Nutrition, Health and Dietary Trends

John L. Sievenpiper, Gabriele Riccardi, Camillo Ricordi, and Katarzyna Dembska

1 Nutrition and Global Non-communicable Diseases

Over the past several decades the world has seen a dramatic shift in the way people eat, drink and move (Popkin et al. 2012), leading to a public health crisis that threatens the economies of all nations, particularly developing countries: few countries are immune to the parallel rise of overweight, obesity, and non-communicable diseases (NCDs). NCDs, also known as chronic diseases, tend to be of long duration and are the result of a combination of genetic, physiological, environmental and behavior factors. The main types of NCDs are cardiovascular diseases (like heart attacks and

J. L. Sievenpiper (✉)
Faculty of Medicine, Department of Nutritional Sciences, University of Toronto, Toronto, ON, Canada

Division of Endocrinology and Metabolism, Department of Medicine, St. Michael's Hospital, Toronto, ON, Canada

Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, Canada
e-mail: john.sievenpiper@utoronto.ca

G. Riccardi
Diabetes, Nutrition and Metabolism research group, Department of Clinical Medicine and Surgery, Federico II University, Naples, Italy
e-mail: gabriele.riccardi@unina.it

C. Ricordi
Diabetes Research Institute and Cell Transplant Center, University of Miami, Miami, FL, USA
e-mail: ricordi@miami.edu

K. Dembska
Barilla Center for Food and Nutrition (BCFN), Parma, Italy
e-mail: katarzyna.dembska@external.barillacfn.com

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stroke), cancers, chronic respiratory diseases (such as chronic obstructive pulmonary disease and asthma) and diabetes (World Health Organization 2018).

A nutritional transition started in the 60s: diets are converging on what we often term the "Western diet" (Popkin et al. 2012) characterized by increased consumption of meat, dairy, sugars, fats and energy-dense food (Alexandratos 2006; Grigg 1995) and the decline in adherence to the so-called 'healthy diets' such as the 'Mediterranean diet'. Although highly heterogeneous among countries, the Mediterranean diet presents several common features: a high consumption of plant foods such as legumes, cereals, fruits and vegetables, nuts and seeds, low consumption of meat and dairy products, olive oil as main source of fat and moderate consumption of wine (Da Silva et al. 2009).

Simultaneously, the epidemiological transition with developments in healthcare and medicine, is drastically reducing mortality due to infectious disease, and extend average life expectancy, which accompanied by increasing prevalence of chronic and degenerative diseases which were more important causes of death today (Omran 2005).

The 2030 Agenda for Sustainable Development adopted at the United Nations recognizes NCDs as a major challenge for sustainable development. Heads of State and Government committed to develop national responses to the overall implementation of this Agenda, including to reduce by one third premature mortality from NCDs.

2 Evolution of Nutrition Guidelines: A Shift from Nutrients to Dietary Patterns

Nutrition remains the cornerstone of therapy for the prevention and management of chronic diseases. The Global Burden Disease (GBD), the largest comparative analysis of the 79 leading risk factors, confirms that poor nutrition is the single most important contributor to the burden of premature morbidity and mortality, accounting for more than 10% of disability adjusted life years (DALYs) especially from cardiovascular diseases and diabetes (Forouzanfar et al. 2016). If poor nutrition is combined with other modifiable lifestyle related risk factors, then it accounts for 25% of premature morbidity and mortality (Forouzanfar et al. 2016). The combination of a healthy dietary pattern with other low-risk lifestyle behaviours that include achieving and maintaining a healthy body weight, regular physical activity, smoking abstinence/cessation, moderate alcohol consumption, and moderate sleep duration is associated with >70% reduction in incident cardiovascular disease (Anderson et al. 2016) and diabetes (Ford et al. 2009; Hu et al. 2001; Mozaffarian et al. 2009).

2.1 Nutrient-Disease Risk Model

Identification of the specific dietary factors that explain disease risk reduction has been of great interest since the time of Hippocrates (Jouanna 2012) and the subject of intense clinical investigation for more than 250 years (Milne 2012). The earliest examples are of investigations of the causal role of specific nutrients (vitamins, minerals, essential amino acids, and essential fatty acids) in diseases of deficiency. An investigation of citrus fruit (vitamin C) for the treatment of scurvy in the Royal Navy by James Lind in 1747 is considered the earliest recorded example of a clinical trial (Milne 2012). Within 200 years of this discovery, the major vitamins and their deficiency diseases were identified: vitamin A (xerophthalmia) vitamin B1 (beriberi), vitamin B3 (pellagra), folate (anemia, spina bifida), vitamin C (scurvy), vitamin D (rickets), vitamin B12 (pernicious anaemia), iron (anemia), iodine (goiter), etc. Despite the incredible public health success of this reductionist model in the prevention of nutritional deficiencies (Mozaffarian et al. 2018), a focus on single nutrients for the prevention of chronic diseases has met with less success.

There are innumerable examples of nutrients supported by biologically plausible mechanisms and/or epidemiological observations that did not produce the anticipated benefits or even resulted in important harm. Large, carefully conducted randomized controlled trials and subsequent systematic reviews and meta-analyses of the available randomized controlled trials have shown that beta-carotene increases lung cancer mortality and all-cause mortality (Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Alpha-Tocopherol Beta Carotene Cancer Prevention Study Group 1994; Omenn et al. 1996); vitamin E, prostate cancer incidence (Klein et al. 2011; Vinceti et al. 2018), selenium, diabetes incidence (Vinceti et al. 2018), antioxidants, all-cause mortality (Jenkins et al. 2018), and niacin, all-cause mortality (Jenkins et al. 2018), while fish oils (Abdelhamid et al. 2018), calcium (Jenkins et al. 2018), and vitamin D (Jenkins et al. 2018) have failed to demonstrate a cardiovascular benefit or mortality benefit. The same is true for a focus on single macronutrients (e.g. “low fat”, “low carb”, or “high protein”). Network meta-analyses of randomized controlled trials comparing diets of varying proportions of macronutrients show only minimal differences in weight loss between diets at 6 and 12-months of follow-up, suggesting that there is no one best macronutrient-based approach and adherence to anyone diet is the dominant consideration (Johnston et al. 2014). The culmination of these failures has been an important paradigm shift.

2.2 Dietary Pattern-Based Clinical Practice Guidelines

Clinical practice guidelines for nutrition therapy in obesity, diabetes, and cardiovascular disease have begun to move away from a focus on single nutrients to a focus on food and dietary patterns (Sievenpiper and Dworatzek 2013). These guidelines had been historically very macronutrient-centric, recommending a narrow acceptable macronutrient distribution range (e.g. 55% energy from carbohydrate and 30% energy from fat) that became progressively broader (45–65% energy from carbohydrate, <35% energy from fat and 15–20% energy from protein), as more emphasis was placed on quality over quantity of carbohydrate, fat, and protein (Sievenpiper and Dworatzek 2013). The transition to more dietary pattern-based recommendations has occurred with the recognition that a focus on single nutrients misses important nutrient-nutrient and nutrient-food (matrix) interactions that better explain chronic disease risk than single nutrients alone.

Dietary pattern-based clinical practice guidelines have provided clinicians, patients, and the public with a number of evidence-based options for the prevention and management of chronic diseases (Sievenpiper et al. 2018; Anderson et al. 2016). Although the evidence may be stronger for some dietary patterns, these guidelines consider the advantages and disadvantages of all dietary patterns for which evidence is available. The Mediterranean dietary pattern is a dietary pattern with some of the highest quality evidence for benefit. The Prevención con Dieta Mediterranea (PREDIMED) trial, a large Spanish multi-centre randomized trial of a Mediterranean dietary pattern in 7447 participants at high CV risk, showed that a Mediterranean diet supplemented with either extra-virgin olive oil or mixed nuts compared with a low-fat American Heart Association control diet decreased major cardiovascular events over a median follow-up of 4.8 years (Ramón Estruch et al. 2018), a finding supported by systematic reviews and meta-analyses of the available randomized controlled trials and prospective cohort studies (Becerra-Tomás et al. 2019). Secondary analyses of the PREDIMED trial have also shown evidence of modest weight loss, decreased diabetes incidence (single centre) and increased metabolic syndrome reversion (Ramon Estruch et al. 2016; Salas-Salvadó et al. 2011). Other dietary patterns with evidence of benefit include low-glycemic index (GI) (Mirrahimi et al. 2012; Viguiliouk et al. 2018b), Portfolio (Chiavaroli et al. 2018), vegetarian (Glenn et al. 2019; Lee and Park 2017; Viguiliouk et al. 2018a; Fenglei Wang et al. 2015), Dietary Approaches to Stop Hypertension (DASH) (Chiavaroli et al. 2019), and Nordic (Adamsson et al. 2011; Galbete et al. 2018a; Lemming et al. 2018; Poulsen et al. 2013, 2015; Roswall et al. 2015; Uusitupa et al. 2013) dietary patterns as well as dietary patterns emphasizing specific foods including pulses (beans, peas, chickpeas, and lentils) (Ha et al. 2014; Jayalath et al. 2013; Kim et al. 2016; Li et al. 2017; Viguiliouk et al. 2015, 2017), fruit and vegetables (Huang et al., 2016; Xia Wang et al., 2014), nuts (Afshin et al. 2014; Flores-Mateo et al. 2013; Mejia et al. 2014; Sabaté et al. 2010; Viguiliouk et al. 2014), whole grains (Aune et al. 2016; Bao et al. 2014; Ho et al. 2016; Hollænder et al. 2015; Schwingshackl et al. 2017), and dairy (Gijsbers et al. 2016; Imamura et al. 2018). Systematic reviews and meta-analyses have shown that these other dietary patterns improve established cardiometabolic risk factors in randomized controlled trials (Chiavaroli et al. 2018, 2019; Viguiliouk et al. 2014, 2015, 2017, 2018a, b; Fenglei Wang et al. 2015; Adamsson et al. 2011; Ha et al. 2014; Jayalath et al. 2013; Kim et al. 2016; Li et al. 2017; Poulsen et al. 2013, 2015; Uusitupa et al. 2013; Huang et al. 2016; Flores-Mateo et al. 2013; Mejia et al. 2014; Sabaté et al. 2010; Bao et al. 2014; Ho et al. 2016; Hollænder et al. 2015) and are associated with decreased diabetes and cardiovascular disease incidence and mortality in prospective cohort studies (Glenn et al. 2019; Lee and Park 2017; Mirrahimi et al. 2012; Viguiliouk et al. 2017, 2018b; Chiavaroli et al. 2019; Galbete et al. 2018a; Lemming et al. 2018; Roswall et al. 2015; Afshin et al. 2014; Wang et al. 2014; Aune et al. 2016; Gijsbers et al. 2016; Imamura et al. 2018; Schwingshackl et al. 2017).

The approach to nutrition therapy is to integrate the assessment of the evidence for these different dietary patterns into a shared clinical decision making model to individualize nutrition therapy. The algorithm for nutrition therapy from the Diabetes Canada 2018 clinical practice guidelines provides a good example of this approach (Fig. 1) (Sievenpiper et al. 2018). The algorithm encourages the clinician and patient to align the evidence of advantages and disadvantages of each dietary pattern with the values, preferences, and treatment goals of the patient. As adherence is considered one of the most important determinants of achieving the benefit of any dietary pattern, the overarching goal is to use the available evidence to find the dietary pattern that will allow the patient to achieve the greatest adherence over the long-term and so achieve the intended benefits.

Dietary pattern-based clinical practice guidelines continue to evolve. The most recent clinical practice guidelines for nutrition therapy in diabetes and cardiovascular disease in Canada (Anderson et al. 2016; Sievenpiper et al. 2018), the United States (American Diabetes Association 2019; Grundy et al. 2018), and Europe (Catapano et al., 2016) have further expanded their focus on dietary patterns. Other clinical practice guidelines have also begun to adopt this focus, including Obesity Canada which will release its updated CPGs in 2019 (https://obesitycanada.ca/resources/clinical-guidelines/) and the European Association for the Study of Diabetes (EASD), which has commissioned a series of systematic reviews and meta-analyses of dietary patterns for diabetes to inform the update of their Clinical practice guidelines (Chiavaroli et al. 2018, 2019; Glenn et al. 2019; Viguiliouk et al. 2018a). As the evidence for different dietary patterns increases, an even greater shift toward dietary patterns is expected.

3 The Relationship Between Dietary Patterns and Chronic Non-communicable Diseases: The Mediterranean Diet

There is ample evidence that the cardiovascular risk can be modulated by lifestyle factors and, in particular, by dietary habits. In the last decades, the science of human nutrition has shifted from a reductionist approach focused on specific nutrients to a broader view emphasizing the role of food groups/dietary patterns in modulating people's health. This paradigm change is due to convincing scientific evidence showing that body functions are influenced not only by single nutrients, but also by

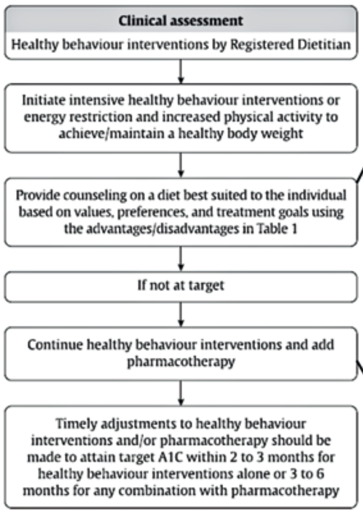

Table 1
Properties of dietary interventions*†‡

Properties of dietary interventions (listed in the order they are presented in the text)

Dietary interventions	A1C	CV benefit	Other advantages	Disadvantages
Macronutrient-based approaches				
Low-glycemic-index diets	↓ (32,44,46,47)	↓CVD (52)	↓LDL-C, ↓CRP, ↓hypoglycemia, ↓diabetes Rx	None
High-fibre diets	↓ (viscous fibre) (57)	↓CVD (69)	↓LDL-C, ↓non-HDL-C, ↓apo B (viscous fibre) (54,57,59)	GI side effects (transient)
High-MUFA diets	↔	↓CVD	↓Weight, ↓TG, ↓BP	None
Low-carbohydrate diets	↔	-	↓TG	↓Micronutrients, ↑renal load
High-protein diets	↓	-	↓TG, ↓BP, preserve lean mass	↓Micronutrients, ↑renal load
Mediterranean dietary pattern	↓ (50,139)	↓CVD (143)	↓retinopathy (144), ↓BP, ↓CRP, ↑HDL-C (139,140)	None
Alternate dietary patterns				
Vegetarian	↓ (145,251)	↓CHD (152)	↓Weight (148), ↓LDL-C (149)	↓vitamin B12
DASH	↓ (159)	↓CHD (161)	↓Weight (159), ↓LDL-C (159), ↓BP (159), ↓CRP (160)	None
Portfolio	-	↓CVD (162,163)	↓LDL-C (162,163), ↓CRP (162), ↓BP (163)	None
Nordic	-	-	↓LDL-C+, ↓non-HDL-C (169–171)	None
Popular weight loss diets				
Atkins	↔	-	↓Weight, ↓TG, ↑HDL-C, ↓CRP	↑LDL-C, ↓micronutrients, ↓adherence
Protein Power Plan	↓	-	↓Weight, ↓TG, ↑HDL-C	↓Micronutrients, ↓adherence, ↑renal load
Ornish	-	-	↓Weight, ↓LDL-C, ↓CRP	↔ FPG, ↓adherence
Weight Watchers	-	-	↓Weight, ↓LDL-C, ↑HDL-C, ↓CRP	↔ FPG, ↓adherence
Zone	-	-	↓Weight, ↓LDL-C, ↓TG, ↑HDL-C	↔ FPG, ↓adherence
Dietary patterns of specific foods				
Dietary pulses/legumes	↓ (176)	↓CVD (181)	↓Weight (179), ↓LDL-C (177), ↓BP (178)	GI side effects (transient)
Fruit and vegetables	↓ (183,184)	↓CVD (79)	↓BP (186,187)	None
Nuts	↓ (188)	↓CVD (143,181)	↓LDL-C (190), ↓TG, ↓FPG (189)	Nut allergies (some individuals)
Whole grains	↓ (oats) (194)	↓CHD (99)	↓LDL-C, FPG (oats, barley) (57,193)	GI side effects (transient)
Dairy	↔	↓CVD (199,200)	↓BP, ↓TG (when replacing SSBs) (197)	Lactose intolerance (some individuals)
Meal replacements	↓	-	↓Weight	Temporary intervention

Fig. 1 Algorithm for nutrition therapy for type 2 diabetes from the Diabetes Canada 2018 Clinical Practice Guidelines. *↓ = <1% decrease in A1C. †Adjusted for medication changes. ‡References are for the evidence used to support accompanying recommendations. *A1C* denotes glycated hemoglobin, *apo B* apolipoprotein B, *BMI* body mass index, *BP* blood pressure, *CHD* coronary heart disease, *CHO* carbohydrate, *CRP* C reactive protein, *CV* cardiovascular, *CVD* cardiovascular disease, *DASH* Dietary Approaches to Stop Hypertension, *FPG* fasting plasma glucose, *GI* gastrointestinal, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *MUFA* monounsaturated fatty acid, *SSBs* sugar-sweetened beverages, *TC* total cholesterol, *TG* triglycerides. Adapted from Canadian J Diabetes, 42, Diabetes Canada Clinical Practice Guidelines Expert Committee, Sievenpiper JL, Chan CB, Dworatzek PD, Freeze C, Williams SL., Nutrition Therapy, S64–S79, Copyright (2018), with permission from Elsevier

	Cardiovascular diseases	Cancer	Diabetes
High energy intake	X	X	X
Inadequate consumption of fruit, legumes, nuts and vegetables	X	X	X
Too much processed and red meat	X	X	X
High intake of refined starch and sugar	X	X	X
Too much trans and saturated (animal and tropical) fat	X		X
Low fish consumption	X		X
Too much salt	X		
Too much alcohol	X	X	X

Fig. 2 Food choices associated with higher risk for the most relevant chronic diseases at the population level

their complex interactions and by their interplay with other active substances present in food. These are likely to act synergistically and, therefore, their impact on human health may not be appreciated unless evaluated within the context of the whole diet. Furthermore, characteristics other than nutrients combination (i.e. physical features of the foods, technological processes, cooking procedures) may influence the absorption and bioavailability of nutrients and in turn modulate their metabolic effects. Therefore, awareness is growing of the relevance of dietary patterns in relation to the risk of disease or death. The Mediterranean Diet is one of the dietary patterns that has been more extensively evaluated and strong evidence from observational and intervention studies has accumulated on its health benefits for primary and secondary prevention of cardiovascular disease and other major chronic diseases such as type 2 diabetes, cancer and probably cognitive impairment (Fig. 2) (Bonaccio et al. 2018; Ramón Estruch et al. 2018; Galbete et al. 2018b).

3.1 The Mediterranean Diet for Prevention of Cardiovascular Disease, Diabetes and Cancer

The so called "Mediterranean Diet" is a model of healthful eating habits for the prevention of coronary heart diseases (CHD), the major cause of premature death and disability in industrialized countries. It was first proposed by Ancel Keys in the fifties: he was interested in the relationship between dietary habits and cardiovascular diseases and in order to clarify this issue he undertook an epidemiological study, the Seven Countries Study, which is still considered a milestone of research in cardiology and nutrition. This study demonstrated that cardiovascular diseases were half as common in populations living in the Mediterranean area than in those living in northern Europe or in the USA; this was largely accounted for by dietary habits which were markedly different in the populations with a high or a low rate of cardiovascular diseases.

The health benefits of the traditional Mediterranean diet have been tested over the year in hundreds of studies that have consistently shown that people following a diet resembling that model have a longer lifespan and a lower of mortality rate. (1) Other studies have shown that this type of diet is also associated with a lower risk of diabetes, cardiovascular diseases and cancer. Even cognitive decline or chronic digestive diseases occur less frequently in people following such a diet. These findings have been reproduced in different countries and in various ethnic groups and, therefore, cannot be ascribed to genetics but must be due to the features of this dietary regimen (Galbete et al. 2018a).

3.2 Characteristics of the Mediterranean Diet

Mediterranean Diet is a broad term used to describe the traditional food choices of people living around the Mediterranean basin. They are largely similar in the different populations and are characterized by a relatively high intake of vegetables, fruit, nuts and legumes, a moderate consumption of fresh and processed meat and by the use of olive oil as the main culinary fat while animal fat is utilized only occasionally (Fig. 3) (Fidanza et al. 2004; Vitale et al. 2018).

However, socially-and culturally-driven differences in food habits exist between Mediterranean Countries. Dietary patterns based on local foods may lead to specificities in the nutrient composition and other characteristics of the diet which, in turn, may lead to diverse health effects (Karamanos et al. 2002).

One relevant example is wheat which is consumed in different quantities and under different food forms (i.e. pasta, bulgur, couscous, bread, porridge) in the various populations. Other differential features of the Mediterranean diet according to local habits are the consumption of specific types of legumes (dry beans, chickpeas, lentils, or fresh peas) as well as the quantity and quality of fat and the amount of added sugars and sugary beverages.

Fig. 3 Features of the traditional Mediterranean Diet

⇑ Vegetables and fruit
⇑ Cereals (pasta and whole-meal bread)
⇑ Legumes and nuts
⇑ Olive oil
⇑ Fish
One or two glasses of wine

⇓ Meat
⇓ Dairy products
⇓ Animal fat

3.3 Mediterranean Diet and Chronic Degenerative Diseases: Insights on Potential Mechanisms

3.3.1 Dietary Fat

Available epidemiological data indicate that while vegetable/unsaturated fat intake is associated with a lower cardiovascular risk, the opposite is true for the consumption animal/saturated fat and trans-fatty acids. In support of this evidence, intervention studies in humans have clearly shown that replacing saturated fat with monounsaturated fat, largely present in olive oil, or with polyunsaturated fat, derived mainly by seed oils like sunflower or corn oil, lowers plasma low-density lipoproteins (LDL) cholesterol, a very atherogenic[1] lipoprotein. The high consistency of the evidence has prompted the European Food Safety Authority (EFSA)—an independent and authoritative body appointed by the European Community to issue opinions on the scientific substantiation of health claims—to state that "consumption of saturated fat increases blood cholesterol concentrations; consumption of mono- and/or polyunsaturated fat in replacement of saturated fat has been shown to lower/reduce blood cholesterol. Blood cholesterol lowering may reduce the risk of (coronary) heart disease".

Substitution of saturated fat with monounsaturated or polyunsaturated fat improves also other cardiovascular risk factors (RF) and, in particular, endothelial dysfunction, blood pressure, insulin sensitivity subclinical inflammation (Catapano et al. 2016).

3.3.2 Carbohydrate Rich Foods

Elevations of plasma glucose levels in the postprandial period represent an important risk factor not only for type 2 diabetes but also for cardiovascular diseases and cancer. In fact, high glucose levels are paralleled by increased plasma concentrations of insulin and triglycerides; all together, these metabolic abnormalities facilitate the occurrence of cardiovascular diseases and promote cell proliferation, a crucial mechanism involved in the development of cancer. Not all carbohydrate-rich foods are equally hyperglycaemic: differences in the postprandial blood glucose response to various carbohydrate-containing foods have been demonstrated in both healthy subjects and diabetic patients, even if they were consumed in portion sizes containing identical amounts of carbohydrate (Riccardi et al. 2003).

In this context, the amount and the physico-chemical properties of fibre present in each carbohydrate rich food is of paramount importance in relation to the impact on postprandial metabolism. In fact, dietary fibre, which is not digested and absorbed in the small intestine delays the absorption of glucose and fat from the small intestine; moreover it ferments in the gut and produces short chain fatty acids which can contribute to the modulation of glucose and lipid metabolism in the liver.

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[1] That initiates or accelerates an abnormal fatty deposit within the walls of arteries.

The vast majority of the studies in this field consistently show a protective role of dietary fibre in relation to the development of major chronic degenerative diseases. Good sources of dietary fibre are legumes, vegetables, fruit, wholegrain, nuts; they are also rich in antioxidants, vitamins and minerals which could contribute to their protective role against most chronic diseases (Catapano et al. 2016; Mann et al. 2004; Parillo and Riccardi 2004).

The physical structure of the foods can also contribute to slow down carbohydrate digestion and this explains why foods like pasta or parboiled rice or potato dumplings have a lower impact on postprandial glycemia, although they are not particularly fibre rich (Riccardi et al. 2003).

3.4 *Towards a Comprehensive Nutritional Approach to Prevent Chronic Non Communicable Diseases: The Role of the Traditional Mediterranean Diet*

Consistent evidence indicates that a diet rich in carbohydrate and fibre, with a low glycaemic index and a high vegetable/animal fat ratio, may contribute to the prevention of many chronic non communicable diseases. Therefore foods with a low glycaemic index and/or high fibre content (e.g. legumes, pasta, parboiled rice, fruits, vegetables, wholegrain, nuts) should replace, whenever possible, those with a high glycaemic index, while unsaturated fat (olive oil) should be a preferential source of dietary fat instead of butter or cheese or fatty meat (Fig. 4) (Mann et al. 2004; Parillo and Riccardi 2004).

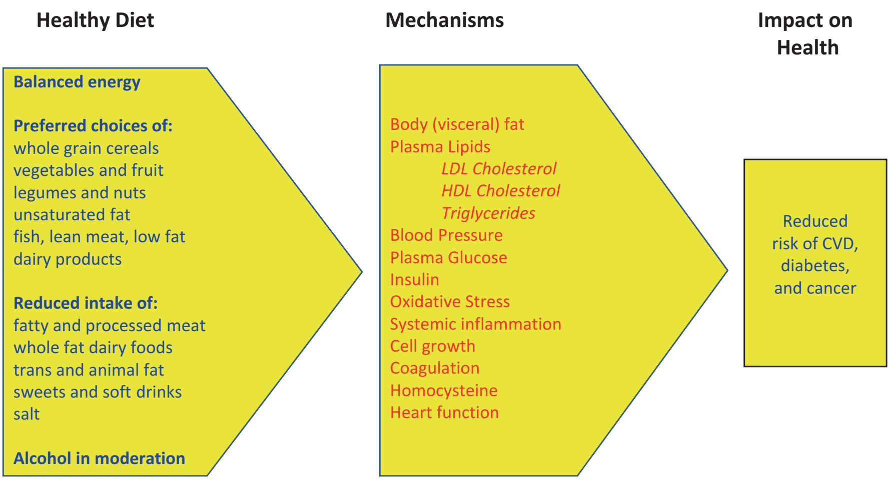

Fig. 4 Features of a healthy diet leading to a lower risk of chronic non-degenerative diseases

This dietary pattern resembles the traditional diet of people living in the Mediterranean region, which is still popular today, especially in the countryside; however these people, too, are experiencing westernization and their nutritional habits are changing towards increased consumption of energy-dense fat-rich products. However, a number of traditional meals and healthy foods are still present in the habitual diet of people living in Greece, Spain or Southern Italy, and it may therefore be wise to make this heritage available to other populations, giving them the opportunity to take advantage of a gastronomic culture that so well links health with pleasure. This is extremely important for the implementation of feasible programs for prevention of chronic non communicable diseases. Long lasting lifestyle changes are difficult to be achieved and, although health motivations may help compliance in the short term, palatability remains an important determinant of any dietary change aimed to last (Grimaldi et al. 2018; Vitale et al. 2018).

4 Possible Role of Nutrition to Prevent Chronic Degenerative Diseases and Improve Health Span

Traditional nutrition and dietary guidelines have focused on easy to understand food groups, such as protein, fats, carbohydrates (carbs), fiber content, etc. Understanding the difference between "good carbs" and "bad carbs", or glycemic index, has been a difficult concept to introduce in nutrition educational programs. It has been even more challenging to understand how nutrition could affect diet-induced inflammation that can be detected by changes in the blood and in the intestinal microbiome (Lopetuso et al. 2014; Sears and Ricordi 2010, 2012). Unfortunately, the evolution of western diets has resulted in an increase of this inflammatory background signature, associated with a progressively increasing rate of chronic degenerative conditions, including obesity, diabetes, auto-immune and neurodegenerative conditions (Ricordi et al. 2015). An interesting example is the potential impact of inflammation on metabolic syndrome and the development of type 2 diabetes, a disease condition typically associated with silent inflammation in the bloodstream (Ricordi et al. 2015; Sears and Ricordi 2010, 2012).

Inflammation is not only associated to the disease condition itself, but could be involved in its pathogenesis and progression, as diet-induced epigenetic changes can occur over time and have been associated with the increase in chronic degenerative diseases that are now affecting over 95% of Americans over age 65. Genetic transcription factors involved in inflammation can in fact be triggered by nutrition (Ricordi et al. 2015; Sears and Ricordi 2012), which can therefore assume a central role in either prevention or progression to many pathologic conditions. We certainly need inflammation to survive, as an inflammatory response to infection, injury, trauma, or poisoning, is essential to keep us alive. However, in these cases it is an acute inflammatory response that is needed in response to an infection or traumatic event. But there is third kind of inflammation that cannot be easily detected, as it is not associated with the typical inflammation cardinal signs of “rubor, calor, tumor and dolor”. This is in fact a kind of inflammation that cannot be detected unless a blood test is performed, the so called “silent” inflammation. This is typically a chronic, subliminal (below the threshold of pain) inflammation that is associated to nutrition and lifestyle patterns (Ricordi et al. 2015; Sears and Ricordi 2010, 2012).

This kind of chronic inflammation is thought to result in consumption of repair mechanisms necessary to regenerate injured tissues and organs. For example, endothelial progenitor cells can be “consumed” to repair of the atherosclerotic microscopic lesions that are associated with chronic inflammation associated with atherogenic diets. It is thought that diet-induced silent inflammation (Ricordi et al. 2015; Sears and Ricordi 2010, 2012) could therefore progressively “consume” the cell types that are needed to repair the chronic tissue micro-injury associated with this subliminal “background” inflammation. In the long term, this chronic process could progressively deplete the native regenerative potential, for example, in atherosclerotic plaque deposition, once the repair potential is exhausted, progression of coronary disease accelerates, and progressive plaque deposition can be interpreted not as progressive injury mechanism, but rather a progressive failure of repair mechanisms (Ricordi et al. 2015).

Several markers of silent inflammation, such as oxidative stress, arachidonic acid and hyperglycemia are often related to inflammation. The importance of the glycemic index of food has been well documented (Brand-Miller et al. 2015). The way our diet has evolved over the past 30 years (Sears and Ricordi 2010, 2012), has resulted in a progressive increase omega-6 fatty acids whose precursors present for example in some refined vegetable oils (rich in linoleic acid) could be synergistic in their negative effects with refined carbohydrates with high glycemic index, since insulin-induced metabolism of linoleic acid to arachidonic acid results in activation of the intracellular proinflammatory cascade (Ricordi et al. 2015; Sears and Ricordi 2010, 2012). At the same time the evolution of western diets has produced a progressive decrease in anti-inflammatory, anti-oxidant, protective factors, such as omega-3 fatty acids and polyphenols.

This led to two negative and synergistic effects:

1. The promotion of inflammation by the combination of foods with a high linoleic acid content and high glycemic index, because insulin catalyzes (through desaturase enzymes) the conversion pathway of linoleic acid to the pro-inflammatory arachidonic acid.
2. A decrease in anti-inflammatory protective factors associated with the decreased consumption of polyphenols and omega-3 (Ricordi et al. 2015; Sears and Ricordi 2010, 2012).

This nutritional change has become evident even in countries traditionally close to the Mediterranean diet, such as Italy. In fact, in recent years the Italian population has adopted poor eating habits (e.g., fast food and sugar-added beverages) and the obesity epidemic has now reached Italy as well, where children and young adults have some of the highest rates of overweight in Europe (Ricordi et al. 2015). This trend was associated with the highest degree of silent inflammation measured by blood markers, such as the arachidonic acid: eicosapentaenoic acid (AA:EPA) ratio that was comparable to the ratios observed in inflammatory disease conditions such as diabetes. Normally this ratio should be less than 3. In fact, the population of Japan, which benefits from one of the longest healthy life spans on Earth, has an AA:EPA ratio of approximately 2, whereas a value of 16–18 is found in subjects with inflammatory conditions such as diabetes (Ricordi et al. 2015). It is worrisome that this generation of children could be the first one with a life span inferior to their parents (Ricordi et al. 2015). It is difficult to study longevity or its impact on health or life span, because studies with projections of many decades should be conducted. However, a recent study reported that simple changes in lifestyle can prolong the life span by 14 years (Khaw et al. 2008). The study indicated that adherence to four factors was associated with a longer life span, individually but with an incremental combinatory effect. The four factors were absence of smoking, vitamin C levels greater than or equal to 50 nmol/L in the blood (as a surrogate marker for sufficient consumption of vegetables and fruit servings), alcohol consumption up to 14 servings per week, and moderate physical activity. These four simple factors combined could result in a positive effect on longevity (Khaw et al. 2008).

An interesting emerging research branch, resoleomics, studies native mechanisms of self-healing that occur when the human body repairs itself and resolves inflammation; but this natural process can be prevented by some of the anti-inflammatory or pain medication administered. For example, some classes of analgesic used to treat pain associated with inflammatory conditions could in fact suppress self-healing mechanisms and their chronic systemic use may not be indicated. Now there are much more integrated approaches under consideration. For example, for arthritis there are groups recommending more combinatorial, integrated approaches to therapy, including diet, medication, and changes in lifestyle. To simplify the impact of diet on long-term reparative systems and their possible impact on longevity, we could assess telomere length. If we assume, for example, that the life potential could be 140 years, this could be reduced to 70 years or less when we are exposed to pro-inflammatory nutrition and/or environment. Therefore, an inflammatory diet could be associated with faster "consumption" of repair potential and subsequent accelerated aging, compared to an anti-inflammatory diet. This diet-induced consumption of the native regenerative potential is supported by recent evidence indicating that adherence to a Mediterranean diet is associated with longer telomeres (Crous-Bou et al. 2014).

At the base of an anti-inflammatory diet, there are six basic rules described in the book "The End of Pain" by Peter Wehling, in which innovative approaches are proposed for the treatment of arthritis (Wehling and Renna 2011). Wehling based his book on nutrition rules to follow for the treatment of arthritis, with several requirements considered in addition to avoidance of foods that are direct triggers of inflammation. These requirements/guidelines include avoidance of allergies and other inflammatory reactions to foods, avoidance of foods rich in starch and sugar that affect the level of glucose in the blood and therefore insulin requirements, and eating foods that reduce inflammation. Additional recommendations include taking supplements that reduce inflammation and keeping one's weight down, because obesity increases inflammation (Ricordi et al. 2015). This book also pointed out that while focusing on the rules one by one, we must remember that it is necessary to implement a global approach where each element enhances the other synergistically, as it is impossible to get full results using only an individual component or element that may appear easier to adhere to (Ricordi et al. 2015; Wehling and Renna 2011). Several studies are in progress to evaluate the effect of anti-inflammatory interventions in the prevention and treatment of cardiovascular disease, stroke, cancer and diabetes. The data emerging are indicating that dose and assessment of markers of reduced diet-induced inflammation may be important to assess potential benefit and tailor intervention guidelines (Sears 2018). In fact, it has been shown that a daily dose of 5 g/day of EPA and DHA is generally required to reduce AA/EPA ratios from 23 to 2.5, with a corresponding reduction of pro-inflammatory cytokines including IL-1 (Endres et al. 1989), and a recent trial (CANTOS) has shown that reduction of IL-1 had significant cardiovascular benefits (Ridker et al. 2017). It is unlikely that any cardiovascular benefits could be observed in the absence of a significant lowering of the AA/EPA ratio.

A dose higher than 60 mg/kg EPA and DHA was recently reported to be necessary to reduce the AA/EPA ratio to less than 3 in patients with type 1 diabetes (Cadario et al. 2017). With such a reduction in the AA/EPA ratio, significant improvements in glycemic control were noted, as measured by decreased insulin requirements, lowered HbA1c, and increased stimulated C-peptide production, suggesting preservation of beta cell function (Cadario et al. 2017; Sears 2018). This has led to the recent FDA allowance of the POSEIDON trial to study the effect of high-dose omega-3 fatty acids and high-dose Vitamin D on beta cell function (Baidal et al. 2018). It should be noted that the initial dosing level in the POSEIDON trial will be a daily dose of 150 mg EPA and DHA/kg body weight to titrate each subject to reach an AA/EPA ratio between 1.5 and 3. Future studies will be necessary to determine the potential usefulness of anti-inflammatory nutritional interventions, omega-3 fatty acids and other immunomodulatory/anti-inflammatory supplements in the prevention and treatment of cardiovascular disease, diabetes and other degenerative conditions, to prolong healthy lifespan.

5 Conclusion

Epidemiologic, clinical, and laboratory data have a clearly linked diet with chronic diseases that are largely preventable. The issue is complex, and without action, NCDs are set to become more acute, posing even more challenges for society as a whole.

The evolution of western diets has resulted in an increase of this inflammatory background signature, and besides being associated to the NCDs themselves, it could be involved in its pathogenesis and progression. Also, anti-inflammatory nutrition has been associated with increased lifespan.

Clearly, optimal nutrition plays a key role in keeping people healthy and long-lived. In order to have the greatest impact possible, nutrition science should continue to study important nutrient-nutrient and nutrient-food interactions, with dietary guidelines moving away from a focus on single nutrients to an approach based on food and dietary patterns.

The Mediterranean Diet is one of the dietary patterns that has been more extensively evaluated and strong evidence from observational and intervention studies, and its adoption is a unique opportunity for the achievement of SDG 3 "Ensure healthy lives and promote wellbeing for all at all ages".

Scientific evidence must be translated into effective intervention programs aimed at changing eating behaviors, from individual-level approaches to community-wide campaigns, with a joint effort of the science community, government and policy-makers, citizens, NGOs and the private sector.

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