



ARISTO VOJDANI

*Effects of Vitamin C levels on relationship
of Immune Function & Cancer*

Cubberly Community Center
4000 Middlefield Road, Room H1, Palo Alto, California

October 10, 2003 at 7:00 pm

MEET DR ARISTO VOJDANI

Dr. Vojdani obtained his Ph.D. in the field of microbiology and clinical immunology with postdoctoral studies in tumor immunology. His area of expertise includes early detection of cancer signals and markers, immune function disorders, immunotoxicology, chemically induced immune deficiency and autoimmune diseases, and immunoassay technology development. In the aforementioned areas, he is regarded as an inventor and currently has more than 20 different U.S. patents, awarded and pending.

Dr. Vojdani has published almost 100 articles in peer-reviewed journals. He is a member of the International Society for Preventive Oncology, the American Association of Immunologists, the American Association for the Advancement of Science, the Society of Toxicology, and the California Association for Medical Laboratory Technology.

He has testified before the US Senate Committee on Veterans Affairs, providing crucial evidence on the effect of chemical agents on veterans who fought in the Persian Gulf War. His testimony helped secure the passage of legislation that enabled the veterans to receive free medical care for neuroimmunological disorders acquired during service in the

Persian Gulf.

Plasma and Intracellular Levels of Antioxidants (ISL Patent No. 6,020,205)

Did you know that the majority of elderly people over 60 years of age often have vitamin deficiencies that can be detected only by measuring intracellular levels of antioxidants? The appreciation of the role of diet in determining the level or state of health continues to grow. A substantial body of research has now solidly established that certain dietary practices cause, as well as prevent, a wide range of diseases. In addition, the research has also shown that certain diets and foods can provide immediate therapeutic benefits. Diet and nutrition are both essential for sustenance, health and the overall well being of an individual. But it is also true that dietary factors contribute substantially to the burden of preventable illness and premature death in the United States. Dietary factors are associated with 5 of the 10 leading causes of death. They are:

- Coronary Heart Disease
- Cancer
- Stroke
- Non-insulin-dependent Diabetes
- Atherosclerosis

Diet can play a major role in the prevention of these diseases. Based on a recent research study, it was found that the international differences in cancer incidence are largely accounted for by lifestyle practices that include nutrition, exercise, as well as alcohol and tobacco use.

About 50% of cancer incidence and 35% of cancer mortality in the US (represented by cancers of the breast, prostate, pancreas, ovary, endometrium, and colon) are associated with Western dietary habits.

Many dietary components are involved in diet and health relationships. Chief among them is the disproportionate consumption of foods high in fats, often at the expense of foods high in complex carbohydrates and dietary fiber that may be more conducive to health. The Dietary Guidelines for Americans recommends that to stay healthy, one should eat a variety of foods; maintain healthy weight; choose a diet low in fat, saturated fat, and cholesterol; and choose a diet with plenty of fruits and vegetables, which contain high levels of fiber and antioxidants. It is well known that both synthetic and natural antioxidants inhibit carcinogenesis and mutagenesis. Natural antioxidants include ascorbic acid (vitamin C), selenium, oxidized glutathione (GSSG), and reduced glutathione (GSH),

which are water-soluble, and the fat-soluble antioxidants α -carotene, β -carotene (precursor of vitamin A), α -tocopherol (vitamin E), γ -tocopherol, lycopene and coenzyme Q10. These antioxidants may be obtained from various food sources, or can be taken as nutritional supplements. Vitamin deficiencies (hypovitaminosis) underlie many human diseases or, conversely, many diseases lead to vitamin deficiencies. It can therefore be said that the measurement of endogenous antioxidant levels is of great importance because the resultant values may be used as indicators of future health. Most methods of determining antioxidant levels focus on serum and adipose tissue. However, because serum levels reflect only those antioxidants, which cannot be absorbed, this is not an accurate indication of intracellular levels. Moreover, serum or plasma levels of these vitamins are associated with the most recent intake and do not reflect current vitamin status. Likewise, the determination of simple circulating concentrations of fat-soluble vitamins is also inappropriate. These vitamins are associated with body fat and are most often stored in specific tissues with circulating concentrations kept relatively constant. For example, vitamin A is stored in the liver and transported by specific binding proteins in the serum. A drop in the vitamin levels in serum or plasma may not be indicative of a deficiency or an increased requirement. Therefore, serum or plasma levels also reflect only the antioxidants, which cannot be absorbed. For a more thorough evaluation of vitamin deficiency, samples used to determine intracellular levels may need to be assayed before a definite diagnosis of nutritional and antioxidant deficiencies can be made. In this light, and based on many years of research and publications in peer-reviewed scientific journals, Aristo Vojdani, Ph.D., M.T. and the Immuno-sciences Lab., Inc. were awarded United States Patent Number 6,020,205 for the Determination of Intracellular Antioxidant Levels. By means of measuring the intracellular antioxidant levels, we are able to make an assessment of the overall oxidative health of an individual and rule out absorption defects. Using the highly sensitive HPLC method, we measure both plasma and intracellular levels of the following antioxidants:

- Reduced Glutathione (GSH)
- Lycopene
- Oxidized Glutathione (GSSG)
- Coenzyme-Q₁₀
- Ascorbic Acid
- α -Carotene
- Lutein
- β -Carotene
- γ -Tocopherol
- Retinol
- α -Tocopherol

- Vitamin-K₁

Intracellular levels of these antioxidants have been measured in more than a thousand samples obtained from healthy subjects and cancer patients. As shown in the chromatograms, significant increases in the intracellular levels of these antioxidants were observed within 16 – 24 hours after vitamin consumption.

Cancer

Cancer is the result of inappropriate cell growth and differentiation due to changes in signaling pathways occurring within the cells, as well as rearrangements in the cell cycle clock. In other words, any alteration in the biodynamics of equilibrium may ultimately result in cancer. Cancer is a disease of multiple stages and causes, some of which lie within control and others far beyond the confines of individual control. For instance, genetics, background, radiation, nutrition, hormones, smoking, chemical exposure, dust, fumes and different kinds of viruses all contribute to the likelihood of cancer development. Fat and salt intakes are also closely associated with increased risk of some forms of cancer, while vegetables and other antioxidant-containing foods are linked to reduced cancer risk. More than 50% of all cancer cases occur in cells that are in direct contact with the outside environment, including the skin, lungs, genitals, and the digestive tract. Variations in these particular types of cancer may provide especially useful clues about key opportunities for prevention. Epidemiologists predict that within this year alone, 600,000 U.S. cancer patients will die (up from 331,000 deaths in 1970). Cancer, which is being diagnosed more accurately today, actually began to rear its ugly head and show telltale signs around 10-20 years ago. If there was a reliable way to detect these critical clues or signs early enough in the process (to catch cancer in the act of damaging healthy tissue and to prevent and reverse the damage already done) wouldn't anyone in his right mind take advantage of it? Nowadays, we live in more fortunate times since technological advancements have enabled clinicians to detect or predict a potential cancer problem decades before it actually occurs and becomes serious. It has been estimated that 75% of cancers are caused by exposure to toxic chemicals. The other 25% consists of hardcore cancers that would eventually arise no matter how healthy a lifestyle the individual leads. Based on years of studies and research work, scientists have come to understand that the onset of cancer is a gradual, step-by-step process that may unfold over decades, rather than a single event. Just as a volcano may take several years to accumulate enough force to erupt, it may also be said that cancer is the end result of an accumulation of injuries at several different levels. And just as little volcanic emissions act as telltale signs of the eruption that is to come, cancer also has different levels or stages that actually give the clinician a clue or a warning before its onset. At each of these stages, there is an

opportunity for intervention – a chance to prevent, slow down or even halt the gradual march of healthy cells towards malignancy. See the next illustration for a summation. Biomarkers for cancer detection may be classified in three separate categories:

- Cancer signals originating from the base of the cancer volcano (A-E in the previous illustration).
- Early cancer markers resulting from continuous oxidative stress, DNA damage, changes in signal transduction, which may end up with cell mutation, and the expression of oncoprotein on the cell surface (F-H in the previous illustration).
- Late tumor markers, which are substances secreted or released by malignant cells in the blood. These can be related to the presence or progress of tumors and appear in the blood only after the onset of cancer (eruption of the cancer volcano).

Biomarkers for early detection of cancer signals.

Biomarkers are physiological manifestations of changes that may occur on the pathway to cancer. If detected early enough, intervention reduces the incidence of these signs and signals in a population and chances are that this strategy will lower the incidence of cancer as well. These markers aid clinicians in evaluating a patient's risk of acquiring cancer in the same way as blood lipid levels are used in standard medical practice to monitor heart disease. Like heart disease, cancer diagnosis today is the culmination of 10-20 years of subtle pathology. It is never too soon to intervene—but it is often too late. Based on the success in cardiovascular intervention strategies in reducing the incidence of death from heart disease, we should revise our cancer research and treatment techniques and put more emphasis on the disease's beginnings, rather than its terminal stages

Early Markers of Cancer

Oxidative stress proto-oncogenes and oncogenes have the ability to change signal transduction and induce cell mutation. In general, mutations that lead to uncontrolled proliferation may result in cancer. Mutations of a cell cycle regulator gene are widespread in cancers. The expression of cell surface molecules, oncoproteins and growth factors on cancer cells and in the blood may be of clinical significance as early markers of cancer.

Late Markers of Cancer

Research conducted over the last decade on the mechanisms involved in cell growth regulation has provided us with better tools for screening, diagnosing, and monitoring the progression of tumors and the efficacy of available treatments. In recent years, several

internal cancer markers have been identified and corresponding commercial assays were developed for these established markers. The usefulness of any marker is predominantly dependent on its level of sensitivity and specificity. In order for it to be truly useful, the concentration of any cancer marker should reflect the changes in the tumor burden and pave the way for the prediction of responses to therapy, as well as the course of the disease. The aforementioned markers are often positive when the tumor has already grown to a significant size. Therefore, all of these markers may be utilized for the baseline determination, intervention, prognosis, and classification of tumor staging. With this in mind, it can be said that a single marker, or a panel combining several individual markers, is a useful tool that can indeed provide a clearer picture of cancer progression. A late tumor marker is any substance that can be related to the presence or progress of a tumor. In practice, the clinical biochemistry laboratory measures markers which may be present in blood, although the term "tumor markers" may also be applied to substances found on the surface of or within cells fixed in frozen or paraffin sections. Tumor cells have been known to release or secrete a tumor marker in plasma. Such markers are not necessarily unique products of the malignant cells, but may simply be expressed by the tumor in amounts greater than that of normal cells. Tumor markers fall into one of several groups. They may be classified as hormones (e.g. human chorionic gonadotropin or HCG secreted by choriocarcinoma), enzymes (e.g. prostatic acid phosphatase in prostate carcinoma), or tumor antigens (e.g. carcinoembryonic antigen or CEA in colorectal carcinoma).

Overall, it may be said that the primary use of tumor markers in monitoring the efficacy of treatment. However, markers may also be of use in screening, diagnosis, prognosis, and in long-term follow-ups.

The Usefulness of Tumor Markers

Usefulness in Diagnosis

No

Usefulness in Prognosis

Yes

Usefulness in Assessing Follow-ups

Yes

Usefulness in Monitoring Treatment

Yes

Proper diet and nutrition play a major role in cancer prevention. The international differences in the incidence of cancer are largely accounted for by lifestyle practices, such as nutrition, exercise, as well as alcohol and tobacco use. As a matter of fact, nowadays,

it is possible to avoid most cancers or delay their onset by taking specially formulated pills or foods since the onset of cancer is a gradual stepwise process that may unfold over the course of decades. The attempt to make use of natural and synthetic compounds to intervene in the early precancerous stages of carcinogenesis (before invasive disease begins) is known as chemoprevention. This should be started as early as possible and at the base of the cancer volcano (see previous illustration), and not at the top, when the volcano is ready to erupt. Cancer prevention must be enforced as early as childhood and should focus on managerial approaches that will ensure optimal nutrition and a healthy balance of food components. This is important since cancer is a "chronic" condition that develops over a long period of time, and certain cancers may actually have their inception during our childhood years. Moreover, food preferences are established in childhood. As a general guide, an attainable goal after adolescence is a diet comprising 25% or less calories from fat (no more than 40 grams per day for an adult) and between 25-35 grams of fiber. Genetic predisposition is clearly important in the etiology of cancer in some individuals, especially those with breast and colon cancer, for which inherited mutations in cancer suppressor genes have been identified. Nevertheless, genetic predisposition as a major determinant has been calculated to account for only 2-3%, at most, of the current cancer burden. Individuals in any population have varying susceptibilities to cancer, but nutrition and food-borne components clearly affect cancer risk in the majority of the world's populations.

Future Speakers :

November 6 (1st Thursday) **Dr. Len Saputo** on Infrared Scanning and Photonics for Pain Relief and Healing

December 4 (1st Thursday) **Dr. Robert Rowen** on New Treatment Modalities for Chronic Diseases

January 22 (4th Thursday) **Dr. Richard Kunin**, on Health Implications of Vitamin Related Genomic Mutations

February 12 (2nd Thursday) **James Wilson** on Optimizing Immune Functions

March 18 (3rd Thursday) **Kelly et al** (Kaiser Hospital) on Theory and Practice of Accupuncture

