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Preface

This is the second volume on Mediterranean diets in the series of *World Review of Nutrition and Dietetics*. The first volume, *Mediterranean Diets*, was published in the year 2000 (vol. 87). Since then, many studies have been published on the beneficial effects of the diets in the Mediterranean region. In addition, studies in which the traditional diet of the country was modified to resemble the traditional diet of Crete (Greece), by increasing the intake of fruits, vegetables, fish, and flax oil, have led to decreases in the omega-6:omega-3 ratio in the plasma and inflammatory biomarkers, indicating that the traditional diet of Greece has anti-inflammatory properties. Investigators have carried out epidemiological and cross-sectional studies using a diet 'score' to define adherence to the Mediterranean diet and its relationship to various chronic diseases. Such studies have shown decreased mortality from cardiovascular disease and cancer, while others have related the Mediterranean diet score to levels of adiponectin. But, the Mediterranean diet score is a crude measurement that does not provide any information on the nutritional composition or nutritional quality of the diet, particularly on fatty acids, types of antioxidants, or other nutrients with antithrombotic, anti-inflammatory and anticarcinogenic properties. Furthermore, it is well known that foods in different climates have different nutritional composition and properties on health. When a dietary score is used, two major requirements have to be achieved in order to obtain an accurate and valid nutritional methodology, namely a precise definition of the composition of the Mediterranean diet, and the validation of the dietary score by means of biomarkers. Therefore, in this volume specific nutrients and their mechanisms of action are discussed and their relationship to health and disease are presented. Because many of the beneficial

effects of Mediterranean diets are synergistic with the health effects of physical fitness, a special paper is included on this subject.

In the previous volume, the papers included dietary patterns of different Mediterranean countries and precise descriptions of olive oil and wine, two major constituents of the Mediterranean diets, and for the first time, the concept that there is no such thing as one Mediterranean diet was extensively discussed. In the current volume the emphasis is on the contribution of foods and nutrients in clinical intervention studies and updated information on olive oil as well as new discoveries of nutrients, such as melatonin, which is high in purslane (*Portulaca oleracea*), nuts, cherries, and other foods that are commonly eaten in some of the Mediterranean countries. Melatonin is a potent antioxidant and anticarcinogenic agent.

The volume begins with the paper 'Modified Cretan Mediterranean Diet in the Prevention of Coronary Heart Disease and Cancer: An Update' by Michel de Lorgeril and Patricia Salen. The authors clearly show that a modified diet of Crete, just like the one used in the Lyon Heart Study, i.e. a dietary pattern that combines high intake of natural antioxidants, low intake of saturated fat, but high intake of oleic acid, with low intake of omega-6 fatty acids, and high intake of omega-3 fatty acids, has a high cardioprotective effect. The Lyon Heart Study (which was a randomized single-blind clinical trial) was the first clinical trial to pay particular attention to the omega-6:omega-3 ratio, with the experimental group having a ratio of 4:1 of omega-6:omega-3. The traditional diet of Crete (Greece) has an omega-6:omega-3 ratio of 2:1 to 1:1, similar to the Paleolithic diet. In addition to the importance of omega-3 fatty acids in the secondary prevention of coronary heart disease, the authors discuss the role of folate, homocysteine, and the nitric oxide pathway. The role of selenium in cancer protection is reviewed along with an extensive discussion of polyphenols that are the most abundant dietary antioxidant.

A number of studies have shown a decreased prevalence of the metabolic syndrome in patients following a Mediterranean diet. Drs. Leighton and Urquiaga in their paper 'Endothelial Nitric Oxide Synthase as a Mediator of the Positive Health Effects of Mediterranean Diets and Wine against Metabolic Syndrome' present a critique and focus on the influence of omega-3 fatty acids, antioxidants, and red wine as the important enhancers of endothelial nitric oxide synthase (eNOS) in the prevention of the metabolic syndrome. The authors provide data from their laboratory as well as other laboratories to support their hypothesis that metabolic improvements following consumption of Mediterranean diets, including red wine, are mediated by eNOS. Although many genes are involved, the participation of eNOS is a constant feature. The recent findings that the eNOS knockout mice present a cluster of cardiovascular risk factors comparable to those of the metabolic syndrome, suggest that

defects in eNOS function may cause human metabolic syndrome. These mice are hypertensive, insulin resistant, and dyslipidemic. Further support for a pathogenic role of eNOS comes from the finding in humans, that eNOS polymorphisms are associated with insulin resistance and diabetes, hypertension, inflammatory and oxidative stress markers and with albuminuria. The data support the hypothesis that eNOS enhancement should reduce the incidence of metabolic syndrome and its consequences. The authors conclude that the hypothesis is supported by epidemiological and observational studies but needs experimental validation with human intervention studies.

Drs. Friberg and Johansson in their paper 'Effects of an Omega-3 Enriched Mediterranean Diet (Modified Diet of Crete) versus a Swedish Diet' comment on the various components and their function of a modified diet of Crete and describe their own study in normal Swedish volunteers. The purpose of the study was to change from the standard Swedish diet to a Mediterranean-inspired diet rich in fish and flaxseed oil, similar to the modified diet of Crete used in the Lyon Heart Study, and to measure anti-inflammatory biomarkers, and changes of the omega-6:omega-3 ratio in the plasma. This is a very important study because it shows that (1) changing the diet was not a problem; (2) the omega-6:omega-3 plasma ratio decreased, and (3) the inflammatory biomarkers decreased.

The next paper by Drs. Marangoni, Martiello and Galli on 'Dietary Fat Intake of European Countries in the Mediterranean Area: An Update' focuses on the contribution of various components of the diets in European Mediterranean countries to the overall fat consumption versus Northern European countries. The authors discuss the protective effects of oleic acid, omega-3 fatty acids, and especially the land-based omega-3 fatty acid alpha-linolenic acid (ALA), and their interactions, and provide practical recommendations on how to formulate menus, including specific amounts of health-promoting fatty acids.

Although changes have occurred in the diet of both Greece and Italy in comparison to the diets prior to 1960 at the time of the beginning of the Seven Countries Study, and despite the effects of globalization, Greeks continue to eat more fish, fruits and vegetables along with increasing intake of meat and dairy products. Rubba's group provides a review and critique of epidemiologic studies, and diet and health, in various parts of Italy, and the consequences of dietary changes on health. It appears that for the past 10 years there is a return to a much healthier and traditional dietary pattern. The authors discuss micronutrients and coronary heart disease, hypertension and stroke, vitamins, Mediterranean diet and obesity, and Mediterranean diet and cancer in Italy. The authors are puzzled that obesity is so prevalent in the European area where diet is still of the Mediterranean type and ask, 'Could the high consumption of bread, pasta, pizza, olive oil and wine facilitate adiposity?' But, the high fiber content

of green vegetables and fresh fruit typical of Mediterranean diets reinforces satiety, a strong anti-obesity effect. Diet alone is not enough to prevent obesity. Physical activity is a very important aspect of health and the prevention of obesity. Epidemiological studies show an increase in sedentary life styles in the Mediterranean region as in other parts of the world, particularly in Western countries.

This point is reinforced in the next paper ‘A Mediterranean Diet Is Not Enough for Health: Physical Fitness Is an Important Additional Contributor to Health for the Adults of Tomorrow’ by Dr. Castillo-Garzón and co-workers. In addition to diet, a sedentary life-style is another major risk factor for non-communicable diseases. Diet and physical activity interact in the development (or prevention) of coronary heart disease and several other health conditions. Regular physical activity stimulates the functional adaptation of all tissues and organs in the body (e.g. improves fitness and decreases fatness), thereby also making them less vulnerable to lifestyle-related degenerative and chronic diseases. The authors explain that it is not only physical activity. Results obtained from Spanish adolescents and other European and American peers have shown that physical fitness (especially cardiorespiratory fitness and muscle strength) is strongly associated with cardiovascular risk factors. Cardiorespiratory fitness has been shown to be associated with traditional risk factors such as triglycerides, total cholesterol, high and low density lipoprotein cholesterol, glucose, waist circumference, total body fat, but also with emerging risk factors such as C-reactive protein, C3, and homocysteine. Muscle strength has been suggested to be inversely associated with all-cause mortality in adults; however, less is known about the association between muscle strength and risk factors in adolescents. For public health strategies and preventive purposes it is of interest to understand the associations of diet, physical activity and fitness on cardiovascular risk factors from an early age.

A book on the Mediterranean diets would not be complete without an update on the dietary and health aspects of the North African region called the ‘Maghreb’. Drs. Sabrina Zeghichi-Hamri and Stamatina Kallithraka in their paper ‘Mediterranean Diet in the Maghreb: An Update’ present data on recent dietary trends in Algeria, Libya, Morocco and Tunisia. These four countries do not have a uniform dietary pattern but relatively specific diets. For example, Moroccans have the highest intake of cereals and sweeteners, and the lowest milk, fats and oils among the four Maghreb countries whereas Tunisians consume the highest amount of fish and other seafood and fruit. In general, the diet of the Maghreb is relatively low in total fat and animal products but high in cereals and vegetables. Alcohol and wine – an important aspect of a healthy diet in Greece, Italy, France and Spain – is very low due to religious restrictions. The authors illustrate the differences among the Maghreb countries by calculating

the contribution of the various food groups to total energy supply for the period 2000–2003. Their paper clearly illustrates that the ‘Mediterranean diet’ is not a homogenous nutritional model because there are several Mediterranean dietary patterns as a result of different cultures, traditions, religions and income, resulting in a wide variety of the dietary patterns within the Mediterranean region.

In epidemiological studies, high amounts of fruits and vegetables in the diet are associated with lower levels of coronary heart disease and cancer. Because fruits and vegetables are high in antioxidant vitamins and minerals, polyphenols, etc., intervention studies with vitamin E, vitamin C, and carotenoids were carried out but failed to support the hypothesis. In fact, the opposite was shown. Studies examining total antioxidant capacity revealed a higher level of total antioxidant capacity than those based on the sum of the antioxidant vitamins and minerals. This finding has led to studies looking at the antioxidant effect of other constituents in fruits, vegetables, wine, olive oil, and wild plants. In their paper on ‘Antioxidants in the Mediterranean Diets: An Update’, Drs. Bogani and Visioli define antioxidants and their relationship to cancer. The authors report on Mediterranean antioxidants and give selective examples, specifically, lycopene and its properties, olive oil and wine, and conclude with a section on phenolic antioxidants, wild plants and endothelial function. In their studies, edible wild plants increase the production of nitric oxide. The authors conclude, ‘... the answer to the debate on the efficacy of antioxidant supplements is likely to be found in the adoption of a Mediterranean-style diet, in which the abundance of bioactive compounds provided by fruits, vegetables, wine, and olive oil grants a higher protection toward ROS (reactive oxygen species)-induced diseases’.

Dr. Dimitrios Boskou’s paper on ‘Olive Oil’ presents the latest information on olive oil composition, fatty acids and triglycerides, partial glycerides, free fatty acids, and minor constituents, which are divided into two categories (1) fatty acid derivatives, and (2) components with different chemical structures. Special focus is given to squalene sterols, fatty alcohol, waxes, diterpene alcohols, tocopherols, volatile and aroma compounds, and other minor constituents. Triterpene acids and various phospholipids, such as phosphatidylcholine, phosphatidylinositol and phosphatidylserine. A major section is devoted to polar phenolic compounds in terms of shelf life, sensory properties, antioxidant properties, isoprostane formation, and scavenging of radicals and other reactive species. There is a section on olive oil quality. The quest for quality is based on the applications of clearly defined rules during the growing and processing of olives, and retail packing of the oil. Dr. Boskou provides definitions of the various types of olive oil, the characteristics of extra virgin olive oil and virgin olive oil, organoleptic assessment, metals, moisture, and volatile matter. There is a special section on olive oil extraction and the changes that have taken place over the past 30–40 years, the culinary aspects and new applications. The pheno-

lic compounds in olive oil diminish during heating. Therefore, the antioxidant activity of the oil, determined by the ABTS radical decolorization assay or the DPPH radical test, diminishes. It is therefore important to further study the nature of the monoglyceride components of olive oil and to improve methods to quantify and preserve functional ingredients.

Edible wild plants have been one of our areas of investigation in attempting to precisely define the traditional diet of Greece prior to 1960. In the past, we focused our studies on the contribution of omega-3 fatty acids from both animal and plant sources. More recently, we studied the antioxidant content of edible wild plants in terms of vitamins, minerals, glutathione and melatonin. Melatonin is a broad-spectrum direct radical scavenger and indirect antioxidant.

Melatonin, *n*-acetyl-5-methoxytryptamine, was long thought to be an endogenously generated molecule found exclusively in vertebrates (pineal gland, retina) that synchronizes circadian and circannual rhythms. Lately, melatonin has been found in insects, unicellular organisms, bacteria, and most recently in plants. Because physiologic concentrations of melatonin in the blood are known to correlate with the total antioxidant capacity of the serum, consuming food stuffs containing melatonin may be helpful in lowering oxidative stress.

Melatonin directly detoxifies the hydroxyl radical ($\cdot\text{OH}$), hydrogen peroxide, nitric oxide, peroxyxynitrite anion, peroxyxynitrous acid, and hypochlorous acid. The products from each of these reactions have been identified in pure chemical systems, and in at least one case in vivo: The interaction product of melatonin with the $\cdot\text{OH}$, i.e. cyclic 3-hydroxymelatonin is found in the urine of humans and rats. Melatonin increases the efficiency of mitochondrial oxidative phosphorylation and reduces electron leakage (thereby lowering free radical formation). Melatonin reduces the initiation of cancer by limiting oxidative damage to DNA. It also curtails the growth of tumors once they are established by inhibiting the uptake of growth factors, such as omega-6 fatty acids, by cancer cells. Melatonin's effects on cancer inhibition are achieved at physiological concentrations, and phytomelatonin such as that found in purslane has been proven as a potential means of limiting the growth on established tumors.

In the paper by Reiter, Simopoulos and co-workers on 'Melatonin in Edible Plants (Phytomelatonin): Identification, Concentrations, Bioavailability and Proposed Function', the authors indicate that except for the potato tuber, all other plants that have been investigated contain various amounts of melatonin ranging from nanograms to picograms per gram of tissue. The paper contains information on the melatonin levels of some edible plant foods, indicating a wide variation in the concentration of melatonin. Purslane (*Portulaca oleracea*), a commonly eaten wild plant in Greece and other parts of the world, has been shown to have the highest amount of the omega-3 fatty acid ALA. It is not surprising that purslane also has one of the highest amounts of melatonin.

Melatonin, being a potent antioxidant, is needed to stabilize the high amount of ALA found in the purslane. Purslane in the diet further contributes to the antioxidant and anticarcinogenic properties of the Greek diet. At the level of 19 ng/g, it has one of the highest amounts of melatonin among edible plant foods. Here, then is another dietary constituent that adds to the armamentarium of the beneficial constituents of the traditional diet of Greece contributing to health.

The new advances reported in this volume should serve as a strong incentive for the initiation of clinical intervention trials and studies that will test the effects of specific dietary patterns as well as specific nutrients in the prevention and management of chronic diseases.

This volume should be of interest to physicians, cardiologists, cancer specialists, nutritionists, dietitians, agriculturists, food scientists and policy makers in government, private industry and international organizations, as well as the informed public.

Artemis P. Simopoulos, MD

