eating disorders since 1988. He is also an Assistant Clinical Professor at Tufts University Medical School, Department of Psychiatry.Dr. Greenblatt explained that, although genetics plays a role, nutritional deficiencies during puberty may affect gene expression in the onset/maintenance of anorexia nervosa. A SAD diet, stress, excess estrogen, vegetarianism can all contribute to a depletion of key nutrients, particularly zinc, that can trigger the onset of AN.

Dr. Greenblatt highlighted prevention strategies for AN based on better understanding of risk factors and triggers. Although risk factors may not all be reversible, environmental and nutritional modulators can be.

Aileen Burford-Mason, PhD
Orthomolecular Treatment for Insomnia

Aileen Burford-Mason, PhD, is an immunologist, cell biologist and nutritionist with a focus on orthomolecular medicine. She co-founded the Holistic Health Research Foundation Canada.

Dr. Burford-Mason presented evidence of the significant effect of sleep deprivation on cognitive function, immunity, weight gain and mood. Recommended prophylaxis included lifestyle changes such as sleeping in complete darkness and an optimal diet rich in nutrients for the brain, Key supplements for insomnia are l-theanine, 5-HTP, melatonin and magnesium. Dr. Burford-Mason recommended the amino-acid or protein chelated forms for oral ingestion, magnesium gel for use topically and Epsom salts for the bath. With these nutrients considered a deep, healthy and regenerating sleep can be assured.


Aileen Burford-Mason, PhD


Gary Ginsberg, DrPH


Alexander Schauss, PhD


Maret Traber, PhD

Gary Ginsberg, PhD
Prioritizing Mainstream and Non-mainstream Interventions

Dr, Ginsberg's presentation applied statistical cost-benefit analysis to compare orthomolecular and conventional medicine for the benefit of governments and health care insurers-in short those who hold the purse strings of our health-care system. A concept in the health industry, termed QALY, or "quality adjusted life year" is a new measure for cost-benefit analysis. A QALY measures a disease burden, including both the quality and the quantity of life lived and is based on the number of years of life that would be added by the intervention. As it turns out, this metric makes orthomolecular therapies score quite favorably.

Nutritional therapies can cause huge reductions in mortality and morbidity, but to demonstrate this through the QALY measure, high level studies are needed. The highest levels are randomized clinical trials, while the lowest are studies of before/after; or expert opinion. Orthomolecular medicine in its current state languishes in the evidence basement-very few of the studies are at the highest level. Ginsberg appealed to his colleagues to produce higher quality orthomolecular studies which would surely demonstrate a better way to care for the overall health of the population.

Alexander G. Schauss, PhD
Acai: The World's Richest Antioxidant

Alexander Schauss, is senior director of natural and medicinal products research for AIBMR Life Sciences. He gave a presentation on Acai, a type of Amazon palm fruit which is one of the most powerful antioxidants discovered. The Acai palm, said Schauss, can produce up to 1,000 kilos of fruit in a 7-10 year period, but because of its volatility and distance from western markets, it can only be handled by vacuum freeze drying. It is the freeze dried plant which is used in studies because only this form preserves the phytochemical content, enzymatic activities, nutritional value, antioxidant activity and taste. Schauss also detailed the mineral, amino acid, lipid, fiber and phytochemical content and antioxidant capacity of Acai.

Schauss spoke of brain health and oxidative stress and presented some studies on how Acai can be used to quench excessive free radicals which are implicated in many brain health issues such as Alzheimer's, Parkinson's, stroke and dementia.

Maret Traber, PhD
Vitamin E Revisited

Dr. Traber's presentation attempted to make sense of the years of equivocal studies on the efficacy of vitamin E in preventing chronic disease. The signs of vitamin E deficiency were discussed and despite the fact that 90% of men and 96% of women do not consume adequate Vitamin E, she noted that deficiencies are almost never due to low intake but rather poor fat absorption or impaired lipoprotein synthesis in the liver. The deficiency symptoms can be as diverse as peripheral neuropathy and muscle weakness

Maret went into the possible reasons the legacy of inconsistent conclusions


Michael Schacter, MD


John Hoffer, MD, PhD


Ron Hunninghake, MD


Jeffrey Bland, PhD

in vitamin E research. She ventured that some negative studies may be due to insufficient dose, type of participants and the use of the synthetic form of vitamin E.

Michael Schachter, MD
Making Decisions about Cancer Treatment

Dr. Schachter has been the medical director of the Schachter Center for Complementary Medicine in Suffern NY. His presentation focused on what patients need to consider before making decisions on conventional or orthomolecular cancer treatments, treatment course.

Integrative medicine evaluation is about treating the patient as a person, assesses strengths and weaknesses and evaluates their support systems, with a full clinical history and physical exam, assessment of lifestyle factors and a nutritional and laboratory testing. Schachter's Integrative lab testing checks for particular vitamins and any immune-supressive heavy metal burdens such as lead or mercury. Schachter's integrative cancer therapies use organic food, exercise, stress management, sunlight, sleep, supplements, detoxification and energy treatments. His advice to patients was simple: we are all entitled to make our own decisions about health, and we should be empowered not bullied by the medical establishment.

John Hoffer, MD, PhD
High Dose Ascorbic Acid and Cancer

Dr. John Hoffer has long been involved in investigating the effects of high-dose vitamin C in cancer therapy. He is not a voice in the wilderness by any means. It is estimated, he said, that 64-82% of cancer patients use nutritional supplements of their own, 14-32% start after diagnosis, and 68% of their physicians are unaware of this adjunctive therapy. Mainstream oncology's bias against vitamin C seems to be centered on conjecture that it may reduce the effectiveness of standard chemotherapy. To address this issue, Dr. Hoffer put forward a hypothesis that vitamin C may amplify the cytotoxicity of chemotherapy for cancer cells while quenching it for normal cells.

Whether antioxidants are beneficial or harmful is now a critical question, but one without a clear scientific answer at this time. When the evidence is inconclusive, Dr. Hoffer suggested that patient values, preferences and circumstances will loom larger than when the evidence is strong. Future evidence should focus on polished case histories, disseminated statistics.


David Quig, PhD


Patrick Holford

Ronald Hunninghake, MD
Oral vs Intravenous Vitamin C

Dr. Hunninghake, current chair of the ISF and director of the Kansas' Center for the Improvement of Human Functioning presented a talk which weighed the differences in oncology paradigms-what he termed allopathic vs orthopathic cancer therapies. Allopathic oncology represents establishment medicine and falls into a predictable pattern of treating the disease by determine the grade, killing cancer cells, and creating more oxidative stress with the quality of survival rather ignored.

The orthopathic approach, by comparison, is a path which Dr. Hunninghake follows and first and foremost concerns itself with treating the patient as a person, correcting the underlying causes of disease, strengthen healthy cells, lessening oxidative stress and improving the overall quality of life. Dr. Hunninghake also described the orthopathic approach created by his late colleague, Dr. Hugh Riordan. This is the "RECNAC" approach

which first developed the doctor-co-learner relationship and created a goal for the patient to heal themselves through learning and using the healing power of nature and food as medicine. Vitamin C is the main biological response modifier in cancer treatment which is known to boost immunity, stimulate collagen, inhibit hyaluronidase and relieve the general scurvy of cancer.

Jeffrey Bland, PhD
The Past, Present and Future of Orthomolecular Medicine

Jeffrey Bland has been teaching functional medicine to physicians, health care practitioners, students, and audiences around the world for over 20 years. Bland's presentation, laid out an historical overview of the early progenitors of orthomolecular medicine, the emergence of orthomolecular medicine per se, 40 years ago, and the issues practitioners will face in the future and ideas on how we may overcome them. In the present we are faced with a curious stand-off in assessing the efficacy of orthomolecular medicine. There often seems to be a discrepancy between the positive effects of orthomolecular therapy in observational studies which often fails to be confirmed in large randomized trials.

Bland then speculated on the future of orthomolecular medicine and he believes epigenetics will factor strongly in future studies of human diseases. Epigenetics may help explain the relationship between the genome and the environment and may provide clues for modifying these effects in disease prevention and therapy.

David Quig, PhD
Safe and Efficacious Metal Detoxification

Metal detoxification an oft-overlooked health optimizer, according to Dr. Quig. His talk covered hair and blood analysis, the best ways of assessing chemical and metal toxicity and also outlined the various ways of treating heavy metal overload in the body. Some ways are not generally known, such as boosting the body's endogenous chelating molecule, glutathione by supplementing with its precursors vitamin C, NAC, lipoic acid and glycine. Another of Quig's strategies is to increase dietary protein which helps to excrete metals, and use IV chelation for heavier metal burdens. Assessment is done in two basic ways. Hair analysis because metals irreversibly bind to hair and blood tests which can be used to assess recent acute exposures which is the gold standard, but not indicative of the body burden. Dr. Quig explained that particular metal burdens may respond to specific chelating strategies and provided the example of the amino acid, glycine, which if taken orally has the advantage of going right into cell, bringing metals to the extracellular surface, and pulling toxins out of cells. Glycine is best used in conjunction with other agents to remove toxins from the body.

Patrick Holford
Dysglycemia–The Common Factor in Mental Disorders

In 1984 Patrick Holford founded the Institute of Optimum Nutrition, the Food for the Brain Foundation and has also written a total of 29 best-selling books.

Mr. Holford presented studies linking high sugar diets and insulin resistance to depression, aggressive behaviour, dementia, memory loss and heart disease. Other studies showed an inextricable link between depressive disorders and metabolic syndrome, indicating that either condition often follows the other. This is consistent with an orthomolecular approach to treating disease.

In his book "The GL Revolution" Mr Holford recommends simple rules such as eating no more than 40/60 GLs a day; eating protein with carbohydrates; and grazing rather than gorge. These three simple steps can stabilize blood sugar levels, support weight loss and treat a plethora of physical and mental illnesses.

Information for Manuscript Contributors

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