Food, Nutrition and Mediterranean Diet
Historical, Health and Cultural Aspect

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INTRODUCTION

Nutrition is the process of provision and availability of food to sustain and preserve life, a fundamental necessity, akin to life per se, similar in man and living beings. Diet is the sum and type of foods and drinks habitually consumed. Dietary patterns are habitual preferences of foods and drinks, determined and shaped by family, tradition, culture, religion, climate, terrain, economy and community customs.

Dietary patterns have changed considerably throughout history, as a result of migration, industrialization and more recently globalization, which has affected food processing distribution and consumption.

The purpose of this review is to provide historical, medical and cultural aspects of nutrition with emphasis on Mediterranean diet.

Food Systems

Food systems evolved over millennia, shaped and influenced by climate, terrain, seasons, geography, culture and technology. Food systems are grouped into three types, based on historical evolution and transformation: a) the Gatherer-Hunter, b) Peasant – Agricultural and c) Urban – Industrial (1).

These food systems coexisted historically until the 18th century when the industrial system developed, as a consequence to industrial revolution. In current times globalization of economy and technology affected significantly food systems regarding production, processing, preservation, distribution and consumption. In some communities, the peasant – agricultural system in rural communities still coexists with the industrial system in urban centers.

Gatherer – Hunter System

Since the emergence of homo sapiens 300,000 years ago, the provision of food depended on the environment he lived, vegetation and animal life. His nutrition was rich in animal protein, derived from meat, sea food and fish, and starch derived from fruits and vegetables. Gathered food was characterized by high fiber and energy from hunted food (2). Gathered food provided higher bulk than hunted food, which originated from animals. Prehistoric data from Stone Age indicates that gatherer-hunter people were lean, mainly the hunter type due to intense physical activity. Life expectancy was short due to increased risk of exposure to nature elements and infection. The incidence of cancer is reported low, probably related to short life expectancy (3).

Peasant – Agricultural

It first developed 9,000 years ago in Mesopotamia, between Euphrates and Tigris rivers, with cultivation of wheat (4), rice in Asia and corn in the Americas. Around 6,000 years ago, people in Egypt started producing bread from wheat (5). The agricultural system was based on land settlement, cultivation of crops and breeding of animals.
Diet was rich in dietary fiber and cereals, supplemented with animal protein. The food composition was derived from variable crops including fruits, vegetables, fish and food from domesticated animals. Storage of food was essential in times of crop failure or wars. People were generally lean, with variable physical activity depending on the difficulty of cultivation. Life expectancy was higher than in gatherer-hunter in primitive age.

Sources of information regarding nutrition in prehistoric period derive from artifacts dating from the Neolithic and Bronze Age, food debris, pottery, utensils, inscriptions and tombs. In ancient Egypt other sources are depiction of food in temples, reliefs, statues, models, papyrus texts and lists of food offerings (6).

In ancient Greece there is reference to food in Homeric texts (7). The food of heroes and warriors consisted of meat, bread and wine. Fruits and vegetables were not considered food fit for noblemen. The diet of ordinary people in ancient Greece was plant-based and wheat. Occasionally, there was consumption of fish and meat (8). It was in the 2nd and 3rd century BC that variety of foods and drinks became available at home or banquets (Symposia), accompanied by wine and philosophical discussions. Life expectancy in ancient Greece was short, with average 30 years, considering nutrition, which was satisfactory. This was due to epidemics, which were common and wars resulting in food crises (9).

**Urban – Industrial System**

It developed in the 18th century with the industrial revolution, first in England and then in America. The evolution of urban – industrial system is based on technology applications of food processing, preservation and distribution. The system is high in animal protein (meat and dairy products), sugar, baked foods, soft drinks, alcohol and low in fiber, fruits and vegetables. In the western world and developed countries the system is efficient to provide available food to large segments of populations (10).

Globalization and spread of urban-industrial food system transformed food industry and distribution (11) and contributed to doubling life expectancy since the 18th century with efficient methods of preservation and improvement in quality and safety of food. Nutritional deficiencies decreased, especially in the western world, which benefited significantly from these developments. The negative effects were an increase in chronic diseases and cancer due to food composition (12). Obesity, diabetes, hypertension and coronary artery disease increased in developed countries as a result of the prevailing dietary pattern rich in sugar and fat (13). A significant decrease was also noted in breast feeding, by the entry of women in the work market. Physical activity was also drastically reduced from the peasant-agricultural system to urban-industrial. Energy balance was also increased due to high caloric intake, sedentary life style and mechanical transportation, leading to decreased physical activity (14). Chronic diseases related to diet have increased in the western world and developed countries with increased morbidity and mortality and a heavy burden on economy and resources (15-17). Overeating, obesity, food high in animal fat and protein, sugar, high calorie and energy intake have led to serious public health problem. This raises concerns regarding the measures to be taken and the need for education of the public, starting with the diet in childhood due to the epidemic of obese children. The inequality of food distribution and availability in developing countries adds another moral and social issue, which needs to be addressed urgently and effectively by governments and international organizations.

**MILESTONES IN THE HISTORY OF NUTRITION**

**Hippocrates (460 BC – 370 BC)**

Hippocrates was born in the island of Cos in 460 BC and died in Larisa, Thessaly in 370 BC, at an advanced age. He is considered the father of Western Medicine. He established Medicine on a scientific and professional base. The Hippocratic Oath is a time-honored legacy which guides the young doctor to follow the principles and ethics in the practice of Medicine. He promoted observation and reasoning in Medicine in his teachings in the Hippocratic School in Cos and in Asklepeia (Hospitals).

He taught that disease had natural causes and not divine and considered nutrition an important component for health. This is reflected in his works “On Food”, “On Diet” and “Dietary Therapeutics”. The famous aphorism to his students and physicians “Let food be thy medicine and medicine thy food”, exemplifies the importance of food in maintaining
In the 1750s, recorded the first observations on the lack of nutrients as a cause of disease and the beneficial effect of supplementing the lacking nutrient. He observed than in long voyages sailors suffered from bleeding, a manifestation of scurvy, due to lack of fruits and vegetables. He noted the therapeutic effect of lime juice due to vitamin C, which was not known at that time.

In the 19th century, in France, Francois Magendie, a physiologist, identified in dog experiments, one of the earliest experimented observations, the essential role of protein in nutrition. Magendie was the mentor of Claude Bernard, who is regarded as one of most eminent scientists in the history of Medicine. His observations in the 1860s that body fat is synthesized from carbohydrates and protein, laid the foundations of human metabolism and the role of homeostasis in biology.

At the end of the 19th century, in the 1880s, a Japanese physician named Takaki Kanehiro observed that ingestion of white rice was associated with beri-beri, whereas unprocessed rice, cured the disease, which was attributed to the nutrient thiamine contained in the husks of rice.

The Age of Vitamins – First Half of the 20th Century

The first half of the 20th century is characterized by a flurry of discoveries of vitamins. Sir Frederick Hopkins (1861-1947), a British scientist, was the first to describe the concept of vitamins, as “accessory food factors”, i.e. organic substances essential to health. His contributions broke new ground in physiology and earned him the Nobel Prize for Medicine and Physiology in 1929.

It was Casimir Funk, a Hungarian in UK who coined the term vitamins, a composite term of vita (life) + amines, which referred to the “accessory food factors”, described earlier by Hopkins. Funk defined also the cause of beri-beri, which was due to deficiency of Vitamin B1 (thiamine).

In the 1920s Adolph Otto Windaus in Germany synthesized vitamin D3 (cholecalciferol) a cure for rickets. He received the Nobel Prize for Chemistry in 1928.

In 1922 Albert Szent-Gyorgi (1893-1986) in Hungary synthesized vitamin C (ascorbic acid) to prevent and treat scurvy, usually a fatal deficiency of vitamin C. He received the Nobel Prize for Medicine and Physiology in 1937.
Second Half of the 20th Century

Two major advances in Nutrition and Food Safety took place in the 1940s. In 1941 in England the first draft of Recommended Daily Allowances (RDA) regarding the daily requirements of nutrients was recorded by the National Research Council. This development was prompted by food rationing during WW II, and served as a guide for adequate nutrition of civilians and military personnel, taking into account availability of food. The first draft of RDA, a forerunner of Recommended Daily Intake (RDI), was introduced in USA by the National Academy of Sciences and Nutrition Board.

The second milestone in the technology of food safety the application and wide use of the electric refrigerator introduced in 1940s which provided effective storage, thus preventing food contamination, gastrointestinal infections and generation of nitrosamines, which are carcinogenic and related to gastric cancer.

In the second half of the 20th century due to high incidence of coronary artery disease, there was a surge of interest and sensitization regarding dietary factors and lipids and the role of cholesterol as a predisposing factor. This started in the USA and spread subsequently to Europe. It was at that time that the eminent American physiologist Ancel Keys (1903-2004) started a campaign for Mediterranean diet, rich in olive oil with beneficial effect on blood lipids and cholesterol. This led to the pivotal Seven Countries Study on the role of diet on coronary artery disease.

In the 1990s a significant development was the launching of the European Prospective Investigation into Cancer and Nutrition (EPIC Study) still continuing, on the effect of nutrition on cancer and chronic diseases, namely coronary artery disease, obesity, hypertension, diabetes type 2, hyperlipidemia and neurological disorders. These studies based on multinational participation confirmed earlier observations that diet plays an important role on cancer and chronic diseases and Mediterranean diet exerts a beneficial effect, associated with healthy living and longevity.

Current Issues of Nutrition

The current issues pertaining to the role of nutrition on health and disease are the following.

1. Obesity, a global epidemic

The prevalence of overweight and obesity worldwide is steadily increasing and constitute major health problem, with serious consequences on health, co-morbidities, life expectancy, society, resources and economy. Obesity is closely related to diet, lifestyle, sedentary life and the emphasis on food and eating at a family and society level. Obesity is more common in urban than in rural populations. It is estimated that in industrialized, high-income countries 22% of the adult population is obese, effecting significantly morbidity and mortality (13).

Diet plays an important role in the development of obesity. Daily foods are high in fat and carbohydrates with consumption of soft drinks, energy dense and high caloric. Abundance and availability of these foods in developed countries provides a social environment conducive to obesity and overweight in childhood, evolving to obesity in adult life. Overweight or obese children have increased incidence of cardiovascular risk, hypertension, hyperlipidemia and diabetes type 2.

2. Increased public awareness of the role of nutrition

There is increased awareness and sensitization of the public on the importance of diet and nutrition to maintain good-health. This is reflected on publication of pamphlets, TV programs, seminars, healthy diet magazines, healthy diet stores, physical fitness and diet establishments. The interest is directed to management of obesity and overweight, coronary artery disease, diabetes, hyperlipidemia, hypertension, cancer, metabolic syndrome, cancer prevention related to foods of increased or decreased risk.

3. Sensitization of public to dietary constituents

There is increased sensitization of public to certain dietary constituents linked with a beneficial effect on health. These include antioxidants, phenols, omega-3-fatty acids, vitamins and food supplements, a controversial subject. All these items should be recorded in food labels for public information.

4. Sensitization for a healthy diet

The food labels attract the attention of the consumer more than before, when the selection of groceries and foods was at random and not guided by knowledge of nutrition labels and the effect on health. There is increased awareness to avoid foods high in fat, sugar, calories, preservatives, as well as foods containing chemicals.
The selection of foods is between highly processed foods, which are cheaper, high fat and sugar and minimally processed foods, which are more expensive but closer to natural products. The knowledge of food and food constituents render the consumer, especially in developed countries, more sophisticated in following a healthy dietary pattern based on scientific evidence.

The study and application of the principles of healthy diet and nutrition has evolved in our times an important field that scientific evidence is transmitted to the public to guide selection of healthy products.

5. Organic farming, biological products

Organic farming is a return to agriculture methods which were standard until the introduction of chemical fertilizers, pesticides and biocides. Organic farming excludes, to a significant degree, fertilizers, plant growth substances, pesticides and additives in livestock. In order to sustain soil productivity organic farming utilizes crop rotation, animal manure as fertilizer and plant nutrients. Biological products, which carry the label of validation, have increased since 1990s due to high consumer demand. The nutritional value of biological products is comparable to products of conventional farming, but they contain fewer residues of chemicals and fertilizers, higher concentrations of vitamin C and dietary fiber. The issue of biological and nutritional superiority products compared with products of conventional farming is controversial, but the avoidance of high concentration of fertilizers and chemicals is beneficial in the long run, especially regarding the carcinogenic effect.

6. Genetic modification of foods

Genetic modification applied in agriculture has raised interest and controversy. Foods are modified genetically by transmission of gene within and between species to increase yield, to change nutritional composition, crops and resistance to pest and herbicides. Genetic modification involves also transfer of gene from one species to another, from plants to animals or inactivation of genes.

Genetic modification of foods requires strict regulation by state agencies. The aim is to produce foods of the same safety and nutritional value to those which they replace. However, not all countries have regulating agencies for genetically modified foods. Concerns are also raised regarding the long term effect of genetically modified foods on cancer, although at the present there is no clear epidemiological evidence, due to the fact that the biology of carcinogenesis is a long term process and long periods of prospective observation are required. The opinion of the author is that the consumption of genetically modified foods requires caution and should not be included in the daily foods staples. The same caution and awareness also apply to the use of pesticides and herbicides on methods of food production.

Policies and Social Issues of Food

Safety is of prime importance for the public and it is the responsibility of state agencies and governments to enforce all regulations in the chain of food production, processing, storage, transportation and distribution. This is necessary for the control of contamination of chemicals and additives in all stages of food from production to distribution.

Another crucial humanitarian and ethical issue is the inequality in food production, availability and distribution. Food shortage and food crises are rampant in war zones, drought seasons and crops failure. Famine and hunger are extreme manifestations of human destitution and dehumanization, crimes against humanity, which go unpunished in our times.

A moral issue of social injustice is the gross imbalance and inequality in food production and the vast gap between rich and poor countries. The repercussions of this inequality are paradoxical and extreme. In rich countries abundance of food and consumption leads to overeating, overnutrition, overweight, obesity and increased morbidity and mortality.

By contrast, in poor countries scarcity of food is associated with undernutrition, malnutrition, emaciation, high morbidity and mortality. State governments and international agencies carry great responsibility to ameliorate food inequality and shortage and apply policies to secure availability of basic food staples in poor countries as well as during food crises.

International agencies involved in food politics are Humanitarian Aid, Food and Agricultural Organization (FAO), International Red Cross, Organization of Economic Cooperation and Development, United Nations Organization and Charity Organizations.
**DIETARY PATTERNS**

*Food Systems Determine Dietary Patterns*

Dietary patterns are defined as the type, quantity, quality, frequency and proportions of foods and drinks, which are consumed in human nutrition. Dietary patterns in populations and geographic regions have developed over a long historical process over centuries. They are determined by local tradition, climate, terrain and geography. Communities living by the seashore, lakes and rivers have different dietary patterns and different local products from communities living in arid land or high altitude and mountains.

The components of dietary patterns, namely foods and drinks, are not only important in the composition of diet per se, but they may affect health and disease in the chain of food production, storage, processing and distribution. In all these stages, contamination of toxic substances or microbial organisms may occur with detrimental short and long-term effects on health. Accordingly, the process of food from terrain to the table is a complex procedure in order to investigate the effect of individual foods and drinks in health and disease. Large cohort or case control epidemiological studies are based on individual components of foods and drinks on their effect as predisposing factors in certain disease processes. Human nutrition and diet are based on dietary patterns, consisting of consumption of a variety of foods and drinks and not individual components.

In recent decades, namely from the 1980s, dietary patterns and the effect on disease, have attracted considerable interest in the investigation of cause and effect. Scientific methodology of research and rigorous statistical analysis became the framework of important large scale, prospective epidemiological studies to assess the effect on diet on disease. The state of knowledge today regarding the effect of diet on neoplastic diseases is substantial to promote dietary patterns, notably Mediterranean diet, associated with prevention of coronary artery disease and cancer.

Dietary patterns and food consumption have been affected, in recent times, by rampant globalization and worldwide distribution of food products, which render them available in distant lands long ways from the place of production. Technology of food industry has significantly influenced production, processing, standardization, packaging and distribution of export-import of foods on a global scale (World Health Organization, 2000). Issues regarding food safety and consumer protection have evolved with an unprecedented scale of mass food distribution, in sharp contrast with the gross inequality and food shortages in certain regions and war zones, resulting in famine and malnutrition.

It is of historical interest to note that foodstuffs and drinks, namely wine, were transported to distant lands, mainly by the sea, in ancient times, as recorded in archaeology and by ships sank in Mediterranean basin. Food culture is a characteristic component in the history of civilization. Dietary patterns are based on local traditions, ethnographic and anthropological characteristics. These are intertwined with the terrain, family and community life, religious practices, folk art and social interaction.

The following dietary patterns are characterized, determined by terrain, climate, culture, technology and the food industry (Table 1):

1. Mediterranean diet – Traditional diet of countries, bordering the Mediterranean littoral, in southern Europe, Middle East and North Africa. It is characterized by high consumption of olive oil, fruits and vegetables, breads and cereals, fish, nuts and wine.
2. Asian diet in India, China, Japan, Thailand, Vietnam, Korea, based on rice, vegetables, plant foods, herbs and spices.
3. Plant-based – Mediterranean and Southern – East Asia based on starch, vegetables, plant foods, herbs and spices.
4. Western Europe, USA, Canada, South Africa, Australia, New Zealand, based on food industrial systems and processed food, rich in sugar, fat and calories.
5. Vegetarian and vegan diet – Heterogeneous dietary pattern, excluding meat and animal products.

**Table 1. Dietary patterns**

- Mediterranean
- Asian
- Plant-based
- "Western"
- Vegetarian – Vegan
- Religious
The principal aspects of Mediterranean diet are presented schematically in the pyramid model (Figure 1), a graphic representation, initiated by Willett and co-workers (23), based on dietary patterns in Crete and Southern Italy in the early 1960s. The base and lower part of the pyramid represent foods, which should be included daily, namely breads, pasta, rice, cereals, fruits, vegetables, olive oil, as the principal source of fat, pulses, legumes, olives, nuts. Dairy products, fish, poultry, eggs and sweets are recommended few times per week. At the top of the pyramid red and processed meat, consumed 1-2 times per month, not exceeding 100 g/meal. It is worthy to note that red meat includes not only beef, but also pork and lamb, whereas white meat, which is preferable, includes fish, chicken and turkey. An important factor for the benefits of Mediterranean diet is daily physical exercise which augments the health effects.

Olive oil with high concentration of unsaturated fatty acids, mainly oleic acid, is the principal characteristic of Mediterranean diet. Oleic acid is linked with the reduction of risk of coronary heart disease (Keys et al., 1986). Oleic acid has antioxidant, anti-inflammatory and anti-hypertensive effects, improves cholesterol regulation and reduces LDL cholesterol. In addition, oleic acid has a beneficial effect on composition of secondary bile acids which exert a deleterious effect with polyamine metabolism on colonic epithelial cells. There is also evidence that it inhibits progression of adenoma to cancer, which may explain the protective effect of Mediterranean diet to colonic cancer.

Consumption of fish and fish oil have also a protective effect on coronary artery disease and cancer, attributed to omega-3 polyunsaturated fatty acids and eicosapentaenoic acid (EPA). By contrast, animal fat consisting of saturated fatty acids increases colonic composition of secondary bile acids, which exert a carcinogenic effect on colonic mucosa.

In terms of classification of dietary factors of the traditional Mediterranean diet, there are nine key components, which are used in a diet score on a scale of 0-10 (22). 1) High ratio of unsaturated to saturated fat, 2) High consumption of fruits, 3) High consumption of vegetables, 4) High consumption of legumes, 5) High consumption of breads and cereals, 6) Moderate consumption of dairy products, 7) Moderate consumption of fish and seafood, 8) Moderate consumption of...

**Mediterranean diet**

The concept of Mediterranean diet as a healthy diet was first publicized in 1945 by Ancel Keys, an American scientist, when he was stationed in Salerno, Italy. He was impressed by the healthy state of the population, which was attributed to the diet, rich in olive oil, fruit and vegetables, breads and cereals. Early observations on the beneficial effect of Mediterranean diet in 1960s were related to low incidence of coronary artery disease and myocardial infarction in the island of Crete and regions of Southern Italy. Another supportive factor on the healthy model of Cretan diet was the data of longevity, which was the longest in the island of Crete (18).

Keys and co-workers launched the Seven Countries Study, investigating dietary factors on the incidence of coronary heart disease on seven countries, namely Greece, Italy, former Yugoslavia, Japan, USA, Finland and the Netherlands (19, 20). Subsequent studies confirmed the early observations on low incidence of coronary heart disease in Mediterranean populations related to diet (21).

The interest generated by the effects of the Mediterranean diet on coronary heart disease was expanded to investigate its role in the prevention or lowering the risk of other diseases, namely certain cancers, metabolic syndrome (obesity, hyperlipidemia, diabetes, hypertension), mental disease (depression) and neurological disease (Parkinson and Alzheimer). Studies and metaanalysis data showed that adherence to Mediterranean diet is an important contributor to health status, mortality, survival and longevity (22).

**Characteristics of Mediterranean diet**

Mediterranean diet is basically a plant-based dietary pattern, characterized by 1) olive oil, as the principal source of fat and low in animal fat and protein, 2) daily consumption of fresh fruit and vegetable, cereals, grain, pulses, beans, legumes, pasta, rice and nuts, 3) moderate consumption of dairy products, and fish, 4) low consumption of sweets and salty foods, 5) very low consumption of red and processed meat. Moderate amount of wine, preferably red wine rich in polyphenols and flavonoids supplements meals.

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Consumption of meat is low, as well as animal fat and sugar. As with Mediterranean diet, traditional South Eastern Asia diet is associated with low incidence of cardiovascular disease, obesity and some types of cancer. The main difference with Mediterranean diet is scarce consumption of olive oil and the narrow spectrum of cuisine.

**Plant based diet**

Plant based diets consist mainly but not exclusively of foods of plant origin, cereals, starchy foods, vegetables, fruits, pulses, herbs, spices and plant oils. Meat, poultry, fish and dairy products are usually consumed in small quantities in everyday life, but more abundantly on feast days.

There are similarities with Mediterranean and Asian dietary pattern. Nutrition in the majority of world’s population, over...
4 billion people, is plant based in most rural communities in middle and low-income countries. Plant based dietary pattern is adopted by choice, due to economic reasons, since animal food is more costly or as an attitude of religion, philosophy of life and ideology to abstain from animal food. Plant based diet is associated with low incidence of obesity, coronary artery disease, diabetes and some types of cancers. This diet is becoming increasingly popular as a healthy in high-income countries, due to protective role for chronic diseases.

Vegetarian and Vegan diets
Vegetarian dietary pattern is essentially a plant-based diet which excludes meat and processed meat products. It is a plant-based diet practiced for health, religion, ecology and ideology reasons. Lacto-ovo vegetarians consume dairy products and eggs. Vegetarian dietary pattern is heterogeneous and it is associated with lower incidence of coronary artery disease, obesity and mortality, as it is the case in general with plant based diets. Vegetarians in developed high-income countries adhere to this diet by conviction and motivation for healthy diet and living, associated with physical activity, weight control and abstention of smoking and alcohol.

Vegan diet is common in Hindus and excludes foods of animal origin, including eggs, due to religious reasons.

“Western” diet
The “Western” dietary pattern first evolved in Europe and spread to the USA, Australia and New Zealand, South Africa and parts of Latin America, as a result of the legacy of British and European settlers in new lands and globalization of the industrial food system. It is an energy dense pattern, high in calories, fat and sugars, characterized by consumption of meat and processed meat products and low consumption of fruits and vegetables. It consists mainly of meat, dairy products, pastries, bakes foods, soft sugary drinks and alcoholic beverages. It is associated with overweight and obesity, diabetes, cardiovascular disease, cerebrovascular accidents, hyperlipidemia, hypertension and some types of cancer (colon, rectal, gastric, breast, prostate).

Religious diet
Islamic religion forbids consumption of pork and alcoholic beverages. Jewish religion forbids pork and Hinduism beef, considered a sacred animal. Seventh-day Adventists, a Christian denomination, avoid meat and meat products, spices, tea, coffee, alcohol and smoking. Religious diets have been the subject of research in a number of studies for a healthy way of living, associated with lower incidence of chronic diseases.

NUTRITION and CANCER
The etiology of cancer is multifactorial. According to data from the World Health Organization (WHO) nutrition and diet accounts for 30% of all cancer cases(24). Smoking accounts for 30%, followed by genetic predisposition (18%), obesity and lack of physical activity (5%), infections (5%), occupational exposure (5%), alcohol (3%), pollution (2%), UV radiation (2%) and drugs (2%).

Genetic predisposition play an important role in cancer (20% of all cases), but the majority is sporadic, due to other etiologies unrelated to genetic predisposition. In these cases, food, nutrition, exposure to food carcinogens in processing and storage, obesity and lack of physical activity are factors which influence fundamental processes of carcinogenesis (25). The effect of nutrition and diet on carcinogenesis attracted considerable interest and has become a major focus of cancer research regarding protective or causative effects of nutrients and dietary components in certain types of cancer. This association carries important implications for public awareness, based on scientific evidence to adopt a dietary pattern of healthy diet to minimize or prevent cancer risk and avoid diets and nutrients which potentially predispose to cancer.

Particular attention is required to avoid natural or man-made food carcinogens. A natural carcinogen for primary hepatocellular cancer is aflatoxin B, derived from the fungus Aspergillus fumigates, which contaminates grains and peanuts during storage, especially in humid conditions. Man-made carcinogens are produced by cooking, e.g. cooking meat at high temperatures with generation of carcinogenic polycyclic hydrocarbons and heterocyclic amines. Food preserved with salt and smoked foods contain nitrates, which generate carcinogenic nitroso compounds related to gastric and colorectal cancer.

The injudicious use of pesticides in fruits, vegetables and other agricultural products also carry a risk of cancer.
Veterinary drugs in industrial husbandry and animal production are another source of concern. These include use of antimicrobial drugs to treat or prevent infections in animals, which pass to foods and drinks, which may exert a carcinogenic effect. Hormones and anabolic agents are also used in animal husbandry to prevent pregnancy or stimulate growth which carries a carcinogenic effect. These hormones include estrogens, progesterone and testosterone.

Obesity, related to overnutrition and overeating, associated with lack of physical activity predispose to cancer and increased morbidity, mortality from cardiovascular disease and cancer (26, 27).

The mechanisms regarding the association of obesity and cancer are related to a) increased levels of hormones and b) chronic low grade inflammation in adipose tissue. These two factors act synergistically with the carcinogenic effect of hormones (Table 2).

### Dietary Factors of Increased and Decreased Risk of Cancer

Extensive research on the role and association of nutrition and cancer based on metaanalysis of large prospective cohort or case-control population studies classified decreased or increased factor into four categories by degree of evidence: 1) Convincing, 2) Probable, 3) Suggestive and 4) Inconclusive (28). Only convincing, probable and suggestive factors of increased and decreased risk are included in this review (29).

A panel of international experts analyzed the data based on evidence derived from large scale epidemiological studies utilizing statistical methodology for individual cancers. It should be taken into account that nutrition consists of food intake and not individual nutrients and it is the summation of nutrients contained in food regarding the increased or decreased risk of cancer.

The following cancers were analyzed regarding the predisposing or protective effect (Table 3).

### Cancer of Mouth, Pharynx and Larynx

These cancers derived from squamous cells, they are more common in men and the 5-year survival is 50%. Alcohol is an important increased risk factor, augmented when alcohol is combined with smoking, as it is usually the case, i.e. alcohol drinkers are also, to a large extent, smokers. “Mate”, a popular hot herb beverage, popular in South America is also a predisposing factor. There is probable evidence that vegetables, fruits and foods containing carotenoids and lycopene decrease the risk due to the antioxidant effect reducing cellular and DNA damage, as well as oxidative stress, a precursor to carcinogenesis.

### Cancer of the Esophagus

It is the sixth most common cause of death from cancer. There are two types of esophageal cancer, squamous cell carcinoma more common in men and adenocarcinoma. Increased risk factors for squamous cell carcinoma of convincing evidence are smoking and alcohol drinks, notably calvados. Hot drinks in general increase the risk. In the adenocarcinoma type of esophageal cancer, increased risk factor is Barrett’s esophagus (ectopic gastric mucosa), chronic gastroesophageal reflux disease and achalasia.

In terms of dietary factors red and processed meat predispose to esophageal adenocarcinoma (29). There is probable evidence that foods containing dietary fiber, folate, pyridoxine and vitamin C decrease the risk of esophageal adenocarcinoma and exert a protective effect (30).

### Table 2. Obesity-Mechanisms predisposing to cancer

<table>
<thead>
<tr>
<th>A. Increased levels of hormones</th>
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<tr>
<td>• Insulin</td>
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<td>• Insulin resistance</td>
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<tr>
<td>• Insulin-like growth factor 1 (IGF-1)</td>
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<tr>
<td>• I-Hyperinsulinemia (colorectal and endometrial cancer)</td>
</tr>
<tr>
<td>• Leptin (colorectal and prostate cancer)</td>
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<td>• Steroids</td>
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<th>B. Chronic low level inflammation of adipose tissue</th>
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<tr>
<td>• Tumor Necrosis Factor a (TNF-a)</td>
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<tr>
<td>• Interleukin 6 (IL-6)</td>
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<td>• Leptin as inflammatory cytokine</td>
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### Table 3. Cancers and effect of nutrition

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<tr>
<th>Hepatocellular</th>
<th>Breast</th>
<th>Endometrial</th>
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<tr>
<td>Mouth, pharynx and larynx</td>
<td>Esophagus</td>
<td>Colorectal</td>
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<td></td>
<td>Stomach</td>
<td>Pancreas</td>
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Cancer of the Stomach

It is the fourth most common cause of cancer and the second most common cause of death from cancer. The incidence is decreasing in developed countries, attributed to the wide use of electric refrigerators and proper food storage.

There is convincing evidence that infection with *Helicobacter pylori* predisposes to gastric cancer by causing atrophic gastritis, intestinal metaplasia, dysplasia and cancer. Additional increased risk factors are high salt and salted foods intake, as it is the case in Japan (31). There is suggestive evidence of increased risk of chili, processed meat, smoked foods, grilled or barbecued meat. Regarding decreased risk, there is probable evidence that non-starchy vegetables, fruits rich in flavonoids and vitamin C exert a protective effect for gastric cancer (32, 33). In regard to alium vegetables there is a decreased risk related to increased intake of garlic, related to antibacterial properties inhibiting bacterial colonization of the gastric mucosa, particularly in cases of gastric atrophy (33).

Colorectal Cancer (CRC)

It is the third most common cancer, after lung and prostate in men and breast and lung cancer in women. The incidence varies from 50-60 cases / 100,000 / year in Europe, North America, Australia, New Zealand to 8-10 cases / 100,000 / year in African and Asian Countries. This marked difference reflects the importance of diet and dietary factors in the development CRC, namely high intake of animal fat, protein and calories (“Western” diet) vs plant based and Mediterranean diet.

It is estimated that 15-20% of CRC are etiologically related to genetic / familial predisposition, whereas the majority of cases (75-80%) are sporadic, i.e. related to nutrition, obesity and lack of physical activity (35, 36).

Factors of increased risk of CRC

Factors of increased risk of CRC are summarized in Table 4. Red and processed meat are major dietary factors which predispose to CRC. Red meat refers to beef, porc, lamb and goat, whereas white meat which is preferable, includes fish, chicken and turkey. The evidence based on metaanalysis of large scale prospective epidemiological studies is convincing of the increased risk related to higher intake of meat and meat products (38, 39).

The mechanisms of increased risk of meat intake with CRC are: 1) generation of N-nitroso compounds which are carcinogenic, 2) production of heterocyclic amines and polycyclic aromatic hydrocarbons by cooking in high temperatures, 3) high concentration of iron in meat generates reactive oxygen species and cytokines which are cytotoxic and promote colonic cell proliferation.

### Table 4. Factors of increased risk of CRC

<table>
<thead>
<tr>
<th>Factor</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red meat</td>
<td>Convincing</td>
</tr>
<tr>
<td>Processed meat</td>
<td>Convincing</td>
</tr>
<tr>
<td>Alcohol (men)</td>
<td>Convincing</td>
</tr>
<tr>
<td>High energy intake</td>
<td>Convincing</td>
</tr>
<tr>
<td>Obesity – Body fatness</td>
<td>Convincing</td>
</tr>
<tr>
<td>Abdominal fat</td>
<td>Convincing</td>
</tr>
<tr>
<td>Adult-attained height</td>
<td>Convincing</td>
</tr>
<tr>
<td>Lack of physical activity</td>
<td>Convincing</td>
</tr>
<tr>
<td>Alcohol (women)</td>
<td>Probable</td>
</tr>
<tr>
<td>Animal fat</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Sugar</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Foods containing iron</td>
<td>Suggestive</td>
</tr>
</tbody>
</table>

Data based on metaanalysis by American Institute for Cancer Research and World Cancer Research Fund (Ref 28, 2007) and European Investigation into Cancer and Nutrition (EPIC), (Ref 37, 2008)

### Table 5. Factors of decreased risk of CRC

<table>
<thead>
<tr>
<th>Factor</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity</td>
<td>Convincing</td>
</tr>
<tr>
<td>Weight control</td>
<td>Convincing</td>
</tr>
<tr>
<td>Dietary fiber</td>
<td>Probable</td>
</tr>
<tr>
<td>Garlic</td>
<td>Probable</td>
</tr>
<tr>
<td>Milk</td>
<td>Probable</td>
</tr>
<tr>
<td>Calcium</td>
<td>Probable</td>
</tr>
<tr>
<td>Fish</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Non-starchy vegetables</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Fruits</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Foods with folate</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Foods with vitamin D</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Selenium</td>
<td>Suggestive</td>
</tr>
</tbody>
</table>

Data based on metaanalysis by American Institute for Cancer Research and World Cancer Research Fund (Ref 28, 2007) and European Investigation into Cancer and Nutrition (EPIC), (Ref 37 and 40, 2009)
There is also conclusive evidence that heavy alcohol intake is a risk factor in men, whereas in women the evidence is probable, attributed to gender differences in alcohol metabolism. The metabolite acetaldehyde is carcinogenic and induces DNA mutations. High energy intake due calories, obesity, body fatness, abdominal fat and adult attained height and lack of physical activity are factors of increased risk, based on convincing evidence.

Factors of decreased risk

Factors of decreased risk of CRC are summarized in Table 5. Physical activity is by convincing evidence a protective factor of CRC, which reduces risk by 30-40%. The degree of protection is increased linearly with increments of duration and intensity of physical activity.

Physical activity increases metabolic rate and oxygen uptake, lowers blood pressure and insulin resistance and improves colonic motility. Combined with weight control physical activity is a significant protective factor of CRC. Foods associated with decreased risk of CRC on probable evidence are dietary fiber, garlic, milk and calcium and on suggestive evidence fish, vegetables, fruits, foods containing folate, vitamin D and selenium. The protective role of dietary fiber on CRC is attributed to increased bulk of fecal content, shorter bowel transit and generation of short chain fatty acids which induce apoptosis. Dairy products and high milk intake due to calcium and garlic inhibit induce apoptosis and inhibit cell growth.

There is suggestive evidence that fruits and vegetables decrease risk of CRC, attributed to antioxidant properties. In a metaanalysis of 14 cohort studies involving 750,000 men and women followed from 6-12 years showed that regular intake of fruits and vegetables is associated with a lower risk of distal colon cancer but not with overall decrease of CRC. The study conducted by the European Prospective Investigation into Cancer and Prevention (EPIC) showed that high consumption of fruits and vegetables is associated with decreased risk of colon cancer (40). Consequently, the protective role of fruits and vegetables on CRC remains valid and contributes with other factors to decreased risk of CRC.

Regarding the mechanism of decreased risk of CRC, fish is rich in omega-3 and polyunsaturated fatty acids which inhibit cyclooxygenase implicated in carcinogenesis. Calcium and vitamin D promote apoptosis of intestinal epithelial cells, selenium has anti-inflammatory and antioxidant properties and folate plays an important role in DNA synthesis, repair and methylation. Errors in DNA methylation are associated with aberrant gene expression.

It should be taken into account that we do not ingest individual nutrients but different foods with different nutrient composition, a fundamental principle in nutrition (42). Accordingly, it is the food consumption and food synergy which determine an increased or decreased risk of developing cancer or other diseases (43), depending to a significant degree on genetic predisposition, physical activity and weight control.

Cancer of the Pancreas

Cancer of the pancreas has a poor prognosis and the 5 year survival is less than 5%. The incidence is high in developed countries. There is convincing evidence of increased risk of chronic pancreatitis, smoking, body fatness and probably diabetes. Cessation of smoking decreases the risk significantly. Nutrition does not play a significant role in decreasing the risk factor.

Hepatocellular Carcinoma

Etiological factors of hepatocellular carcinoma are chronic hepatitis B and C, alcoholic cirrhosis and cirrhosis from other causes. Exposure to aflatoxin B derived from Aspergillus fumigates, due to contamination during storage of cereal grain, pulses, seeds and nuts, is a predisposing factor with increased risk. There is limited evidence that dietary factors, i.e. fruits, vegetables, fish and foods containing folate or selenium decrease the risk.

Breast Cancer

Worldwide it is the most common cancer in women and a leading cause of death from cancer. It is hormone related and family history is a predisposing factor. The incidence is higher in industrialized nations and urban population, but the incidence is increasing in emerging economies in countries of Asia and South American.

In premenopausal breast cancer alcohol, greater birth weight and adult height are increased risk, whereas lactation, physical activity and body fatness are decreased risk. In postmenopausal breast cancer alcohol, body fatness, adult height and
adult weight gain are increased risk. Lactation and physical activity are decreased risk. There is probable evidence that fruits and vegetables decrease the risk.

**Endometrial Cancer**

It is more frequent in developed countries and accounts for 2% of all cancer deaths in women. The risk increases with age and most diagnoses are made in postmenopause. Regarding risk factors, there is convincing evidence that body fatness and abdominal fatness increase the risk. There is limited evidence that red meat and adult attained height increase the risk. Dietary factors do not play a role increasing or decreasing the risk.

**Ovarian Cancer**

There is probable evidence that adult attained height increases the risk. By contrast, late menarche, childbirth, lactation and early menopause have a protective effect. All these events are related to reduction of menstrual cycles and lower exposure of estrogens to the ovaries. There is limited evidence that fruits and vegetables confer protection or lower the risk.

**Cancer of the Prostate**

It is the second most common cancer in men after lung cancer. It is a hormone related cancer with high degree of genetic penetrance in first or second degree relatives with prostate cancer.

The incidence is high in industrialized countries and high income populations. The diagnosis is made earlier with the wide use of prostatic specific antigen (PSA).

In term of dietary factors, high calcium intake from dairy products increases the risk of prostate cancer. This is due to down-regulation of 1,25 dihydroxy vitamin D3 synthesis from vitamin D, which stimulates prostate cell proliferation. There is evidence that foods containing lycopene, selenium, carotenoids and vitamin E decrease risk. Lycopene is a potent carotenoid antioxidant with antiproliferative action which reduces inflammation and improves immune function. Tomatoes, especially cooked (tomato sauce) are rich source of lycopene. There is no evidence that dietary fibre, vitamins A and C, physical activity, body fatness, abdominal fatness and energy intake increase or decrease prostate cancer risk.

**HEALTH ASPECTS of MEDITERRANEAN DIET**

The first observation of health aspects of Mediterranean diet were recorded in the island of Crete in 1948 in a project under the auspices of Rockefeller Foundation in USA, invited by the Greek Government to assess and improve health, economic and social condition in postwar Greece. The American epidemiologist Leland Albaugh coordinated a survey on diet and living condition of 765 Cretan households. The results of the epidemiological study was published by Albaugh in 1953 in a monograph (44). Paradoxically, in an “undeveloped area”, as the title of the publication indicates, the spartan dietary conditions in Cretan villages, proved beneficial to health, regarding the incidence of cardiovascular disease. Diet rich in olive oil, grain cereals, nuts, pulses and fish was associated with low rates of coronary artery disease and heart attacks.

It is surprising even by today’s epidemiological standards that this survey was conducted and completed with detailed scientific methodology and statistical evaluation (21). The field work, regarding dietary practices, energy intake and food frequency, was conducted by volunteer nurses from the Hellenic Red Cross, who after a training period they lived in the communities surveyed visited households daily and recorded the data. This was a landmark pioneer study which paved the way to the recognition of Mediterranean diet as the model of healthy diet.

It was a forerunner of the Seven Countries Study which was launched by the American epidemiologist and physiologist Ancel Keys and associates in the 1950s (45). Keys, stationed in Salerno, Italy in the 1952, made the observation that local population in Southern Italy had lower rate of cardiovascular disease, similar to the Cretan population, compared with USA, which was attributed as in the survey in Crete, to the Mediterranean dietary pattern (18). Keys and his associates launched the pivotal Seven Countries Study in 1958, a prospective investigation on diet and risk of cardiovascular disease in 7 countries, namely United States, Greece, Italy, Finland, the Netherlands, former Yugoslavia and Japan (19, 20). The Seven Countries Study showed that in different countries with different dietary pattern food composition and high animal fat intake was related to high cholesterol and coronary artery disease. By contrast, consumption of olive oil, cereal grains, fruits and vegetables, which constitute
Finally, there are some preliminary data that Mediterranean diet may have a preventive or ameliorating effect in depressive disorders (65), but further longitudinal prospective studies are needed to confirm these observations.

In conclusion, there is substantial and convincing evidence based on long-term multinational and multicenter prospective epidemiological studies on large populations that Mediterranean diet constitutes a model of healthy diet. A consistent adherence to Mediterranean diet is associated with lower risk of cardiovascular disease, certain cancers (esophageal, gastric, colorectal), type 2 diabetes, hypertension, obesity, metabolic syndrome and possibly Alzheimer disease and depressive disorders.

It should be emphasized, that in addition to Mediterranean diet, physical activity, good quality of life, open air activities, social interaction and sense of well being are related to mental health, attributes of the Mediterranean culture and landscape.

CULTURAL ASPECTS of MEDITERRANEAN DIET

Mediterranean diet developed over centuries in the countries bordering the Mediterranean Sea, Southern Europe, North Africa, Eastern Mediterranean and Middle East. Despite differences in religion, languages, culture, political systems, economy, climate and landscape, there is a common legacy with its variation of the Mediterranean cuisine and the Mediterranean dietary pattern.

Mediterranean is not only one sea, there is succession and communication of seas. Ancient civilizations sprang from Mediterranean basin, being a crossroad of different people and different lands. It is not only one civilization, but many civilizations evolving on different layers (66). Great civilizations were nurtured and developed over millennia by the Mediterranean Sea, the Mare Nostrum - Egyptian, Phoenician, Minoic, Ionian, Hellenic, Roman, Byzantine, Ottoman, Arab, Norman, Venetian. Civilizations develop when human habitat promotes organization of communities and produce major works of lasting value which glow with grandeur, thousands of years after their creation.

Mediterranean is blessed with a temperate climate, an important attribute of human habitat. Mild winters, glorious springs, hot summers and sweet falls, a succession of seasons...
generate a variety of pleasant milieu, which fosters social interaction and communal life. The landscape is also an important factor with succession of seascapes, islands, mountain, prairies, favorable for agriculture, vineyards and olive trees, olive oil and wine being the most emblematic and ancient Mediterranean products. Communal life, climate and landscape have been the setting where Mediterranean diet developed and flourished, from the soil and sea to the table. It is the ideal setting for a colorful, plentiful, joyous and variable table with Mediterranean food and different tastes.

Mediterranean diet is more than food, it has developed over centuries and transmitted from generation to generation, by tradition, skills, family ties and community life. Women have played a pivotal role in the preservation and transmission of Mediterranean diet safeguarding the art and knowledge of food preparation and the culture of the table.

In recognition of the cultural value of Mediterranean diet the United Nations Educational, Scientific and Cultural Organizations (UNESCO) on November 14, 2010 in Nairobi, included Mediterranean diet in the list of Intangible Cultural Heritage of humanity (67). The file for this recognition was submitted by four model Mediterranean communities of Mediterranean diet and culture, Soria (Spain), Koroni (Greece), Cilento (Italy) and Chefchaouen (Morocco).

The statement by UNESCO for the recognition of Mediterranean diet in the list of Intangible Cultural Heritage of humanity reads as follows:

“The Mediterranean diet constitutes a set of skills, knowledge, practices and traditions ranging from the landscape to the table, including the crops, harvesting, fishing, conservation, processing, preparation and consumption of food. A nutritional model which remained constant over time and space, consisting mainly of olive oil, cereals, fresh or dried fruits and vegetables, a moderate amount of fish and dairy products, low amount of meat, condiments, spices, accompanied by wine, according to the beliefs of each community. It is more than food, it promotes social interaction and communal events, since communal meals are the cornerstone of social customs and festivities. It has enriched knowledge, generated songs and music, tales and legends over centuries in the Mediterranean. The Mediterranean diet is rooted in respect to the territory, biodiversity and is closely related to traditional activities and crafts linked to farming and fishing. Women played a vital role in the transmission from generation to generation, as well as knowledge of gestures, celebration practices and the culture of the table”.

Mediterranean diet, is indeed, a time honored legacy of health and culture, a great contribution to the world, which needs to be preserved, as monuments of ancient civilizations and passed to future generations.

REFERENCES


MAHATMA GANDHI
(1869-1948)

Dünyada görmeyi istediğinize değişimin kendisi olunuz.