

## HEALTH EFFECTS OF CHANGES IN THE STRUCTURE OF DIETARY MACRONUTRIENTS INTAKE IN WESTERN SOCIETIES

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### ABSTRACT

A Western-type diet, characterized by a significant share of highly processed and refined foods and high content of sugars, salt, fat and protein from red meat, has been recognized as an important factor contributing to the development of metabolic disorders and the obesity epidemic around the world. Excessive body fat causes metabolic pathologies, such as insulin resistance, type 2 diabetes, dyslipidemia, cardiovascular diseases, hypertension, non-alcoholic fatty liver disease and cancer. According to the World Health Organization 1.5 billion adults are overweight, nearly 500 million are obese and 220 million suffer from type 2 diabetes. The Western-type diet is also associated with an increased incidence of chronic kidney disease. It is known that a combination of nutrients typical for this diet contributes to impaired renal function, renal steatosis and inflammation, hypertension and dysfunctional renal hormonal regulation. The Western diet is also associated with a chronic inflammatory process that is involved in all stages of atherosclerosis development and is increasingly recognized as a universal mechanism of various chronic degenerative diseases, such as autoimmune diseases, some neoplasms or osteoporosis. The present article is focused on the results of the most recent research investigating the effects of dietary macronutrients and the type of fatty acids on selected mechanisms associated with the occurrence of the most common diet-related diseases.

**Key words:** *Western diet, macronutrients, diet-related diseases*

### STRESZCZENIE

Dieta typu zachodniego tzw. Western diet, charakteryzująca się wysoką zawartością produktów wysokoprzetworzonych, cukrów prostych, tłuszczu i białka pochodzącego z czerwonego mięsa oraz soli, została uznana za istotny czynnik przyczyniający się do powstawania zaburzeń metabolicznych i szerzenia się epidemii otyłości na świecie. Nadmierna masa tkanki tłuszczowej prowadzi do patologii metabolicznych, takich jak insulinooporność, cukrzyca typu 2, dyslipidemia, choroby sercowo-naczyniowe, nadciśnienie, niealkoholowa stłuszczeniowa choroba wątroby czy nowotwory. Światowa Organizacja Zdrowia oszacowała, że 1,5 miliarda ludzi dorosłych ma nadwagę, blisko 500 milionów jest otyłych i 220 milionów choruje na cukrzycę typu 2. Dieta typu zachodniego wiąże się także ze zwiększoną częstością występowania przewlekłej choroby nerek. Wiadomo, że połączenie składników pokarmowych charakteryzujące tę dietę przyczynia się do zmniejszenia czynności nerek, ich stłuszczenia i powstawania stanów zapalnych, nadciśnienia tętniczego i zaburzeń nerkowej regulacji hormonalnej. Dietę zachodnią łączy się ponadto z toczącym się przewlekłym stanem zapalnym, który bierze udział we wszystkich etapach rozwoju miażdżycy i jest coraz częściej uznawany za uniwersalny mechanizm powstawania różnych przewlekłych chorób degeneracyjnych, takich jak choroby autoimmunologiczne, niektóre nowotwory, osteoporoza. Artykuł poświęcony jest przede wszystkim przedstawieniu wyników najnowszych badań dotyczących wpływu makroskładników diety i rodzaju kwasów tłuszczowych na wybrane mechanizmy odpowiedzialne za procesy związane z występowaniem najczęstszych chorób dietozależnych.

**Słowa kluczowe:** *dieta typu zachodniego, makroskładniki, choroby dietozależne*

### INTRODUCTION

Incorrect proportions of macronutrients in the diet contribute to the occurrence of numerous metabolic disorders and are associated with the development of many diseases of civilization. Many studies have revealed

various mechanisms, primarily based on ongoing chronic inflammatory processes, through which the Western diet may cause the development of chronic diseases [49].

According to the data of the United States Department of Agriculture from 2006, the percentage of food

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energy, derived from three main macronutrients, was as follows: carbohydrates (48.1%), fat (40.6%) and protein (11.3%). Changes in the consumption of various food groups can be followed thanks to the data provided by the United States Department of Agriculture, which since 1909 has been collecting data on food consumption in the United States and provides them free of charge on the Internet [33].

The data on three countries: Russia, the Czech Republic and Poland are disturbing. The authors demonstrated that the percentage of energy derived from the three macronutrients is as follows: carbohydrates (39-45%), fat (36-43%) and protein (17-18%), depending on the country [5]. The mentioned nutrient proportions significantly differ from the 2010 dietary guidelines for adult Americans, aimed at reducing the risk of cardiovascular diseases and other chronic diseases by limiting fat intake to 25-35% of total energy, maintaining the level of protein at 10-35% of total energy and increasing complex carbohydrates consumption to 45-65% of total energy [83].

### HEALTH EFFECTS OF INCORRECT PROTEIN INTAKE

Although the recommended dietary intake (RDI) for protein is 0.8 g/kg body weight, it has been proven that athletes need to consume more protein. The recommended protein intake in sports medicine is 1.4-2 g/kg bw/d [10]. Elderly people also need higher levels of protein in their daily diet in order to prevent or alleviate sarcopenia and osteopenia, as dietary protein increases calcium absorption and exerts anabolic effects on muscle and bone cells [34]. It has been shown that a high-protein diet (20% of energy) can help in combating dyslipidemia and thus reduce the risk of cardiovascular diseases [56], increase tissue sensitivity to insulin [14], and it may be also a potentially effective strategy in fighting against obesity, metabolic syndrome [46] and hypertension [32]. Maintaining a protein-rich diet for a long time does not seem to negatively affect the renal function in patients with no pre-existing renal diseases [77]. *Wolfe* and *Giovannetti* [88] showed that an isocaloric substitution of carbohydrates with protein (23% of energy) in subjects with moderate hypercholesterolemia caused a significant decrease in plasma total cholesterol, low-density lipoprotein (LDL), very low-density lipoproteins (VLDL) and triacylglycerols (TG), and an increase in the plasma level of high-density lipoprotein (HDL). Similar beneficial changes in the lipid profile were observed in patients with type 2 diabetes, and they were associated with improved glucose and insulin metabolism. High-protein diets improve the metabolic control in patients with type 2 diabetes

[58]. In obese women, low-calorie diets rich in proteins increase sensitivity to insulin and prevent muscle loss, while low-calorie diets rich in carbohydrates reduce sensitivity to insulin and decrease lean body mass [65].

Protein, vitamin B12 and folate intake is inversely correlated with blood homocysteine level [74, 80], which is an independent risk factor for cardiovascular diseases. Meat-consuming populations are proven to maintain lower plasma homocysteine levels than those not eating meat [50]. Numerous population studies [57] have reported higher blood pressure to be linked with lower protein consumption. A 4-week dietary intervention showed that a protein-rich diet (25% of energy) efficiently and significantly reduced blood pressure [7]. Moreover, many population studies have confirmed that death due to stroke is inversely proportional to protein consumption [41].

Protein consumption can also modulate renal function [40]. Excessive protein intake that may result in chronic renal disease by increasing the glomerular pressure and hyperfiltration is controversial [6, 52]. However, some studies suggest that hyperfiltration in response to various physiological stimuli is a normal adaptation mechanism [9].

High-protein diets are those in which the level of daily protein intake is equal to or higher than 1.5 g protein/kg body weight/day. A report from the United States Institute of Medicine stated that there was insufficient scientific evidence to recommend an upper limit of protein intake, but it was found that the maximum amount of energy from this macronutrient should be within the range of 10-35% of the total energy requirements of an adult human [23]. In Polish standards, 5% of energy was proposed as the lowest permissible protein intake and 15% of energy as the value that should not be exceeded [35].

Chronic kidney disease (CKD) is defined as renal failure or renal function deterioration manifested by reduced glomerular filtration rate (GFR) over a period of at least three months [48]. In the general population, the deterioration of renal function is considered an independent risk factor for both cardiovascular diseases and all-cause mortality rate [53]. However, it is still unknown to what extent this risk is affected by mild renal function deterioration [17].

As early as in the 1930s it was found that an increased level of dietary protein was associated with elevated levels of creatinine and urea excreted in urine [37] as well as with renal hypertrophy [87]. Data from epidemiological studies indicate that unlimited protein consumption may be associated with renal disease progression [47]. The Nurses' Health study, based on a questionnaire assessment involving semi-quantitative evaluation of the frequency of food intake, was compared with GFRs recorded during more than 11

years of research in patients with pre-existing kidney disease [42]. Regression analysis showed a relationship between increased consumption of animal protein and deterioration of renal function. *Hammond* and *Janes* [29] reported on the relationship between increased protein intake and increased glomerular filtration rate and renal hypertrophy in mice.

Hypertension is one of the most common causes of CKD, accounting for about 30% of all cases in the USA [61]. Although initial estimates of CKD prevalence in patients with hypertension amount to about 2%, the latest data suggest that the prevalence rate may be much higher [30]. In Poland, at the end of 2005, about 10.7% of patients undergoing chronic dialysis therapy suffered from hypertensive nephropathy. In over 14% of patients with end stage renal disease (ESRD), who were started on renal replacement therapy in 2005, the cause of the kidney disease was hypertensive nephropathy [71]. Blood pressure control is particularly important in patients with diagnosed hypertension in the course of CKD. This has been confirmed by studies in which antihypertensive therapy delayed the progression of CKD [89].

The data on the role of dietary protein, as an independent risk factor for both onset and development of renal disease, indicate an inverse relationship between protein consumption and blood pressure [31]. A randomized study published by *Burke et al.* [7] demonstrated the role of dietary protein and fiber in reducing the systolic blood pressure in a group of 36 hypertensive patients. Although these results suggest that a protein-rich diet may be beneficial for people with hypertension, additional studies are necessary, as increased protein intake is often associated with the consumption of micronutrients of proven antihypertensive effects, such as potassium, magnesium and calcium [78].

### **HEALTH EFFECTS OF EXCESSIVE CONSUMPTION OF REFINED CARBOHYDRATES**

Long-term consumption of foods with a high glycaemic load may cause hyperglycemia and hyperinsulinemia, which may contribute to disturbed lipid metabolism (high concentrations of TG and VLDL, and low level of HDL), hypertension, elevated levels of plasma uric acid and insulin resistance [68]. Moreover, postprandial hyperglycemia can intensify oxidative stress and increase the level of proinflammatory cytokines and protein glycation that negatively affect the endothelial function [69].

Total consumption of refined sugar per person in the United States in 2000 was 69.1 kg, while in 1970 it was 55.5 kg [84]. This upward trend in sugar con-

sumption in the United States within the last 30 years reflects the global trend, observed in highly developed countries since the beginning of the industrial revolution about 200 years ago [24]. The average consumption of sucrose in England gradually increased from 6.8 kg in 1815 to 54.5 kg in 1970 [15]. According to a survey on household budgets carried out by the Central Statistical Office, sugar (sucrose) consumption in Poland amounted to 37.2 kg in 1969, and in 2007 it was 39.3 kg per capita [72].

High consumption of refined sugar, and recently also of corn fructose syrup, responsible for high levels of fructose in the Western diet, are important factors promoting the increase in obesity, insulin resistance, dyslipidemia, gout, hypertension, kidney diseases and nonalcoholic fatty liver disease [36].

Monosaccharides such as glucose, galactose and fructose contribute to the formation of advanced glycation end products (AGE) and their intra- and extracellular accumulation. Chronic high intake of sucrose, fructose and galactose and/or following a diet characterized by a high glycaemic load may significantly promote the formation of AGEs. AGE formation increases with age and in the course of some diseases. The presence and role of AGEs and the receptor for advanced glycation end products (RAGE) have been investigated in the pathogenesis of diabetic complications, diseases of the nervous system and renal disease, and liver cirrhosis [38, 39].

There are data indicating that limiting the amount of carbohydrates instead of cutting down on dietary fat may be a better dietary approach in Western societies, especially in patients with metabolic syndrome. This approach may result in reduced insulin resistance, postprandial lipemia, triglyceridemia, HDL cholesterol, total-to-HDL cholesterol ratio and improvement in some inflammation biomarkers, such as tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), interleukin-8 (IL-8), monocyte chemoattractant protein (MCP-1), intercellular adhesion molecule (ICAM) and plasminogen activator inhibitor 1 (PAI-1) [85].

### **THE HEALTH EFFECTS OF FAT CONSUMPTION DEPENDING ON THE AMOUNT AND COMPOSITION**

In the twentieth century, there was a significant increase in the use of vegetable oils. In the United States a 130 per cent increase in salad oil consumption was reported, accompanied by 136 and 410 per cent rises in the consumption of vegetable oils and margarine, respectively [25]. These trends were also observed in other parts of the world, and they were due to the industrialization and mechanization of the oilseed industry.



In Poland, in the years 1970-2007, butter consumption fell from 6.0 kg to 4.2 kg, and vegetable oil consumption rose from 6.6 kg to 20.1 kg [72]. The data of the Central Statistical Office for the years 2005-2009 show a 10 per cent increase in butter consumption from 4.2 to 4.4 kg/person/year. Consumption of crude animal fats in this period decreased by 10 per cent, down to 6 kg per person per year. Total fat consumption decreased in general by 11 per cent, reaching 16.4 kg per person per year. In 2010, the average consumption of oils and fats in individual households amounted to 16.2 kg per person.

Fatty acids (FA) belong to three main categories: 1) saturated fatty acids (SFA), 2) monounsaturated fatty acids (MUFA), 3) polyunsaturated fatty acids (PUFA). Additionally, PUFAs are present in two biologically important families, i.e. *omega*-6 PUFA, also known as *omega*-6, and *omega*-3 PUFA, also known as *omega*-3. Fats containing MUFA and certain PUFA are healthy, while most SFA and *trans* isomers of fatty acids are harmful when consumed in excess. Moreover, balanced consumption of *omega*-6 and *omega*-3 PUFA is an important factor for reducing the risk of chronic diseases and health promotion [43, 72]. The main sources of dietary *omega*-3 PUFA are fish and seafood, as well as vegetable oils – rapeseed and flaxseed. *Alpha*-linoleic acid from vegetable oils is to some extent converted during digestion into *omega*-3 fatty acids and longer and more unsaturated – eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) [13].

The Western diet often contains too much saturated and *trans* fatty acids, and not enough *omega*-3 PUFA as compared to *omega*-6 PUFA. High consumption of SFA and *trans* fatty acids increases the risk of cardiovascular diseases by raising the total cholesterol and LDL levels [79]. *Omega*-3 PUFAs may reduce the risk of cardiovascular diseases through various mechanisms, including the reduction of ventricular arrhythmias, blood coagulation, concentration of triacylglycerols, development of atherosclerotic plaques and blood pressure [43]. Patients with diagnosed ischaemic heart disease seem to have benefited from a 3.5-year long daily supplementation with 850 mg of *omega*-3 fatty acids (with or without vitamin E), showing a 20 per cent reduction in total mortality and a 45 per cent reduction in sudden deaths [26]. Higher consumption of *omega*-3 fatty acids appears to be effective in the prevention and alleviation of many inflammatory and autoimmune diseases [75]. It has been suggested that the risk of ischaemic heart disease depends more on the quality, and not the quantity, of consumed fats. After 50 days of maintaining a low (22% of energy) and a high (39% of energy) fat diet, containing identical ratios of PUFA to SFA, *omega*-6 PUFA, *omega*-3 PUFA and MUFA to total dietary fat, similar effects on total cholesterol and LDL levels were reported [54].

The introduction of vegetable oils to our diet resulted in a higher *omega*-6 PUFA-to-*omega*-3 PUFA ratio, because most vegetable oils have higher content of *omega*-6 fatty acids than *omega*-3 fatty acids [16]. Therefore, the ratio of *omega*-6 to *omega*-3 FA in the diet of people in developed countries is as high as 10:1 [44], whereas in hunter-gatherer societies, it is estimated to be 2:1 to 3:1 [14]. *Kuipers* et al. [45] claimed that the content of *omega*-3 fatty acids (EPA + DHA) and *omega*-6 arachidonic acid (AA) in the paleolithic diet was 1.7-14.2 g/d and 1.81-5.46 g/d, respectively. These values are different from EPA + DHA and AA levels in the Western diet, where they amount to 0.11 g/d and 0.2 g/d. In the United States, current consumption of *alpha*-linolenic acid (ALA) is only 0.6% and of linolenic acid (LA) 6-7% of the total dietary energy intake. A study by *Dybkowska* et al. [20] evaluated the intake of essential polyunsaturated fatty acids *omega*-3 and *omega*-6 in an average food ration in Poland. The consumption of *omega*-6 fatty acids was found to constitute 5.2% of the dietary energy value (13 g daily), markedly exceeding the upper recommended limit (3%), and *omega*-3 FA accounted for only 0.95% of the energy (2.4 g daily). ALA intake amounted to 0.9% of energy and was similar to the recommended 1%, but the intake of EPA and DHA was 0.04% of the dietary energy value, lower than the recommended 0.3%.

Possible beneficial effects of *omega*-3 PUFA in kidney diseases have been studied extensively; however, no clear results have been obtained, as evidenced by recently published review articles [21, 62]. *Omega*-3 PUFA consumption was found to be inversely correlated with the occurrence of CKD. It was demonstrated that high consumption of fish reduced the risk of CKD by about 32 per cent. In contrast, enhanced ALA intake was associated with a 73% increase in CKD probability [28]. However, animal studies have shown that PUFA supplementation reduced the progression of renal diseases [3]. *Gopinath* et al. [28] suggested that *omega*-3 PUFA can protect renal function by inducing anti-inflammatory activity, i.e. reducing the synthesis of pro-inflammatory cytokines, NO and the expression of endothelial leukocyte adhesion molecules [70]. The possible protective effect of *omega*-3 PUFA towards the kidney may be related to the metabolism of eicosanoids, including leukotriene formation [64]. Leukotriene B4 (LTB4) and the by-product 5-hydroxyeicosatetraenoic acid (5-HETE) are formed in the metabolic pathway of *omega*-6 PUFA – arachidonic acid. Leukotriene B5 (LTB5) and the by-product 5-hydroxyeicosapentaenoic acid (5-HEPE) are derived from eicosapentaenoic acid. LTB4 is a known pro-inflammatory agent that can be involved in the development of many diseases [27], whereas LTB5 has much weaker pro-inflammatory properties [69]. Studies conducted in humans and animals

indicate that LTB<sub>4</sub> plays an important role in kidney diseases [55, 90]. EPA and DHA are incorporated into the cell membrane phospholipids depending on the consumed amount, and they partially compete with AA. EPA and AA also compete with regard to the eicosanoid metabolism pathway enzymes. Therefore, increased intake of EPA and DHA may lead to a limited formation of LTB<sub>4</sub> and 5-HETE and enhanced synthesis of LTB<sub>5</sub> and 5-HEPE. Moreover, *omega*-3 PUFAs may lower the production of LTB<sub>4</sub> by inhibiting 5-lipoxygenase (5-LOX), the enzyme initiating the leukotriene synthesis pathway. Decreased synthesis of LTB<sub>4</sub> and LTB<sub>5</sub> increase were observed in response to the consumption of *omega*-3 PUFA [81, 86]. It should also be pointed out that AA serves as a source of lipoxins, which exhibit anti-inflammatory and immunomodulating properties and which are, together with the resolvins derived from EPA and DHA, and maresins and protectins derived from DHA, involved in alleviating the inflammation process. Therefore, increasing the consumption of *omega*-3 fatty acids (EPA + DHA) and cutting down on vegetable oils rich in LA can prove to be an effective strategy for reducing the risk of a various chronic inflammatory diseases [73].

Epidemiological studies suggest that enriching the diet in polyunsaturated *omega*-3 fatty acids from fish and monounsaturated fatty acids from olive oil may help to lower the blood pressure [2]. Contrary to the beneficial effects of *omega*-3 FA, increased consumption of saturated fats increases the blood pressure [79]. In hypertensive patients, a diet rich in polyunsaturated fatty acids from the *omega*-6 family does not induce changes in either systolic or diastolic blood pressure [22].

A high dietary LA/ALA ratio is characteristic for countries with a high prevalence of coronary artery disease [63]. High LA consumption lowers the *omega*-3 index (percentage share of EPA and DHA in the erythrocyte membranes relative to all other fatty acids) [66], which have been proposed as a new risk factor for ischaemic heart disease. The research conducted by *Calder* [8] indicated that LA activated the nuclear factor  $\kappa$ B (NF- $\kappa$ B), thus enhancing the synthesis of pro-inflammatory cytokines such as IL-6 and TNF- $\alpha$ .

*Ramsden* et al. [67] challenged the hypothesis that replacing the dietary SFA with LA reduces the risk of coronary heart disease. No beneficial effects of LA-rich diets in reducing the risk of ischaemic heart disease and the risk of death due to any other cause have been reported. In another long-term study, based on a dietary intervention involving introduction of diets with lowered content of *omega*-6 FA and increased supply of *omega*-3 FA, a 70 per cent reduction in the risk of ischaemic heart disease and mortality rate was observed [19]. The results of these studies strongly suggest that a high intake of LA is not necessary to reduce the risk

of coronary heart disease and may even increase it. Epidemiological and interventional studies indicate, however, that increased intake of *omega*-3 FA reduces the risk of cardiovascular mortality [66].

In the traditional Mediterranean diet, used in the clinical trials as a model proper diet, 35-40% of total energy intake comes from fat, especially from cis monounsaturated fatty acid (cis-MUFA) from olive oil and cis-polyunsaturated fatty acids (cis-PUFA) of the *omega*-3 family, supplied by fish, egg yolk and common purslane. The death rate due to cancer and heart disease in the countries of the Mediterranean region where this diet prevails is one-third lower compared to the United States [76].

A diet rich in cis-MUFA from olive oil reduces the risk of cardiovascular diseases. Studies have shown beneficial effects of cis-MUFA consumption manifested by improved lipid profile, reduced oxidation of LDL cholesterol, increased sensitivity to insulin and reduced thrombogenesis [66]. When monounsaturated fatty acids replace dietary carbohydrates, a reduction in triglycerides and cholesterol levels in blood plasma is observed [51]. Antioxidants and phenolic compounds present in the olive oil help to reduce the blood vessel damage caused by free radicals and may inhibit the activation of NF- $\kappa$ B, inhibit platelet aggregation and increase the availability of nitric oxide [11, 12].

The intake of saturated fatty acids, exceeding the recommended 10% of energy, is associated with increased level of total and LDL cholesterol in the blood plasma, but lower consumption of those fatty acids, combined with increased intake of dietary refined sugars, leads to increased plasma levels of TG and VLDL, and reduced levels of HDL cholesterol. Lipid disorders are often associated with renal diseases [60] and dysfunction [4].

The development of atherosclerosis and cardiovascular diseases in CKD patients is conditioned by a few factors. It is believed that the key factors contributing to the development of coronary heart disease in CKD patients are the non-traditional risk factors, such as inflammation, oxidative stress, anemia, malnutrition, vascular calcification (due to changes in calcium and phosphorus metabolism) and endothelial dysfunction [59]. In the general population, a known traditional risk factor for cardiovascular diseases is dyslipidemia. Renal dysfunctions are also associated with significant changes in lipoprotein metabolism, which in their most advanced form can lead to the development of severe lipid disorders. However, the exact role these changes play in the pathogenesis of atherosclerosis in CKD patients remains controversial [1, 82, 89].

## SUMMARY

Studies investigating the effects of various nutrients on the development of diet-related disorders usually focus on a single component or a type of component. However, to be able to formulate the theoretical basis of an appropriate and effective diet-based prevention and therapy, it is necessary to examine the effects of changes in the quantitative relationships between the dietary components, particularly macronutrients that exert the largest and global impact on the metabolism. The available literature lacks any data on the effects of various proportions of dietary macronutrients on the mechanisms regulating the endocrine function of adipose tissue, renal blood pressure or inflammatory mediators. It is therefore worth finding out whether the modifications of macronutrient proportions can influence these mechanisms and factors that initiate inflammatory processes and that may further lead to the development of civilization diseases.

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