



WORLD SOCIETY OF ANTI-AGING MEDICINE

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Consensus Group of Experts on Nutritional Therapies

CONSENSUS # 1 on "FATTY ACID TESTING AND TREATMENT" of October 30, 2006

After having reviewed the scientific literature and exchanged experiences between physicians from all over the world who are competent in nutritional therapies, we, members of the Consensus Group of Experts of the World Society of Anti-Aging Medicine, think the time is ripe to reconsider current concepts on corrections of fatty acid deficiencies and excesses as they can be measured in a fatty acid profile.

Fatty acids accomplish important functions in our body: they are major components of cell membranes, and they play fundamental roles in the cardiovascular, immunological and nervous systems. Fatty acid deficiencies have been shown in several studies to increase cardiovascular diseases (including myocardial infarction, cardiac arrhythmias, and abnormal lipid profiles such as hypercholesterolemia or hypertriglyceridemia), to facilitate the appearance of psychiatric and neurological diseases, and to increase insulin resistance. Several serious studies have suggested that individuals presenting fatty acid deficiencies may have increased cardiovascular mortality. On the other hand, excesses in trans fatty acids have been shown to be detrimental to health: increases in cardiovascular diseases and mortality, a possible increased cancer risk, a higher incidence of diabetes, etc. Excesses in arachidonic acid increase inflammatory processes; they may alter health and possibly accelerate aging. Excesses in several saturated fatty acids (such as myristic acid) have been demonstrated as atherogenic and hypercholesterolemic.

The evidence is sufficient to justify testing (i.e. realize a fatty acid profile) and corrections of fatty acid deficiencies and excesses. The evidence is sufficient to guarantee the physician a **freedom of choice in fatty acid profile testing**.

As fatty acid imbalances can contribute to serious adverse consequences on the quality of life and health of patients, we recommend that physicians, in light of the solid evidence here collected, request for their patient **a fatty acid profile test** (including the dosage of myristic acid, palmitic acid, stearic acid, margaric acid, pentadecylic acid, oleic acid, palmitoleic acid, elaidic acid, trans-vaccenic acid, linoleic acid, gamma-linolenic acid, dihomogamma-linolenic acid, arachidonic acid, docosapentaenoic acid, alpha-linolenic acid, stearidonic acid, eicosapentaenoic acid, docosahexaenoic acid)) **whenever a fatty acid imbalance is suspected**, such as in case of fatigue, depression and other psychiatric disorders, dry skin, cardiovascular pathology (familial or personal history), rheumatic diseases, insulin resistance, etc. Such a test must be done by measuring the profile of fatty acids included in serum phospholipids (and not just by evaluating free fatty acids) and should be done after a 12 hours fast. If these conditions are respected, it generally offers a stable picture of the fatty acids that a patient consumes (food and possibly supplements) during the preceding weeks, which enables the physicians to adapt either the patient's diet or their advice and treatments.

Treatment of fatty acid imbalances or toxic excesses indeed consists of **dietary advices** such as increasing the intake of fish, of specific cold-pressed vegetable oils and other sources of polyunsaturated omega 3 and 6 fatty acids, of monounsaturated omega 9 or, if necessary, of certain saturated fatty acids; and reducing the intake of sources of fatty acids that may be in excess such as arachidonic acid and trans fatty acids (these may also be produced by faulty cooking processes). Evidence suggests that diet adjustment in our modern society is often not sufficient to optimize the fatty acid composition of our body and makes **fatty acid supplementation** compulsory, in particular among patients showing signs and symptoms possibly linked to fatty acid disturbances. Such a supplementation is best done individually according to a fatty acid profile. Generally, several months of daily intake of fatty acid supplements are necessary before the correction takes place.

CONSENSUS # 2 on "OXIDATIVE STRESS TESTING and SUPPLEMENTATION with ANTIOXIDANTS" of October 30, 2006

After having reviewed the scientific literature and exchanged experiences between physicians from all over the world who are competent in nutritional therapies, we, members of the Consensus Group of Experts of the World Society of Anti-Aging Medicine, think the time is ripe to reconsider current concepts on tests for antioxidant capacity and free radical damage, and supplementation with antioxidants.

Free radicals are generated by the loss of an electron, leaving a molecule with an odd, unpaired electron. This molecule is very unstable and tends to react quickly with other compounds, trying to capture a needed additional electron to gain stability. Generally, free radicals attack the nearest stable molecule, "stealing" its electron, and, which may spread through waves causing free radical damage. This is believed to be one of the essential mechanisms behind senescence and many diseases such as diabetes, cardiovascular diseases, cancer, neurodegenerative diseases (Alzheimer's disease, amyotrophic lateral sclerosis, Parkinson's disease), stroke, asthma, psoriasis, pancreatitis, cataract, in case of transplant as well as in case of emotional stress. In an increasing number of studies, free radical damage, also called "oxidative stress" reflecting increased levels of free radicals, has been reported. Increased levels of free radicals generally result from lower levels of antioxidants and antioxidant enzyme systems. Health is generally associated with adequate levels of compounds (vitamins, trace elements and others) and enzymatic systems with antioxidant activity, plus low levels of lipid peroxides, oxidized lipoproteins, malonaldehyde, 8-OH-deoxy-guanosine and other markers of free radical damage. Laboratories specialized in Nutritional Biology have developed tests to measure the serum levels of these free radical markers as well as those of antioxidants such as vitamin A, vitamin C, vitamin E, beta-carotene, coenzyme Q10, zinc, copper, selenium, plus antioxidant enzymes such as superoxide dismutase and glutathione peroxidase. The testing also measures several markers of free radical damage in order to evaluate the net result of the oxidative stress and the antioxidant protection. Every month, new evidence accumulates to show that adequate antioxidant supplementation can correct the disease-associated and the age-related increases in oxidative stress. In animal studies, antioxidant supplementation has been shown to reduce the progression of cancer, cardiovascular diseases, diabetes, and many other diseases, and even to increase lifespan. Some prospective human studies have shown beneficial results on the incidence and progression of diseases too, although not always as consistent as the animal studies data. In some important human studies, a high dietary intake of specific antioxidant nutrients has been shown to reduce overall or disease-specific mortality.

Recommendations: In face of the growing body of evidence, we recommend **testing** oxidative stress markers, antioxidant nutrients and antioxidant enzymatic systems, in any patient who is suspected, based on familial or personal history, to present or develop the above-mentioned diseases, to show signs of aging and/or to be in a chronic stressful environment. We recommend the physician to work with a laboratory where quality and experience in these tests handling are high (especially sampling and transport).

We recommend also the **treatment** of any oxidative imbalance to be discovered with the tests. Besides dietary advices to reduce free radical pathology such as increasing the intake of fruits and vegetables and avoiding foods cooked at excessive temperature for example, it is of primary importance to prescribe the appropriate antioxidant supplements. Treatments with antioxidant supplements may take months of daily intake before achievement of adequate levels of antioxidants. Patients with disease or persons in prolonged stressful conditions often need to continue the treatment by taking the needed antioxidant supplements in order to keep the antioxidant capacity of their body high and to prevent or counter further aggravation of their disease. The approach 'high-quality tests/personalized supplementation' is the most efficient one and the most recommended. It is for many patients not sufficient to merely take a daily multi-antioxidant complex without any knowledge of the body's levels. Some rare studies have shown moderate increases of disease or mortality risk in case of vitamin E and beta-carotene intake, in particular among smokers, which represents sufficient evidence to recommend caution and avoid excesses in any supplementation. The cost /effectiveness of the available tests are considered by the members of the Consensus Group of Experts of the World Society of Anti-aging Medicine to be good for the best specialized laboratories. In order to treat their patients, we do recommend physicians to search for the highest quality of products as not all brands are equal in composition and availability.

CONSENSUS # 3 on “TESTS and TREATMENTS of INTESTINAL WALL PERMEABILITY and GUT FLORA” November 19, 2006

After reviewing the scientific literature and exchanging experiences with physicians from all over the world who are competent in nutritional therapies, we, the Consensus Group of Experts of the World Society of Anti-Aging Medicine, think it is time to re-evaluate the tests for intestinal health. In particular, we are interested in the tests that measure intestinal mucosal permeability and intestinal microfloral composition. We are also concerned with establishing the best corrective treatments and diet modifications to reduce intestinal mucosal leakiness, and, when indicated, to fight the overgrowth of yeast or any other gut pathogens.

Intestinal mucosa should absorb essential micronutrients without allowing macromolecules to penetrate the digestive system. The loss of this barrier function is referred to as *leaky gut syndrome*. The micronutrient functional permeability of the intestinal mucosa can be measured by having a fasting patient ingest two types of sugar. A monomeric sugar, such as mannitol or rhamnose, will test for intestinal absorption, while a dimeric sugar, such as lactulose or lactitol, tests for pathologic permeability of the intestinal mucosa. Dimeric sugars are not normally absorbed by the brush border of the intestinal mucosa. Therefore, no dimeric sugar should be absorbed or leak through the normally sealed tight junctions. These tests have been available for many years in university hospital pediatric units, but are surprisingly rare in gastroenterology units. Now, however, they are performed by laboratories specializing in nutritional and functional testing. A large number of studies have been published in leading mainstream medical journals, where the quality of these tests is recognized in obtaining valuable information on gut permeability, especially for the indications mentioned above.

Leaky gut syndrome can be caused by malnutrition and the lack of specific factors necessary for adequate selective permeability. Whenever this is the case, we recommend treating the excessive intestinal permeability by improving diet and providing nutrients that improve the intestinal barrier such as L-glutamine, butyrate, zinc, vitamin A, vitamin E, folic acid, omega 3 fatty acids, etc.

Leaky gut syndrome can also be caused by an imbalance of intestinal microflora, i.e. yeast or putrefactive bacteria “overgrowths”. The term “infection” does not apply in that these micro-organisms are normally present in the human gut, however in much smaller amounts. This pathologic permeability can also be caused by amoeba, flagellates, or helminths. Unwanted organisms in the gut are traditionally detected by microscopic identification or by culturing stools in specific nutritive broths. However, yeast (not necessarily alive when excreted in stool) often cannot produce colonies in a Petrie dish because it cannot adapt and reproduce in an incompatible environment.

We have carefully reviewed the recent scientific publications in which the presence of yeast is detected by measuring specific fungal metabolites (arabinose, arabinitol, citramalate, β -cetoglutarate, furanes) in the host's organic fluids, especially in urine. These metabolites are secreted by the fungus in the patient's intestinal lumen, where they are absorbed and then secreted in urine. They then can be evaluated by classic chromatography. We recommend that physicians do this test, as it avoids many false negatives. It also circumvents the many false positive results obtained from culturing stool, as yeast can be detected in the stools of 80% of healthy subjects. Measuring metabolites provides a quantitative evaluation of yeast overgrowth directly within the host's environment. To treat yeast overgrowth, we recommend the administration of antifungals (medications, herbs and/or essential oils), while simultaneously supporting healthy microflora with probiotics (friendly live bacteria), prebiotics (their nutritive fibers) or both together.

Allergic, inflammatory and autoimmune diseases have all been increasing in the last decades. Every month, new scientific evidence is published showing that an imbalanced intestinal ecosystem and especially an increase in intestinal permeability (intestinal leakiness) may lead to these diseases, and that patients who experience intestinal yeast overgrowth may suffer from irritable bowel syndrome, abdominal bloating, excessive production of gas, headaches, fatigue and much more. Patients suffering from an amoeba infection may complain of diarrhea, arthralgia, lumbalgia and fatigue. Patients affected by helminths may lose weight despite an increase in hunger and food intake. They may also become anemic, fatigued and may suffer from bruxism (unconscious tooth grinding).

In light of this growing body of evidence, we recommend testing intestinal mucosal permeability and intestinal microflora quality in any patient who, based on family or personal history, is suspected of having the above-mentioned diseases, or who shows signs of intestinal dysfunction, or who suffers from unexplained fatigue. We recommend that physicians work with specialized laboratories with a reputation for quality and reliability, which have experience in handling these tests, including sampling and transport. The Consensus Group of Experts of the World Society of Anti-Aging Medicine believes that the tests provided by the best specialized laboratories are very cost effective.

As for treatments of intestinal dysfunction, we recommend that physicians use the highest quality products, as not all brands are equal in composition and availability, especially probiotics, where a new generation of better, more potent and more reliable products have been developed and are preferred.

CONSENSUS # 4 on “GENETIC TYPING TESTS” December 4, 2006

After reviewing the scientific literature and exchanging experiences with physicians from all over the world who are competent in genetic typing, we, the Consensus Group of Experts of the World Society of Anti-Aging Medicine, think it is time to provide a consensus on the quality and usefulness of these tests.

Genes are basic working units of hereditary material, the double-stranded DNA (Desoxyribonucleic acid) housed on the chromosomes. A gene is composed of a specific sequence of nucleotides. Genes contain the information for the synthesis of proteins that are at the basis of physical or functional traits. Each gene may have several alternative forms, called alleles, which vary in one or more of their amino acids. Occurrence of more than one allele at the same locus is called **genetic polymorphism**. Different alleles of a gene may be found in different individuals of a population. Variant alleles of a gene may also be expressed in different proportions throughout the body cells in one individual.

Genetic typing tests: Genetic typing tests analyze the genetic polymorphisms. They are performed on the DNA isolated from white blood cells obtained from a blood sample or from epithelial cells obtained from mouth swabs. It is a **fast growing field of medicine:** Everyday, new research on genes and their variants is published. The evidence on links between genetic polymorphisms and various diseases is increasingly growing.

Diseases associated with genetic polymorphisms: Genetic typing tests detect alleles or genetic variants of a gene. A genetic variant may be associated with an increased or reduced relative risk of certain diseases. Up to now, risk variations associated with genetic polymorphisms have been reported in peer-reviewed medical journals for the following multifactorial diseases: obesity, diabetes mellitus, cardiovascular diseases (such as hypercholesterolemia, hypertriglyceridemia, hypertension, coronary heart insufficiency, stroke), osteoporosis, Alzheimer’s disease, Parkinson disease, breast cysts, polycystic kidney disease, thrombophilia (i. e. Factor Leiden), hemochromatosis, gluten and lactose intolerance, periodontitis, Crohn’s disease, different types of allergies, and cancers that may be environmentally-induced such as breast, prostate, colon and lung cancer, melanoma, and secondarily, also gastric, larynx and ENT (ear-nose- throat) cancers, etc. Not all studies in genetic analyses have the same value. Meta-analyses and critical review and some major multi-centre studies can be considered as the reference in genetic analysis. For obesity and diabetes type II, large-scale screening programs are currently going on and their results should further increase our knowledge of genetic polymorphism.

Usefulness of genetic typing tests: Genetic tests for prevention purposes allow physicians to detect the modified susceptibility/ sensitivity to unfavourable environmental factors and the genetic predisposition of increased relative risks for disease early in the life of individuals at a presymptomatic stage. In this way they help physicians provide early and personalized health advices to their patients to improve prevention or delay the outbreak of a disease. For some genes (“modifier risk” genes), lifestyle or diet changes, nutritional or hormone replacement therapies may minimize the expression of a disadvantageous genetic polymorphism. For other polymorphisms, the expression of a gene cannot be influenced, but its associated increased relative risk of disease may be attenuated by improving the life style or diet, or by taking medications. Genetic typing may also help a physician make a better choice of a medication (“pharmacogenetics”) in order to avoid severe adverse drug reactions (ADR) or treatment failure. For example, with some antihypertensive drugs, anticoagulants and antidepressants, the efficacy

and relative risk for ADR depends on the genetic variant of the patient. Similarly, genetic typing may help a physician make a better choice of a nutritional supplementation (“nutrigenetics”) or find more efficient therapies to eliminate pollutants (“toxigenetics”). For the World Society of Anti-Aging Medicine, genetic typing is useful as it improves the overall level of healthcare by personalizing more adequately the therapy of a patient, helping mainly in disease prevention. Once a patient is ill, it is likely that genetic typing tests will become increasingly important as aids to better therapy choices in the future.

Quality of genetic typing tests: The quality of the genetic tests done by experienced laboratories that are accredited and participate to external quality assessment programs, can be considered as good. Some studies have shown possible faults in the tests, namely sample mismatching, cross contamination and interpretation errors. Overall, the number of false positive or false negative tests does not exceed the average percentage found in other laboratory assays. We recommend physicians to send samples to certified laboratories which frequently process such tests, as they have the largest experience in doing them.

Genetic testing procedure: According to the basic international documents of the UNESCO (Universal Declaration of Human Genome and Human Rights), the WHO (International Guidelines on Ethical Issues in Medical Genetics and the Provision of Genetic Services) and the Council of Europe (Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine), genetic testing for personalized prevention measures can be performed for any person, who is considered as major (> 18 years old). Any genetic testing should be confidential and performed on the voluntary basis and only for the health purposes. Any form of discrimination against a person on grounds of his or her genetic heritage is prohibited. .

Conclusion: in the light of the current evidence, the quality and usefulness of genetic typing tests is high enough for the World Society of Anti-Aging Medicine Consensus group of Experts to recommend

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