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# ROCZNIKI PAŃSTWOWEGO ZAKŁADU HIGIENY

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## NUTRACEUTICAL FUNCTIONS OF *BETA*-GLUCANS

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### ABSTRACT

Recent studies have shown that naturally occurring substances found in the food of the daily human diet are important for preventing chronic non-communicable diseases. One of them is *beta*-glucan, which is a natural polysaccharide, occurring in plant cell walls, mainly oats, barley and wheat. It is also present in baker's yeast cells, fungal cell walls, and some microorganisms. *Beta*-glucan belongs to one of the dietary fiber fractions, which are attributed a number of beneficial health properties, including the prevention and treatment of certain digestive diseases and supporting the immune system. This compound has biological activity that depends on the size, molecular weight, conformation, frequency of bonds, solubility and changes in structure. *Beta*-glucan reduces cholesterol and glucose concentrations in the blood, which reduces the risk of cardiovascular disease and diabetes. In addition to its effects on lipid levels and glucose metabolism, *beta*-glucan also exhibits antioxidant properties by scavenging reactive oxygen species, thereby reducing the risk of diseases, including atherosclerosis, cardiovascular diseases, neurodegenerative diseases, diabetes, and cancer. Immunostimulatory and antitumor effects have also been reported. The immunostimulatory activity of *beta*-glucan occurs as a result of its attachment to specific receptors present on the immune cell surface. *Beta*-glucan belongs to the group of prebiotics which stimulate the growth and activity of the desired natural intestinal microbiota, while inhibiting the growth of pathogens. It plays an important role in the proper functioning of the gastrointestinal tract and preventing inflammation as well as colon cancer. Such a number of health benefits resulting from the properties of *beta*-glucan may play a key role in improving health and preventing chronic non-communicable diseases, such as diabetes, hypercholesterolemia, obesity, cardiovascular diseases, and cancer.

**Key words:** *beta-glucans, chronic non-communicable diseases, health properties*

### STRESZCZENIE

Badania ostatnich lat dowiodły, iż w codziennej diecie człowieka znajdują się naturalnie występujące składniki żywności o istotnym znaczeniu w zapobieganiu niezakaźnym chorobom przewlekłym. Między innymi jest to *beta*-glukan, który jest naturalnym polisacharydem, występującym w ścianach komórkowych roślin, głównie owsa, jęczmienia i pszenicy. Obecny jest także w komórkach drożdży piekarniczych, ścianach komórkowych grzybów i w niektórych mikroorganizmach. *Beta*-glukan należy do jednej z frakcji błonnika pokarmowego, któremu przypisuje się szereg korzystnych właściwości zdrowotnych, między innymi w prewencji i leczeniu niektórych schorzeń układu pokarmowego oraz wspomaganiu układu odpornościowego. Związek ten wykazuje aktywność biologiczną, która zależy od wielkości masy cząsteczkowej. *Beta*-glukan obniża poziom cholesterolu oraz pozwala utrzymać prawidłowy poziom cukru we krwi, co wiąże się ze zmniejszonym ryzykiem zachorowalności na choroby sercowo-naczyniowe oraz cukrzycę. Oprócz wpływu na poziom lipidów i metabolizm glukozy *beta*-glukan wykazuje także właściwości przeciwutleniające poprzez wychwytywanie reaktywnych form tlenu, zmniejszając tym samym ryzyko wystąpienia, m.in.: chorób układu krążenia, chorób neurodegeneracyjnych, cukrzycy oraz nowotworów. Substancja ta wywiera również efekt immunostymulujący oraz antykancerogeny. Immunostymulujące działanie *beta*-glukanu polega na jego przyłączeniu się do specyficznych receptorów obecnych na powierzchni komórek układu odpornościowego. *Beta*-glukan należy do grupy prebiotyków, stymulujących wzrost i aktywność pożądaną, naturalnej mikroflory jelitowej, hamując jednocześnie rozwój patogenów. Odgrywa to istotną rolę w prawidłowym funkcjonowaniu przewodu pokarmowego oraz zapobieganiu wystąpieniu stanów zapalnych, jak również nowotworów jelita grubego. Wykazane korzyści zdrowotne wynikające z właściwości *beta*-glukanu mogą odgrywać kluczową rolę w poprawie stanu zdrowia oraz przeciwdziałaniu niezakaźnym chorobom przewlekłym, tj. cukrzycy, hipercholesterolemii, otyłości, chorobom sercowo-naczyniowym oraz nowotworom.

**Słowa kluczowe:** *beta-glukan, niezakaźne choroby przewlekłe, właściwości prozdrowotne*

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## INTRODUCTION

Food safety and nutrition along with other lifestyle factors are major determinants of the health of a population. One of the key tasks in terms of food safety is introducing natural ingredients of plant and animal origins as nutraceuticals that play a key role in preventing chronic non-communicable diseases and maintaining good health. Nutraceutical foods and preparations with new biomedical functions and additional physiological activity can become part of a personalized diet. In view of the huge costs incurred for treating the effects of chronic non-communicable diseases, it seems warranted to develop non-invasive methods of dietary prevention and dietotherapy based on natural functional food ingredients obtained using innovative technologies that guarantee their appropriate biopotential [79].

The most serious health risk factors responsible for the highest number of deaths in European countries are high blood pressure, smoking, overweight, and obesity. Excessive body weight means a significantly increased risk of cardiovascular diseases, type 2 diabetes, most types of cancer, and thus the most common causes of morbidity and death in industrialized countries [1, 4, 21, 62]. According to research by the Polish Central Statistical Office (GUS), cardiovascular diseases are responsible for 45% of deaths in Poland and malignant neoplasms for 26% (Figure 1), and these percentages have increased slightly over the last 4 years [22]. Excessive body weight increases the risk of lipid profile disorders, including elevated triglycerides, total cholesterol and LDL – while lowering HDL cholesterol – as well as carbohydrate metabolism disorders, insulin resistance and inflammation, contributing to the development of cardiovascular diseases and type 2 diabetes [16].

An important indicator of the risk of complications of excessive body weight in children and adolescents, just like in adults, is primarily waist circumference, which indicates the presence of visceral fat [69, 81]. It is therefore important to use a well-planned and effective dietary intervention that will reduce weight and improve the health of people with metabolic syndrome.

Numerous epidemiological studies indicate that consuming dietary fiber from whole grains or whole grain products is associated with a reduced risk of type 2 diabetes mellitus (DMT2), cardiovascular disease, cancer and obesity occurrence. Soluble dietary fiber, particularly *beta*-glucan, which is found mainly in grain cereals, such as barley and oats, as well as *beta*-glucans present in the cell walls of fungi and microorganisms has various beneficial health effects [65].

Due to their properties, *beta*-glucans have a broad spectrum of use, especially in medicine and

the pharmaceutical, food, cosmetics and chemical industries, as well as in veterinary medicine, in the production of medicines and feed [86].

## CHEMICAL STRUCTURE, SOURCES AND THE PRESENCE OF *BETA*-GLUCANS

*Beta*-glucans are polysaccharides made of D-glucose molecules connected by  $\beta$ -glycosidic bonds. They belong to one of the dietary fiber fractions, which are attributed a number of health benefits, including the ability to treat certain gastrointestinal diseases and support the immune system [57]. These glucose polymers are a structural component of the cell wall of some pathogenic bacteria (*Pneumocystis carinii*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Histoplasma capsulatum*, *Candida albicans*), the *Basidiomycetes* class of fungi, baker's yeast (*Saccharomyces cerevisiae*), and plants, mainly oats, barley and wheat [3, 71]. Some authors found that *beta*-glucans are also present in some vegetables and fruits [77], lichen and algae [57]. Depending on their origin, *beta*-glucans differ in their specific properties, such as solubility, degree of branching, and molecule mass and shape, which have a significant impact on their biological activity [41]. Due to the types of glycosidic bonds present in the *beta*-glucan structure, two isomers can be distinguished: one forming the walls of fungi and yeast, made of  $\beta$ -D-glucopyranose molecules connected by  $\beta$ -1,3- and  $\beta$ -1,6-glycosidic bonds, giving a branched structure [47, 59]; and the other one present in unprocessed grain products in the form of unbranched chains consisting of  $\beta$ -D-glucopyranose monomers connected by  $\beta$ -1,3- and  $\beta$ -1,4-glycosidic bonds [52].

## HEALTH BENEFITS OF *BETA*-GLUCANS

The health-promoting properties of *beta*-glucans, which have been confirmed by numerous studies, have been known for several decades. Studies have shown that zymosan, derived from the yeast cell wall, is characterized by high *beta*-glucans content and activates the body's nonspecific immune system response [19, 52]. Based on the accumulated knowledge on *beta*-glucans functions, the fungi-derived lentinan and schizophyllan have been used as drugs in medicine due to their immunostimulatory effect [52]. A diet rich in *beta*-glucans has a positive effect on human health by preventing chronic non-communicable diseases, such as diabetes, hypercholesterolemia, obesity, cardiovascular diseases, and cancer. *Beta*-glucans present in grains (such as oats and barley) have been documented to lower cholesterol and blood glucose (Figure 2) and act as a main factor in preventing obesity and metabolic disorders [14, 29, 75].

The results of both clinical and preclinical studies have confirmed the antioxidant, immunomodulatory,

and antitumor properties of *beta*-glucans [11, 40, 46, 86]. In addition, this compound has a prebiotic effect, supporting the growth of beneficial intestinal bacteria [24] (Figure 2).

### Hypoglycemic properties

The beneficial effect on glucose metabolism is mainly attributed to *beta*-glucans derived from cereal grains. *Beta*-glucan from grains is not digested in the stomach or intestines after ingestion. It also has a high capacity for binding water and forming sticky gels in the gastrointestinal tract, which results in delayed gastric emptying, slowing down enzymatic breakdown of starch and hindering intestinal absorption of digestible carbohydrates [25]. This mechanism results in a reduction of postprandial glucose in the blood, as well as insulin secretion (Figure 2), which may contribute to a decrease in the incidence of type II diabetes [57].

Moreover, *Pick* et al. [58] showed that consuming oat products may also result in a reduced glycemic response after the next meal, due to the fact that slower rising glycemia is also accompanied by reduced insulin secretion. *Biörklund* et al. [7] observed that oat *beta*-glucan significantly affected the reduction of glycemia and insulinemia compared with barley *beta*-glucan. The effectiveness of *beta*-glucan in lowering blood glucose results not only from the ability to form sticky solutions (the higher the viscosity of the layer, the lower the glucose and lower insulin levels in blood plasma), but also depends on its molecular weight and the concentration used [61]. The results of conducted research proved that the addition of *beta*-glucans from oats with a high molecular weight to food products reduced the level of glycemic response the most [9, 80].

### Hypocholesterolemic properties

Grain *beta*-glucans also have a positive effect on lipid metabolism, they reduce blood cholesterol. The hypocholesterolemic effect of *beta*-glucans results from the ability to act as a dietary fiber as well as from the ability to increase the viscosity of food content in the small intestine, which then affects the formation of micelles and their structure and composition [41, 52]. Increased viscosity of the intestinal lumen reduces fat and cholesterol absorption and bile acid binding, increasing their excretion in the feces. Reducing the amount of bile acids results in increased utilization of cholesterol accumulated in the body for bile acid production in the liver. Furthermore, to compensate for reduced bile acid levels,  $7\alpha$ -hydroxylase activity, which is involved in bile acid synthesis, increases [17]. As a result, the cholesterol level in the liver as well as LDL cholesterol concentration in the blood decrease [52]. Due to the properties of *beta*-glucans, lowering the total cholesterol and LDL fraction

levels in the blood (Figure 2) may reduce the risk of cardiovascular diseases [78]. *AbuMweis* et al. [2] showed that consuming barley or *beta*-glucans derived from barley leads to a significant reduction in total cholesterol as well as LDL cholesterol. *Ho* et al. [26, 27] also confirmed the lowering of LDL levels by *beta*-glucans derived from barley and oats. *Lange* [41] showed that oat products exert an independent hypocholesterolemic effect, and the consumption of 3 g of *beta*-glucans daily with the diet promotes not only a decrease in total cholesterol by 2% but also LDL by about 5%, which in consequence may contribute to a 10% reduction in the risk of ischemic heart disease occurrence.

### Antioxidant properties of *beta*-glucans

Various grains, such as barley, oats, millet and rye, have antioxidant properties by scavenging reactive oxygen species (ROS) (Figure 2), i.e. superoxide anion, hydrogen peroxide, and hydroxyl radicals, which are involved in the occurrence of many diseases [45]. Considering that oxidative stress is considered to be one of the main factors affecting aging of the body and is conducive to the occurrence of atherosclerosis, cardiovascular diseases, brain diseases, diabetes, and cancer, among others, eliminating reactive oxygen species minimizes the possibility of these diseases [39]. *Beta*-glucans from oats and barley have the highest affinity for removing reactive oxygen species [14, 23, 67]. However, *Kofuji* et al. [37] showed that *beta*-glucan extracted from barley has significantly higher antioxidant activity compared with *beta*-glucan from oats and yeast, which indicates that the structure of *beta*-glucans also affects their antioxidant properties. The high antioxidant activity of glucans is probably due to the presence of anomeric hydrogen atoms in their molecules, and the polymeric structure provides additional free radical removal capabilities [63]. Studies on rats revealed that the antioxidant properties of *beta*-glucans after oral administration are due to the prevention of oxidative stress in internal organs such as the liver and kidneys [6, 66]. The results of these studies suggest that *beta*-glucan acts as an antioxidant and protects the body from the adverse effects of free radicals.

### Immunomodulatory and antitumor properties

*Beta*-glucans with immunostimulatory properties were also shown to be beneficial in preventing infectious diseases and gastrointestinal cancer, particularly colorectal cancer [32].

Despite advances in medicine, cancer, which is uncontrolled cell growth, is now classified as a chronic non-communicable disease of the 21st century, which is the leading cause of death after cardiovascular diseases (Figure 1).

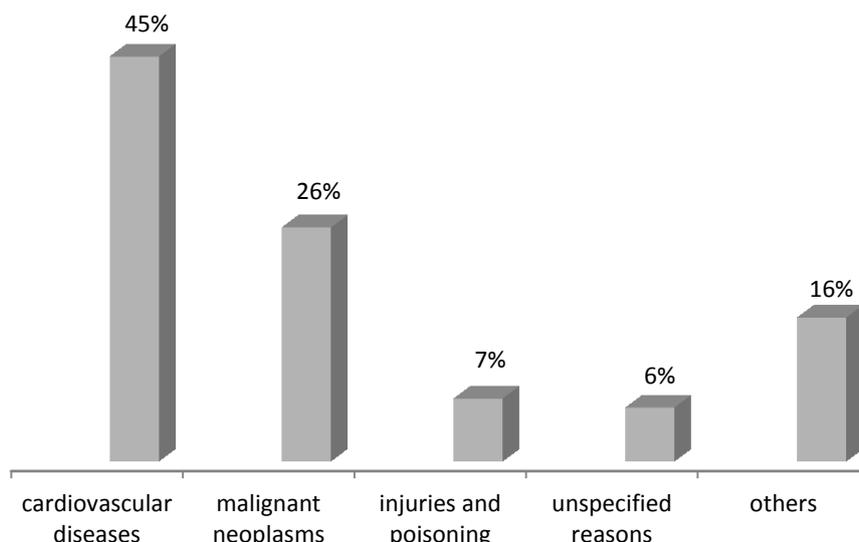


Figure 1. Deaths by cause in Poland in 2013 [22]

Among them, colorectal cancer is diagnosed as the most common malignant gastrointestinal tumor, whose development is a multistage process. Many studies demonstrated the significant role of matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) in the carcinogenesis of colorectal cancer. Colorectal cancer cells were found to have the ability to synthesize metalloproteinases, including matrix metalloproteinase 9 (MMP-9), a collagen-degrading enzyme of the basement membrane and the extracellular matrix, which plays a significant role in invasive growth, distant metastasis, and tumor angiogenesis [51]. Similar results were obtained in the case of colorectal cancer cell lines, where high activity of MMP-9 was found, which determines the ability of cells to metastasize by degrading the extracellular matrix, among others [43].

Moreover, *Kim* et al. [36] observed that higher expression of this enzyme in colorectal cancer cells resulted in increased tumor aggressiveness and a tendency to infiltrate. *Zeng* et al. [82] also demonstrated higher MMP-2 activity in patients with colorectal cancer compared with normal intestinal mucosa. *Oberg* et al. [54] found higher levels of MMP-9 and TIMP-1 in patients with colorectal cancer compared with healthy individuals, as well as a correlation with the stage of cancer. *Murashige* et al. [50] observed higher levels of TIMP-1 and TIMP-2 mRNA expression along with the progression of colorectal cancer as well as in metastatic lesions in the liver and lymph nodes.

*Beta*-glucan leads to an increase in the mass of large intestine content, in which carcinogenic compounds (nitrosamines, phenols, cresols, skatoles, indoles, estrogens, secondary bile acids) and toxic metabolites (ammonia, amines) are more dispersed. It also facilitates cleansing the intestines of residual fecal matter and food particles. Thus, the excreted fecal matter does not stagnate. Stagnation promotes the formation of inflammatory foci leading to ulceration and, consequently, tumor foci [20].

The effect of *beta*-glucan is based on two basic mechanisms of action on cancer cells. One of them is indirect action resulting from the immunomodulatory properties that affect the immune system. The indirect action is the stimulation of defense mechanisms, primarily the activation of granulocytes (neutrophils, eosinophils), monocytes, macrophages, and natural killer cells (NK cells) [85]. *Beta*-glucan is an immune stimulator that activates macrophages and cytokines, among others, which are responsible for the body's defense (Figure 2). Macrophages are elements of the immune system that have the unique ability to kill cancer cells and phagocytosis, and are therefore the immune system's first line of defense. The immunostimulatory activity of *beta*-glucan occurs as a result of its attachment to specific membrane receptors on immunologically competent cells, including macrophages, neutrophils, monocytes, NK cells, and dendritic cells, which affects their immune response, including cytokine production and the induction of an oxygen burst [12].

The immunomodulatory effects occur mainly via receptors such as: dectin-1, complement receptor 3 (CR3), and Toll-like receptor 2 (TLR-2). The dectin-1 receptor (innate immune response receptor), which is mainly present on the surface of macrophages and dendritic cells, induces the secretion of pro-inflammatory cytokines by activating tyrosine kinase Syk and nuclear factor-kappa B (NF- $\kappa$ B) [33, 49, 52]. This receptor works with TLR-2 to activate the pro-inflammatory response by macrophages due to infections caused by mycobacteria [3]. Moreover, it interacts with the TLR-2 receptor to recognize *beta*-glucan and mediates the production of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). The CR3 receptor, interacting with TLR-2, also mediates TNF- $\alpha$  synthesis by activating transcription factor NF- $\kappa$ B as well as monocyte chemoattractant protein-1 (MCP-1) production [85] (Figure 2).

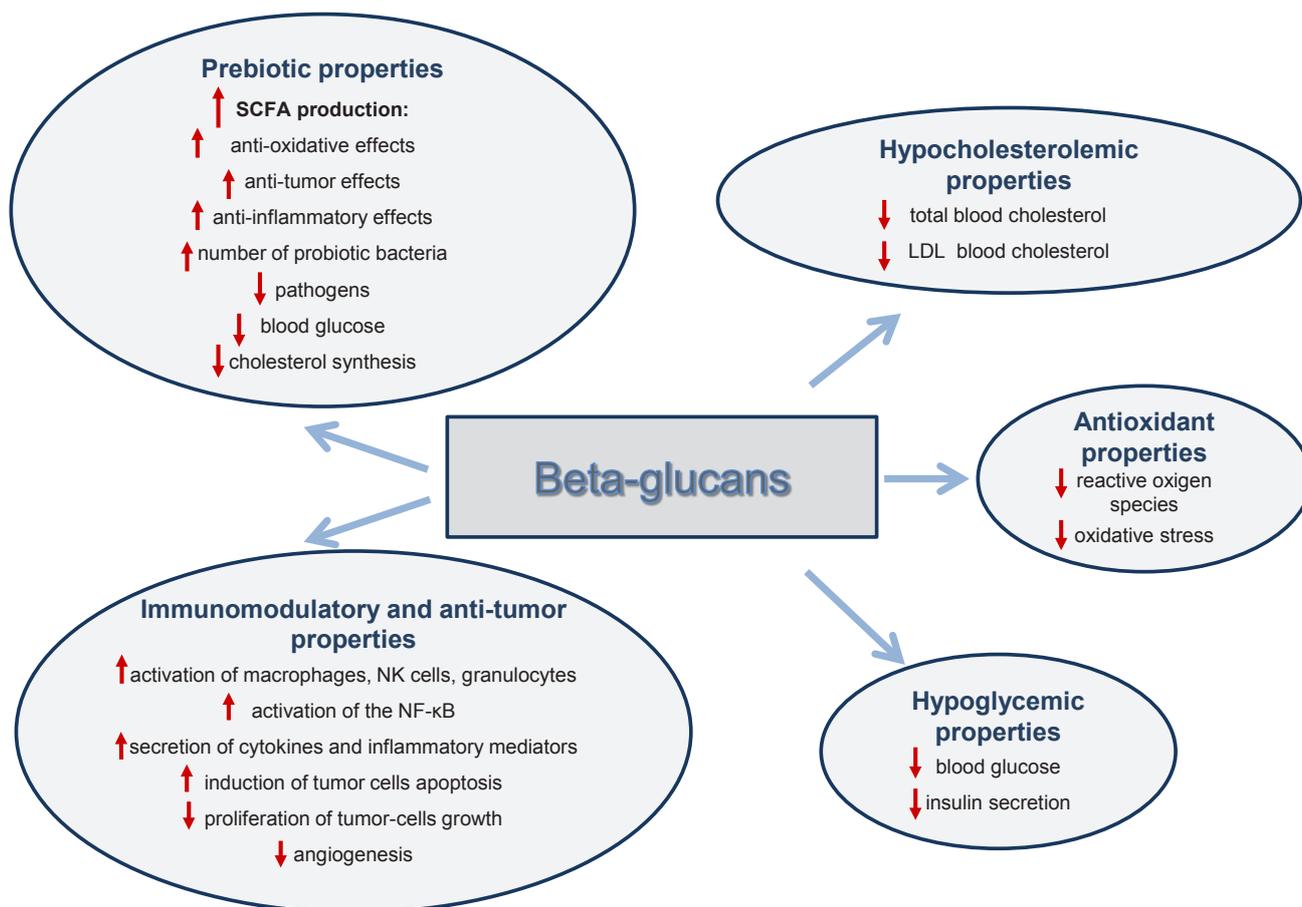


Figure 2. Health benefits of *beta*-glucans [own elaboration]

The CR3 receptor, present mainly on the surface of neutrophils, monocytes, and NK cells, has the ability to recognize the iC3b opsonin, which commonly occurs on the cancer cell surface [3]. Stimulation of phagocytic activity occurs as a result of simultaneous attachment to the CR3 receptor of the complement component iC3b (opsonin) as well as *beta*-glucan, and a lack of any of these components prevents the induction of cytotoxicity [3, 12, 52]. Thus, the antitumor effect of *beta*-glucan associated with the ability to elicit a specific immune response is associated with the activation of the complement system.

The immunostimulatory activity of *beta*-glucan is also based on the macrophage activation mechanism. Due to the presence of specific receptors, such as CR3, TLR-2, dectin-1, macrophages recognize the *beta*-glucan structure, which initiates a cascade of both cellular and humoral immune responses. As a result of *beta*-glucan attachment to macrophage receptors, they are activated, which consists of interconnected processes, such as increased chemotaxis, chemokinesis and degranulation leading to increased expression of adhesion molecules on the macrophage surface. In response to macrophage stimulation, inflammation mediators (interleukins: IL-1, IL-6, IL-8, IL-12, and TNF- $\alpha$ ) and pro-inflammatory factors (including: nitric oxide (NO), inducing a cytotoxic effect on cancer

cells and pathogens, and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>)) are secreted [3] (Figure 2). This leads to pathogen phagocytosis and antibody production.

*Beta*-glucan, referred to as a Biological Response Modifier (BRM), mainly activates the basic cells of the immune system, which are macrophages, the task of which is to absorb and destroy foreign cells in the body, including cancer cells or other pathogens. When crossing the epithelial barrier, a pathogen is phagocytized by macrophages and then digested by lysosomal enzymes released by these cells, which leads to full degradation of the phagocytized material [63]. *Beta*-glucan affects macrophages by intensifying phagocytosis, and by activating transcription factor NF- $\kappa$ B it increases the production of tumor necrosis factor [34].

The conducted research showed that *beta*-glucan isolated from yeast cell walls of *Saccharomyces cerevisiae*, due to its ability to stimulate the body's immune cells, has antitumor effects, as well as plays the role of an adjuvant in radio- and chemotherapy, thanks to which it supports the action of other preparations used in the treatment of cancer [30, 38]. Furthermore, Hofer et al. [28] observed that oral administration of *beta*-glucan from *Saccharomyces cerevisiae* in mice before exposure to radiation induced hemopoiesis as well as secretion of cytokines, such as IL-1, IL-6,

TNF- $\alpha$ , thus increasing the chances of survival after irradiation as well as intensifies the phagocytosis of cancer cells. By activating macrophages, *beta*-glucan contributes to the stimulation of the immune system, thus playing a significant role in infectious diseases and cancer, after treatment with immunosuppressive drugs, antibiotic therapy, and radiation, which significantly burden the immune system [63]. Most pathogenic fungi contain *beta*-glucans in the cell wall, which potentially trigger the body's innate immune response [44]. *Beta* glucans derived from the opportunistic pathogens *Pneumocystis carinii* act as strong inducers of macrophage activation by translocation of NF- $\kappa$ B using cell receptors and signaling pathways. They also stimulate the release of inflammation mediators, including TNF- $\alpha$ , IL-1, macrophage inflammatory protein 2 (MIP-2), eicosanoids, and reactive oxygen species [44, 76].

In addition to indirect effects, *beta*-glucans also have a direct effect on cancer cells. It consists of inhibiting cancer cell proliferation by, among others, inhibiting tyrosine kinases, limiting blood vessel development around the tumor and inducing death via apoptosis of cells that have undergone transformation [5, 70, 74, 83] (Figure 2). The mechanism of direct antitumor activity consists of modulating the activity of transcription factor NF- $\kappa$ B. Excessive activation of this factor was observed in many types of cancer, which consequently intensifies tumor growth by increasing the transcription of genes inducing proliferation, anti-apoptotic activity, and promoting angiogenesis and metastasis [60]. Studies showed that *beta*-glucans inhibit the phosphorylation and degradation of the NF- $\kappa$ B inhibitor, thus preventing the activation of the transcription factor and then the expression of genes subject to this factor [18, 48, 55, 56].

*Beta*-glucans isolated from *Pleurotus ostreatus* and *Lentinus edodes* were shown to have antiproliferative and proapoptotic activity against colorectal cancer cells, which indicates a significant antitumor effect [73]. Similar direct antiproliferative activity against colon cancer cell lines was demonstrated for *beta*-glucan obtained from *Pleurotus pulmonarius* [42]. *Beta*-glucan of bacterial origin also inhibits proliferation and induces apoptosis in human colon cancer cells. In addition, Kim et al. [35] demonstrated the effect of *beta*-glucan on the expression of apoptotic genes such as Bcl-2 and Bax, as well as caspase-3 activity, which was significantly higher in the case of cells treated with *beta*-glucan compared with the control group [35]. Research conducted by Shah et al. [67, 68] showed that grain *beta*-glucans from oats and barley inhibited the proliferation of human colon cancer cell line (Colo-205), human ductal breast epithelial tumor cell line (T47D), and human breast adenocarcinoma cell line (MCF7).

The obtained study results indicate the significant role of *beta*-glucan as a cytotoxic factor in relation to cancer cells, as well as stimulating factor towards the immune system via macrophage activation, among others, which prevents cancer development.

### Prebiotic properties

*Beta*-glucans also have prebiotic properties, which has a beneficial effect on the microflora of the gastrointestinal tract, simultaneously preventing diseases of the large intestine and digestive system. Soluble *beta*-glucans, especially from grains, are fermented by colon microflora, leading to many beneficial health effects. The fermentation of these compounds produces, among others, short-chain fatty acids (SCFA) (Figure 2), such as acetic acid, propionic acid, and butyric acid [10, 31]. SCFAs produced in the colon have an immunomodulatory effect, prevent obesity and colon cell proliferation, thus inhibiting cancer cell growth [52, 64]. In particular, butyric acid has a number of chemotherapeutic effects. By acting as a histone deacetylase inhibitor, it contributes to inhibiting the growth of already degenerated cells and inducing apoptosis in these cells, reducing the risk of developing colon cancer [8, 65].

Due to their antioxidant, antitumor, and anti-inflammatory properties (Figure 2), short-chain fatty acids play an important role in maintaining gastrointestinal and immune system homeostasis [13]. Furthermore, they also have cholesterol-lowering properties [11]. SCFAs are able to regulate glucose and cholesterol metabolism by acting on free fatty acids receptor 2 and 3 (Ffr 2/3). Through these receptors, short-chain fatty acids can increase the concentration of gastrointestinal hormones, such as glucagon-like-peptide 1 (GLP-1) and peptide YY (PYY). PYY induces glucose uptake in skeletal muscles and adipose tissues, while GLP-1 indirectly reduces blood glucose, increasing insulin concentration and reducing glucagon production in the pancreas. Use of propionic acid contributed to the reduction of cholesterol synthesis in rat livers [15, 65] (Figure 2).

By increasing the production of butyric acid and propionic acid, oat *beta*-glucan may also play a significant role in the prevention and treatment of diabetes and cardiovascular diseases [64]. *Beta*-glucans, as a dietary fiber fraction, are an important source of energy, stimulating the growth, activity, and survival of probiotic bacterial strains such as *Lactobacillus* and *Bifidobacterium* while inhibiting the development of pathogenic bacteria (*E.coli*, *Clostridium celatum*, and *Bacterioides*) [24, 72, 84] (Figure 2). This promotes the growth of beneficial intestinal microflora and improves the function of the small intestinal mucosa and colonocytes, thus reducing the risk of nonspecific inflammation and colorectal cancer [53].

## CONCLUSIONS

Research conducted in recent years has shown that *beta*-glucans can be helpful in the fight against chronic non-communicable diseases. Due to their hypocholesterolemic and blood sugar lowering properties, they can be used to prevent cardiovascular diseases and diabetes. In addition, *beta*-glucans have immunomodulatory properties, which are due to their ability to bind specific surface receptors on immunologically competent cells, thereby affecting their immune response. They also affect the secretion of cytokines, the expression of inflammation-related genes, phagocytic activity, and the activation of the complement system. They prevent oncogenesis due to their protective effect from genotoxic carcinogens. Therefore, they may play an important role in cancer prevention and treatment. Stimulation of immune system cells is particularly important not only in the case of cancer but also infections, antibiotic therapy, and long-term use of immunosuppressive drugs.

Moreover, some polysaccharides such as *beta*-glucans may act as a prebiotic and stimulate the growth of probiotic bacterial strains in the large intestine and inhibit the growth of pathogenic bacteria. This plays an important role in the proper functioning of the gastrointestinal tract and preventing inflammation as well as colon cancer. The beneficial effects of *beta*-glucans on so many aspects of metabolism have great potential for using this compound as an immunostimulant in the prevention and treatment of many diseases.

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## SIGNIFICANCE OF LOW-CARBOHYDRATE DIETS AND FASTING IN PATIENTS WITH CANCER

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### ABSTRACT

The differences between the metabolism and the physiology of cancer cells and the cells of the human body are assessed and used in most anticancer treatments. These differences encompass, among others, increased glucose metabolism in the changed cells. The aim of the paper was to discuss the results of studies concerning the relationship between low-carbohydrate diets and fasting and the course of cancer. An inappropriately composed diet consisting of high amounts of simple sugars supplies cancer cells with nutrients, which may impair the effectiveness of cancer patients treatment. Low-carbohydrate diets may, therefore, constitute an element of supplementary therapy in cancer treatment. The mechanism of low-carbohydrate diets in combination with standard treatment has not been completely explained, though. In initial studies it was proven that patients who were able to continue low-carbohydrate diets showed improvement in health and reduction of tumor mass or its slower growth. Moreover, it was observed that the inability of cancer cells to adapt in new environmental conditions that occur while fasting may have toxic effect on them. Introduction of fasting may sensitize cancer cells to chemotherapy, decrease concentration of growth factors and lead to repair of normal cells. On the other hand, fasting may also promote autophagy and, as can be concluded from the literature, its mechanism may have twofold activity: as a process impacting the survival or death of cancer cells.

**Key words:** cancer, fasting, intermittent fasting, low-carbohydrate diets, ketogenic diet

### STRESZCZENIE

W większości terapii przeciwnowotworowych oceniane i wykorzystywane są różnice między metabolizmem i fizjologią komórek nowotworowych, a komórkami ciała człowieka. Różnice te obejmują między innymi nasilony metabolizm glukozy w zmienionych komórkach. Celem pracy było omówienie wyników badań na temat związku diet niskowęglowodanowych i głodówek z przebiegiem choroby nowotworowej. Nieodpowiednio skomponowana dieta składająca się ze znacznej ilości cukrów prostych dostarcza składniki odżywcze komórkom nowotworowym, co może pogarszać skuteczność leczenia pacjentów onkologicznych. Diety niskowęglowodanowe mogą więc stanowić element terapii uzupełniającej w chorobie nowotworowej. Mechanizm działania diet niskowęglowodanowych w połączeniu ze standardowym leczeniem nie został jednak w pełni wyjaśniony. We wstępnych badaniach wykazano, że pacjenci, którzy byli w stanie kontynuować diety niskowęglowodanowe wykazywali poprawę stanu zdrowia, zmniejszenie masy guza lub jego spowolniony wzrost. Ponadto zaobserwowano, że niezdolność komórek nowotworowych do adaptacji w nowych warunkach środowiska, jakie występują podczas głodzenia, może działać na nie toksycznie. Wprowadzenie postu może uwrażliwić komórki nowotworowe na chemioterapię, zmniejszać stężenie czynników wzrostu i prowadzić do naprawy prawidłowych komórek. Z drugiej strony post może również promować proces autofagii, a jak wynika z piśmiennictwa, jej mechanizm może mieć działanie dwukierunkowe: jako proces wpływający na przeżycie lub śmierć komórek nowotworowych.

**Słowa kluczowe:** choroba nowotworowa, głodówka, post przerywany, diety niskowęglowodanowe, dieta ketogeniczna

### INTRODUCTION

In epidemiological studies it was proven that diet plays key role in the process of carcinogenesis. Obesity and metabolic imbalance related to sedentary lifestyle and consumption of wrong foods may induce oxidative stress, insulin resistance and hormonal changes that

are significant in cancer pathogenesis. Inadequate diet is understood as excessive consumption of meat and processed foods and insufficient consumption of plant foods, among others vegetables, fruit, legumes and whole-grain products [37, 59, 66].

Metabolic processes in cancer cells are different than in healthy cells. One of the most frequent

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metabolic changes in cancer cells is increase in glycolysis speed even in the presence of oxygen. The authors confirm the hypothesis according to which metabolism of cancer cells depends on higher supply of glucose for maintenance of *redox* homeostasis related to increased reduction of  $O_2$  to  $O_2 \bullet^-$  and  $H_2O_2$  electrons in mitochondria. In cancer cells, process of glucose fermentation into lactate occurs even with adequate availability of oxygen. The effect, known as the *Warburg* effect, constitutes a separate characteristic feature of cancer cells and may be caused by genetic mutation. Authors of research [1, 60, 77] works made an attempt to reduce the amount of carbohydrates in diet, in order to selectively sever the energy supply to cancer cells and, thus, inhibit tumor growth.

The aim of the study was to assess the relationship between low-carb diets and fasting, and the course of cancer on the basis of literature review.

### CANCER CELL METABOLISM

In most anti-cancer therapies the differences between the metabolism and the physiology of cancer cells, and human body cells are assessed. Cancer cells are characterized by different metabolism in comparison to properly differentiated cells. These differences encompass, among others, increased glucose metabolism that depends on many factors, including increased activity of the GLUT glucose-transporting proteins and some enzymes as well as the level of proliferation. Cancer cells show high level of proliferation; the consequence of it is disturbance in access to nutrients, including glucose and oxygen, and, as a result, switching cell metabolism to anaerobic respiration. Glycolysis becomes the main process in which energy, in the form of high-energy bonds of adenosine triphosphate, is produced (ATP). Pyruvate, produced in the glycolysis process, is transformed by lactic fermentation into lactic acid [6, 40]. The above phenomenon was more broadly described in the second half of the 20th century by a German scientist, *Otto Warburg*. In the research conducted in animal models within the last 60 years, increased uptake of glucose by cancer cells in comparison to the normal cells has been confirmed. Using positron-emission tomography (PET), the authors of the study observed an increased uptake of glucose and release of lactate by malignant cancer cells in comparison to benign cancer cells [68]. It seems that depriving cancer cells of energy source, namely glucose, may result in inhibition of their proliferation which may be related to higher effectiveness of radio- and chemotherapy [40].

Hyperglycemia is of high significance for growth and proliferation of cancer cells. An inadequately composed diet, consisting of high amounts of simple carbohydrates, provides cancer cells with nutrients,

which may negatively affect the effectiveness of cancer patients treatment [15, 19]. Thus, a thesis stating that low-carbohydrate diets may constitute an element of supplementary therapy in cancer has been formulated. Energy production from fats decreases availability of glucose to glycolysis and decreases production of pyruvate and glucose-6-phosphate which may enter the pentose phosphate pathway creating nicotinamide adenine dinucleotide (NADPH) necessary for hydrogen peroxide reduction. As a consequence, lack of NADPH regeneration increases the dynamic of oxidative stress in cancer cells. Lipid metabolism in cancer cells is, in addition, related to the use of energy from mitochondrial metabolism. In cancer cells, damaged respiratory chain in mitochondria occurs. It is related to increased reduction of  $O_2$  electrons that leads to synthesis of reactive oxygen species (ROS) [10, 12]. Many amino acids enter the tricarboxylic acid cycle in the course of the *Krebs* cycle. This process may be related to gluconeogenesis, allowing for NADPH production. Protein metabolism cannot therefore lead to increase in ROS production in cancer cells on the same level as metabolism of fats [34]. Glutamine is used as a substrate and a donor of nitrogen atoms for cancer cells. It enters the *Krebs* cycle by transforming into glutamate and then into  $\alpha$ -ketoglutarate. As a result of further transformation,  $\alpha$ -ketoglutarate may undergo gluconeogenesis, allowing for production of NADPH [95]. *Lieberman* et al. [48] observed that cancer cell lines that they were analyzing showed higher uptake of glutamine than of glucose. Metabolic changes of glutamine may influence protection of cancer cells from oxidative stress and promote tumor growth [16,17]. In restrictive conditions, cancer cells also use ketone compounds as energy source. It is possible only in the presence of adequate oxygen concentration, access to which is limited during fast growth of tumor [30]. *Lin* et al. [49] observed presence of enzymes which condition oxidation of fatty acids in the cells of human glioma. Fatty acids were used as the main energy source by cancer cells.

### THE MECHANISM OF FASTING AND AUTOPHAGY IN THE PROCESS OF CARCINOGENESIS

The term autophagy comes from Greek and means self-consumption. It is an intracellular process that consists in degradation of macromolecular components of cytoplasm [50, 61]. The process of autophagy may be induced by many factors, including fasting, oxygen deprivation, damage to DNA structure and hormone activity [50]. Autphagy ambiguously influences the stages of neoplasm initiation and progression. It is related to overlapping of signal pathways of autophagy and carcinogenesis. In chronic autophagy inhibition

carcinogenesis is promoted, which is related to genome instability, defective cell growth and oxidative stress induction. However, increase in autophagy process may be related to a mechanism that allows for survival of cancer cells in the state of oxygen deficiency, acidosis and under the influence of chemotherapy. Due to those factors the process of autophagy in cancer development should be considered in a two-way manner [56, 94].

The process of autophagy is used as a mechanism that conditions survival of cancer cells and may be inhibited at the early stages of cancer which allows for tumor development. At the late stage of cancer, autophagy and intercurrent cancer cell resistance to chemotherapy are increased [47, 56, 79]. For example, increased autophagy is used in liver cancer cells in order to provide key medium metabolites that are necessary for maintaining energetic processes at the level that allows for cell survival [97].

Autophagy may also act in a completely opposite manner, contributing to cancer cell elimination causing their apoptosis and increasing the effectiveness of treatment. Hunger is one of the most effective ways of promoting autophagy in cancer cells; it enhances immunological response and treatment process in cancer patients [79, 94]. In cancers with mutation in the *Ras* oncogene (including lung cancer, colon cancer and pancreas cancer) increased autophagy, necessary for cell growth, was observed. This process is necessary for cells both at the stage of transformation and at the stage of progression. *Lock et al.* [51] observed that autophagy blocking in cancer cells with *Ras* oncogene mutation was related to the decrease of their proliferation potential. In addition, inhibition of autophagy process decreased the ability of cancer cells to use glycolysis. *Van Niekerk et al.* [86] proved higher immunity of normal cells to negative effects of applied chemotherapy when fasting was introduced. Fasting was related to physiological adaptations, including regulation of autophagy. According to the authors, these processes could have influenced the effectiveness of chemotherapy.

Thus, the role of autophagy in the carcinogenesis process is not unambiguous, because it depends on the type of cells and the conditions in which they dwell. Further studies are needed in order to understand these processes better.

## VERY LOW CALORIE DIETS

While fasting, energy expenditure is decreased and used in processes that are aimed at organism protection and that condition survival [52]. Proliferation of cancer cells occurs in an environment rich in nutrients, in which processes such as glycolysis and protein biosynthesis can take place. Inability of cancer cells

to adapt in new environmental conditions that occur during fasting may have toxic effect on them [65]. The difference between tumor-induced weight loss (TIWL) and fasting is that in the case of cancer cachexia the process cannot be reversed after introducing proper nutrition. It is assumed that cancer cachexia means unintentional weight loss by 5-10% within 6 months. TIWL is observed in, among others, patients with advanced stomach cancer, pancreas cancer, lung cancer and colon cancer. Despite the development in the field of oncology, TIWL remains a significant cause for persisting chronic illness and morbidity of cancer patients [8].

In the research by *Sun et al.* [79] the relationship between the applied fasting and the organism's immunity to cancer was assessed. The authors of the research observed that introduction of fasting for the period of two weeks caused inhibition of tumor growth in mice, without causing decrease in their body weight. It is one of the first works in which the above dependency was described. It was proven that introduction of fasting may induce autophagy in colon cancer cells, which eventually inhibited tumor growth by promoting anti-cancer immunity. From pre-clinical studies, conducted in animal models, it can be concluded that calorie restriction (CR) positively influenced lifespan and delayed occurrence of illnesses related to aging of the organism, including cancers. The above method of nutrition is described as calorie restriction by about 20 - 40%, without allowing for the occurrence of the state of malnutrition [31]. Metabolic changes related to calorie restrictions positively influenced health, including increase in insulin sensitivity, decrease of inflammation and inhibition of angiogenesis [11, 32, 55]. In addition, introduction of CR influenced processes that are directly related to the pathomechanism of cancer, including repair processes of the DNA, removal of damaged cells in result of apoptosis, increased autophagy and protection from toxic factors [14].

Calorie restriction in diet and health benefits related to it are observed in various countries, for example in Japan. High diversification in terms of life length was observed there. The inhabitants of the Okinawa prefecture lived the longest, which is believed to be caused by their traditional, healthy lifestyle which can be characterized as CR [80]. *Suzuki et al.* [80] observed that the people from the island consumed 17% less calories in their diet in comparison with the people living in continental Japan, and 40% less calories than an average resident of the United States. The authors state that the residents' diet consisted mainly of fresh vegetables, fruit, sweet potatoes, soy and fish, and the share of energy from protein in the diet was 9%. Morbidity due to cancer, including prostate, colon and breast cancer, was much lower in comparison with Japanese and American populations [36].

## INTERMITTENT CALORIE

Intermittent calorie restriction (ICR) consists in calorie restriction in a diet for 1-3 days per week. *Kusuoka et al.* [45] studied the influence of ICR in mice with induced colon cancer. The mice were subjected to a 24-hour-long fasting once a week for four weeks. The control group received high calorie diet or diet rich in *trans* fatty acids. It was observed in the study that ICR had no tumor growth suppression effect, and the applied nutrition model promoted proliferation of cancer cells. The researchers suggest that irregular food intake that causes cycles of fasting/eating may give cancer cells the ability to metastasize.

The mechanism of fasting and fasting-mimicking diet (FMD) was assessed in terms of the possibility of protecting the properly functioning cells from the toxic effect of chemotherapy. The fasting described in literature lasted from 12 hours to 3 weeks [11, 21]. In the study by *Brandhorst et al.* [11] introduction of two month-long cycles of FMD in mouse models caused elongation of their life, decrease in the amount of visceral adipose tissue and decrease in the incidence of cancer. The above diet: low in calories, low in protein, high in fats and rich in complex carbohydrates was related to obtaining an effect similar to the results obtained while applying fasting in healthy mice. It was observed that short-term fasting for 48 hours was an effective method of protecting the normal cells of mice from the toxic effect of chemotherapy. Introduction of fasting caused enhancement of the ability to react to chemotherapy applied against cancer cells of melanoma, glioma and breast cancer. In mice with neuroblastoma, cycles of fasting combined with chemotherapy and different methods of treatment caused longer survival with no progression of the cancer [46]. Similarly, in the study conducted by *Di Biase et al.* [21] it was observed that FMD cycles in combination with chemotherapy increased the effectiveness of anti-cancer treatment by stimulating the immune system. Discovering that the FMD cycles may increase the effectiveness of chemotherapy in terms of cancer cells, and, at the same time, limit this toxicity in mice interested the scientists. The above information was used in clinical studies. Currently, studies on the possibility of applying fasting in patients with prostate and breast cancer are in progress [27, 33, 70].

Due to the fact that in animal models evidence concerning the benefits of applied fasting was provided, the above mechanism was assessed in a group of 2413 women between the age of 27 and 70, at early stages of breast cancer. Night fasting that lasted on average 12,5 hours was applied. In the study it was observed that night fasting prolonged to more than 13 hours may be a simple, non-pharmacological strategy of reducing the

risk of breast cancer relapse. The authors of the above study expressed an assumption according to which prolonged night fasting may potentially decrease the risk of type 2 diabetes, cardiovascular diseases and some cancers. However, randomized studies on the subject are needed [54].

In the study by *Safdie et al.* [69] 10 cases of patients with cancer, subjected to chemotherapy (7 women and 3 men) aged 44 to 78 with diagnosed breast, prostate, ovary, uterus, lung and esophagus cancer were analyzed. 48 to 140 hours-long fasting before chemotherapy and/or 5 to 56 hours-long fasting afterward chemotherapy was applied in patients. On the basis of observation of this group of patients the authors concluded that fasting in combination with chemotherapy was feasible and safe, and could reduce chemotherapy-induced side effects. The patients reported reduction of fatigue and weakness and less side effects from the digestive tract in comparison with the state of being before the application of fasting.

At Leiden University Medical Center (NCT01304251) 13 women at early stage of breast cancer were qualified and randomly assigned to a study in order to assess the safety of 24-hour-long fasting before and after applying chemotherapy. In the above pilot study it was confirmed that short-term fasting was well tolerated and safe, and it could limit hematological toxicity and increase protection from DNA damage in normal cells [18]. In addition, fasting could influence destruction of cancer cells by activating the immune system and/or enabling the immunological cells to recognize the cells of malignant cancers [11].

## LOW-CARBOHYDRATE DIETS

According to the recommendations of the World Health Organization (WHO) carbohydrates should constitute 45-65% of daily caloric intake. It is related to the daily need of an organism for, among others, glucose as a source of energy. The brain, the erythrocytes, the leukocytes and the renal cortex are directly dependent on glucose. In the conditions of fasting tissues dependent on glucose may adapt to metabolism of fats. During the process of gluconeogenesis glucose may be produced in the liver and in kidneys from glucogenic amino acids, glycerol and lactate. While fasting, the organism may obtain up to 200g of glucose from the pathway described above. This amount is sufficient to satisfy the needs of glucose-dependent tissues [74, 90].

### The Atkins diet

In the years 1972 - 2003 *Robert Atkins* [4] promoted low-carbohydrate diet as a method in obesity treatment. He recommended restricting carbohydrates to up to 30 g/day and increasing protein and fats intake - those could be consumed without limitation.

He divided this diet program into several phases. The first phase was essential due to ketosis induction in patient, and it lasted 14 days. Then, the share of energy from carbohydrates in the diet was increased by 10 g per week. The final element of the process was the maintenance phase. According to the author, the patient could consume fat-rich dairy products, eggs, meats, fish and vegetables, and, in further phases of the diet, also fruit and nuts.

Safety of applying modified *Atkins* diet in patients with diagnosed cancer was assessed. In the diet, carbohydrates were restricted to 20 to 40 grams per day. The energy value in the diet was not reduced. Due to the declining health of patients, unrelated to the diet, and due to personal reasons the applied dietary program was assessed in 11 out of 17 qualified patients. In all the patients, loss of body weight was noted, yet the hematological, biochemical and lipid parameters remained stable. The survey data showed that the quality of life slightly improved. Scientists believe that modified *Atkins* diet was safe and feasible at advanced stage of cancer, yet, due to lack of results from other studies, the above issue requires further research [81].

### **Ketogenic diet**

In 1921 Dr *Wilder* from the Mayo Clinic proposed a diet that consisted in increasing the share of energy from fats, on the basis of biochemical processes of fasting. He was also one of the first people to use the term of ketogenic diet (KD). The above diet is applied with good results in treatment of drug-resistant epilepsy [5, 93]. During KD, oxidation of fatty acids occurs and ketone compounds - acetoacetate,  $\beta$ -hydroxybutyrate and acetone - are produced. When the concentration of ketone compounds in blood is equal to 4mmol/l they may be used as a source of energy by the central nervous system [24].

As early as in 1987 KD was also applied in cancers. *Tisdale* et al. [82] observed decrease in tumor mass and improvement in health (at the stage of cancer cachexia) in mice with colon cancer when KD was applied. In the research conducted by *Zhang* et al. [98] studies on the influence of KD on cancer cells depending on the expression of key enzymes of ketone compounds catabolism *in vivo* and *in vitro* were conducted. Activity of enzymes (3-hydroxybutyrate dehydrogenase, 1BDH1 and 3-oxoacid CoA transferase 1,OXCT1) responsible for catabolism of ketone compounds *in vivo* and *in vitro*, was studied in two representative cell lines (HeLa and PANC-1). It was proven that response to application of KD was present to a larger extent in cancer cell lines in which low activity of 1BDH and OXCT1 occurred. In meta-analysis published in 2016 by *Klement* et al. [41] 12 studies assessing survivability of mice with cancers in whom KD was applied were analyzed. The authors

of the meta-analysis observed that application of KD in mice delayed tumor growth. The effect of the diet depended on the location of the tumor and the stage of advancement of cancer.

The evidence regarding the beneficial effect of KD in animal models was used in clinical studies in which application of ketogenic diet in terms of its safety and the possibility of its application was analyzed. KD was introduced in 16 patients with advanced cancer (among others: breast, ovary, esophagus, pancreas, colon, lung and stomach cancer). The therapy lasted for 3 months. In 6 patients there was an improvement in emotional well-being and in the quality of sleep [72]. Similar results were obtained by *Fine* et al. [23]. KD was applied in 10 patients for 26 to 28 weeks. Adverse effects were not noted and the diet was deemed possible to be applied in cancer patients. *Klement* et al. [42] also confirmed that introduction of KD during standard therapy was safe and did not cause adverse effects. Loss of body weight in patients was related to reduction of adipose tissue, not muscle tissue. Patients reported well-being on a diet in which carbohydrate intake was below 50 g. Tumor regression at early stages of the illness occurred as expected, however, in one patient progression of illness occurred, and it intensified after the end of KD.

### **Ketogenic diet and brain glioma**

In the recent years, studies on the relationship between KD and the nervous system-related cancers have been commenced. Malignant gliomas have been occurring increasingly within the last 30 years, especially in elderly people. Prognosis for patients with glioblastoma multiforme (GBM) is bad, and the survival median is equal to 12 months [35]. Due to bad prognosis and ineffectiveness of the available treatment methods, new therapeutic methods are being sought for [13]. It has, moreover, been observed that hyperglycemia is related to worse prognosis in patients with GBM [57].

In 1995, on the basis of a study of two cases of pediatric patients with brain cancers (astrocytoma) at an advanced stage of the illness, the KD model with 60% of energy share from medium-chain fatty acids was incorporated. The remaining macronutrients were distributed in the following way: 20% of energy share from proteins, 10% from carbohydrates and 10% from the remaining fats. In the area where the tumor was located glucose uptake was measured using positron-emission tomography. After 7 days of the diet being applied by both patients, reduction of glucose uptake equal to 28,7% was noticed in the area of the tumor. In one of the patients significant clinical improvement in terms of mood and development of new skills were observed. During continuation of KD for 12 months no progression of illness was observed [63].

The other case description concerned a 65 years old female patient, in whom glioblastoma multiforme was diagnosed. After surgical resection of GBM ketogenic diet was also incorporated into the standard therapy in this case, using 4:1 ratio (4 grams of fats to 1 gram of carbohydrates and protein altogether). The daily calorie intake was established at the level of 600 kcal. The patient's body mass decreased by about 20% after two months of KD implementation, and no presence of brain cancer cells was detected. Strict diet was continued for 6 months. 2 months after the end of it, relapse of the illness was detected in the image of magnetic resonance [99].

*Champ et al.* [13] applied KD in 6 patients with GBM during chemotherapy and radiotherapy. The implemented diet was well tolerated, and no episodes of hypoglycemia were observed in patients. Four patients survived; the observation time median was 14 months. However, as the authors of the study state, the benefits of KD incorporation remain dubious.

In the ERGO study (NCT00575146) the possibility of applying KD (60 g of carbohydrates per day) in 20 patients with recurrent glioma 3 months after the end of radiotherapy was assessed. The diet consisted of, among others, fermented milk beverages (500 ml) and plant oils. The dietary model did not encompass calorie restriction, the patients were instructed which products they were allowed to consume. The implemented diet complemented the applied treatment. The average survival time with no progression of illness was 5 weeks, and the survival median - 32 weeks. The authors emphasized that the limited number of patients, lack of control group in the study and no randomization do not allow for unambiguous estimation of the KD effectiveness [67].

### DIET MODIFICATIONS IN BREAST CANCER PREVENTION

The available research on the potential role of the KD in prevention of breast cancer and support of its treatment is based on the analysis of singular cases. There are no randomized clinical studies. Nonetheless, a relationship between high body mass index (BMI) and the incidence of breast cancer among women pre- and post-menopause has been observed. Body mass reduction was proposed as a potential goal reducing the risk of breast cancer; KD may be probably used to obtain this result [7, 38].

In 86 621 participants of the Nurses' Health Study (NHS) the relationship between implementing the DASH diet (*Dietary Approaches to Stop Hypertension*), diets with lower content of carbohydrates (based on plant-based products, animal products and general) and the risk of breast cancer after menopause was assessed. The DASH diet and the plant-based diet

with limited amounts of carbohydrates (the median of carbohydrate content in the diet was 52,9%) was related to lower risk of breast cancer with negative estrogen receptors [25].

In the study conducted by The Finnish Social Institution's Mobile Clinic Health Survey (FSIIMCHS) the relationship between the content of fats in diet and later risk of breast cancer was studied in a group of 3988 women, aged 20 - 69. The authors of the study suggest that occurrence of breast cancer in patients was related to higher energy value in their diets, but not to complete share of energy from fats in the diet [44].

In a prospective cohort study, conducted on the basis of the data from The Canadian National Breast Screening Study (NBSS), the risk of occurrence of breast cancer depending on the glycemic index (GI) and the glycemic load (GL) was assessed in 49 613 Canadian women. In the above study, the GL in the analyzed diets was not related to the risk of breast cancer in particular subgroups, whereas the GI in the diets was related to higher risk of breast cancer in women post-menopause. The GI considers the quality of the consumed carbohydrates along with the product, and the GL additionally considers their amount. According to the authors, the participants of the study in whom cancer occurred could have consumed a wider variety of products with high glycemic index that were also characterized by worse quality of carbohydrates [76].

### DIET MODIFICATIONS AND HEAD AND NECK CANCERS

Due to their similar etiopathogenesis, pathomorphology and clinical course, cancers located in the area of head and neck (HNC) are qualified into one group. Inflammations in the area of mouth cavity before occurrence of HNC and during cancer were observed more often in diabetic patients. Therefore, studies including appropriate nutritional support were undertaken [85, 88].

In a randomized prospective study, using double-blind test, standard enteral nutrition and enteral nutrition specific for the illness containing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were administered in 111 patients with HNC undergoing chemotherapy. Improvement in the nutritional condition and in functioning during chemotherapy was observed in patients in whom feeding model rich in EPA and DHA fatty acids was applied [22].

Patients at advanced stages of head and neck squamous cell carcinoma (HNSCC), treated post-surgically, were qualified for the first phase of the clinical trial. For 5 weeks, the patients underwent chemotherapy with simultaneously incorporated KD, with adequate parameters being monitored. The

average observation time of all the included patients (n=9) from the moment chemotherapy ended was 7,1 month. Out of 9 qualified persons, 3 managed to apply KD for 5 weeks [3]. The foods were administered in the form of cocktails via percutaneous endoscopic gastrostomy (PEG), or were administered orally, depending on patient's capability. Discontinuation of application of KD was related to nausea (3 patients), fatigue (1 patient), hyperruricemia (1 patient) and additional stress for patients, related to following the diet (1 patient).

### The paleo diet

The paleo diet is also considered to be a low-carbohydrate diet. The concept of this diet is to follow the way of eating that is based on eating habits of our ancestors from the Paleolithic era. The ancestors consumed foods that were gathered or hunted by them on their own. In compliance with the description of low-carbohydrate diets, paleo diet is dominated by proteins and fats from meat products, fish, eggs, vegetables and nuts. Supply of carbohydrates in the diet is not specified unambiguously. Eating fruit and selected starch vegetables is permitted. As authors of the study indicate, the paleolithic diet may be used as eating strategy for weight loss [64]. *Whalen et al.* [92] conducted an analysis of two exemplary diets: the paleolithic diet and the Mediterranean diet, the health-promoting effects of which are supported by studies [73]. Consumption of products in accordance with the above diets was verified using the Food Frequency Questionnaire (FFQ). The paleolithic diet that was analyzed in the study consisted of higher supply of vegetables, fruit, lean meat, fish, nuts and low supply of red and processed meat, sodium-rich products, dairy and wholegrain products, sweetened beverages, alcohol. Lower mortality rate of all causes was observed in people who conformed with the paleolithic or the Mediterranean diet. Additionally, decrease in dynamic of oxidative stress and mortality caused by cancers, mostly by colon cancer, was observed in the patients. As the researchers emphasize, it was the first study that analyzed the aforementioned dependencies [92].

Considering the arguments advocating application of KD and the paleolithic diet, the researchers developed a dietary model that is known as the paleolithic ketogenic diet [83, 84]. The paleolithic ketogenic diet was introduced in a 60 years old patient, diagnosed with epithelial-myoepithelial carcinoma of the parotid gland, who did not agree to conventional treatment. Diet consisting mainly of meat and fats was suggested. The ratio of the mass of fats to the mass of protein in the diet was 2:1. The amount of plant products in the diet was less than 30% of all consumed foods. No calorie restriction was applied. The patient did not report adverse effects and his state of being

and physical fitness improved. It can be concluded from the data that introduction of an alternative dietary model inhibited tumor growth. The patient continued the diet for 20 months [83].

In another case description, the authors assessed introduction of the paleolithic ketogenic diet in a 62 years old patient diagnosed with rectal cancer. Radiotherapy combined with the diet was applied in the patient for 6 weeks. Later on, the diet itself constituted independent therapy. Grains, milk, dairy products, oil plant seeds, legume seeds, plant oils, including coconut oil and olive oil, were eliminated from the diet. Vegetables constituted less than 30% of the entire daily range of foods. They were mostly root vegetables. The patient continued the diet for 24 months. Tumor growth was inhibited within the first 5 months when the patient strictly complied with the diet, which could be related to the simultaneously applied radiotherapy. Symptoms suggesting progression of the illness were noted when the patient did not comply with the dietary recommendations strictly. An operation within 24 months revealed metastases to liver. According to the authors, rectum operation was delayed by two years because of the influence of the diet [84].

## ADVERSE EFFECTS OF LOW-CARBOHYDRATE DIETS

In most studies concerning KD negative effects such as: occurrence of kidney stones, decreased weight gain and deficiencies of mineral substances were observed when the diet was applied for 1 - 6 years [9, 71]. In the literature the following are described as the adverse effects: torpor, nausea and vomiting caused by intolerance of the diet, especially in children. In addition, children may be prone to develop hypoglycemia due to low amounts of carbohydrates in the diet. In adults, on the other hand, gastrointestinal discomfort related to high amount of fats in diet and constipation were noted [20]. In a prospective pilot study it was observed that the level of LDL cholesterol in blood serum was elevated after one year if KD was complied with [62]. *Hayashi et al.* [29] monitored the level of selenium, zinc and copper in patients' blood serum and their daily consumption both before and 6 months after the beginning of KD. Due to the occurring deficiencies during the diet, the authors of the study suggest supplementation with these mineral substances.

There is a risk of kidney damage caused by nitrogenous waste products excretion. The authors do not demonstrate definite certainty of the occurrence of KD-related kidney damage, but in 6% of children kidney stones were noted while applying the diet for 1 - 5 years [71]. Introduction of KD may be related to occurrence of elevated concentration of ketone

compounds in blood which is in particular undesired in the case of patients with diabetes in whom there is an increased risk of ketoacidosis - a state that is potentially life-threatening. However, the concentration of ketone compounds and glucose in blood of most adult patients was not elevated [72]. Adaptation of patient's organism related to changing the standard diet to low-carbohydrate diet may be accompanied by: constipation, headache, halitosis, muscle contractions, general weakness, rash, diarrhea. Constipation and digestive tract dysfunctions may result from smaller volume of food, increased share of fats and decreased supply of fiber in the diet [39, 96].

Xia et al. [95] showed that application of KD may result in occurrence of cancer mutations. Elevation of acetoacetate concentration in blood serum led to growth of human melanoma in mouse models. These observations indicate pathological relationships between nutrients and specific oncogenic mutations that occur in human cancers. Selective influence of fat in diet on the increase of proliferation of tumor cancer cells (BRAF V600E) took place via elevated ketogenesis.

According to the Polish standards for nutritional therapy, fasting should not be applied in order to inhibit tumor growth. It can moreover significantly worsen the state of a patient in the course of cachexia, leading to his or her faster death. Combining the above alternative methods is therefore not recommended until there is adequate evidence that confirms their effectiveness [43].

## CONCLUSIONS

Despite the progress in anti-cancer treatment, prognosis for many cancer patients is bad, and most current methods of treatment are limited due to occurring adverse effects. Alternative dietary interventions seem to be a method of cancer patient support that is possible to be applied, yet, due to their restrictive form, they may not be tolerated by patients. The authors of the studies emphasize that limited number of patients, lack of control groups and lack of randomization do not allow for unambiguous estimation of the effectiveness of fasting and low-carbohydrate diets.

The mechanism of KD in combination with standard treatment has not been fully explained. In preliminary studies it was demonstrated that patients who were able to continue low-carbohydrate diets showed: improvement in health, decrease in tumor mass or its slower growth. Molecular mechanisms of the diet-cancer mutation relationship are unclear. Introduction of fasting may sensitize cancer cells to chemotherapy and lead to re-directing energy toward conservation and repair of normal cells. On the other hand, fasting may also increase autophagy regulation and, according to the literature, its mechanism may have two-way activity, hence further studies are needed.

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## IMPORTANCE OF DIET IN REDUCING CANCER INCIDENCE IN POLAND: A REVIEW

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### ABSTRACT

Cancer is one of the leading causes of death in most countries in the world. In Poland, after cardiovascular disease, cancer is the leading cause of death, and the number of malignant tumors has more than doubled in the last three decades. Increased cancer mortality in the immediate future is expected to be mainly associated with lung cancer caused by smoking (both sexes), colorectal cancer (both sexes), breast cancer in women, and prostate cancer in men. It is estimated that 20 to 30% of all malignant tumors are diet-dependent, in which cases the cancer-inducing factors are the nutritional components of the food and the 'hygiene' of eating. Research by the Institute of Food and Nutrition in Warsaw indicates that an important factor in the prevention of cancer is also the individual's state of awareness concerning diet. It is emphasized that running nutritional education programs, especially for children and adolescents, may help to limit the occurrence of diet-dependent cancers in Poland over the next few decades. The aim of this review is to assist the promulgation of knowledge about the importance of a high-quality diet in the prevention of cancer. The need for such knowledge is indicated by the upward trend in the incidence of these types of disease in Poland.

**Key words:** *nutrition, diet, cancer, prevention*

### STRESZCZENIE

Choroby nowotworowe stanowią jedną z głównych przyczyn zgonów w różnych krajach świata. W Polsce nowotwory obok chorób układu krążenia są jedną z przyczyn największej ilości zgonów, a liczba zachorowań na złośliwe rodzaje tych schorzeń wzrosła ponad dwukrotnie w ciągu ostatnich trzech dekad. Umieralność z powodu prognozowania dotyczące dalszego wzrostu ilości tych zachorowań, związane są głównie z paleniem tytoniu i dotyczą nowotworów jelita grubego u obu płci oraz nowotworów płuca oraz piersi u kobiet, jak również prostaty w populacji mężczyzn. Uznaje się, że około 20 – 30% wszystkich nowotworów złośliwych stanowią nowotwory dietozależne, w których czynnikiem indukującym raka są składniki żywieniowe oraz higiena odżywiania. Badania Instytutu Żywności i Żywienia w Warszawie wskazują, że ważnym czynnikiem profilaktyki zachorowalność na nowotwory złośliwe jest również stan świadomości związanej ze stosowaną dietą. Podkreśla się również, że prowadzenie edukacji żywieniowej już u dzieci i młodzieży może ograniczać występowanie nowotworów dietozależnych w Polsce. Celem niniejszego artykułu jest popularyzacja wiedzy na temat jakości diety stosowanej w profilaktyce chorób nowotworowych, z uwagi na niekorzystną tendencję wzrostową zachorowalności na te rodzaje schorzeń w Polsce.

**Słowa kluczowe:** *pożywienie, dieta, choroby nowotworowe, zapobieganie*

### INTRODUCTION

Cancer is one of the leading causes of death in developed and developing countries around the world. The term cancer is understood to mean an abnormal, excessive growth of tissue originating from normal cells of the body that have undergone cancerous transformation. Over time, cancer cells in the case of malignant tumors are transferred by the lymphatic or

blood circulatory systems to other organs of the body, creating secondary foci (metastases). The primary causes of cancerous transformation are mutations in proto-oncogenes, anti-oncogenes and mutator genes regulating the cell cycle, and DNA repair systems. Both genetic factors (affecting about 10% of the population) and environmental factors (affecting about 80% of the population) are involved in the development of tumors. The environmental factors include ionizing

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radiation, excessive exposure to the sun, factory fumes, some metals (asbestos, lead, nickel, chromium), dioxins (from grilled food, cigarette smoke, garbage incineration smoke, car fumes), smoking tobacco, medicines, viruses and bacteria, alcohol and certain types of diet (*DeVita et al. 2011*).

According to reports from the GLOBOCAN project, in 2012 there were about 14.1 million new cases of cancer and 8.2 million deaths related to cancer in the whole world. It is presumed that in the near future cancerous diseases will be the main cause of deaths for both men and women before the age of 65 (*Torre et al. 2015*). In Poland, cancer is the second highest cause of death, and the number of malignant tumors has more than doubled in the last three decades. Mortality from malignant tumors in Poland is higher than the average for other European Union countries. The most common cases of malignant tumors in men are found in the lungs (about 20% of cases), the prostate (13%), the colon and rectum (12%), the bladder (7%), and then the stomach, kidneys, larynx, and circulatory systems (leukemia and lymphoma). Among women the incidence is breast cancer (over 20% of cases), large intestine (10%), lungs (9%), uterine body (7%), ovary (5%), and then cervix, kidneys, stomach and thyroid. The number of deaths from malignant tumors in Poland in the last five decades has increased by almost 2.4 times (*Didkowska et al., 2017, Europejski Raport Zdrowia, 2013*).

Research conducted at the Institute of Food and Nutrition in Poland indicates that the state of health of Poles, including the incidence of malignant tumors, could have been affected by changes in the quality of nutrition. After the political transformation of 1989, dietary habits in the country changed for better and for worse. Among the favorable trends occurring in the period since then were, firstly, an increased consumption of vegetables and fruits, resulting in a higher content of vitamin C in the diet, and, secondly, a reduced consumption of red meat, resulting in an associated reduction in the consumption of animal fats. In addition, there was a reduction in salt intake and an increase in the content of vitamin D. These dietary changes were accompanied by a reduction in the number of cigarettes smoked. However, despite there having been some favorable changes in nutrition, certain negative trends have also become apparent, such as an increase in alcohol consumption, a decrease in dairy product consumption, resulting in a reduced supply of calcium in the diet, a decrease in the consumption of cereal products, resulting in a reduction in foliate and fiber consumption, and an increase in the fat content of the diet (*Jarosz, 2017*). The special relationship between diet and cancer is shown by the incidence of colon and rectal tumors. In the last few decades, there has been an increase in both morbidity and deaths among

Poles from these cancers to the extent of a four-fold increase in the incidence of the cancers among men and a three-fold increase among women. The research of *Didkowska et al. (2009)*, regarding the prognosis of morbidity and mortality of Poles due to cancer, indicates that a significant increase is likely to occur in the coming years, especially due to cancer associated with smoking. These studies suggest a future increase in the incidence of lung and colorectal cancer in both sexes, breast cancer in the female, and prostate cancer in the male population.

The aim of this article is to assist the promulgation of knowledge about the role of diet in the prevention of cancer. This is considered essential because of the unfavorable upward trend in the incidence of cancer in Poland.

## DISCUSSION

### DIETARY MISTAKES STIMULATING THE DEVELOPMENT OF CANCER IN POLAND

Some of the main reasons for the increased incidence of cancer are dietary errors. These include excessive consumption of industrially processed food products. Such products contain significant amounts of preservatives that, in stimulating the production of free radicals, damage the genetic material of cells and thus lead to cancer transformation (*Valko et al. 2006*). Mutations in the genome are very often also caused by toxic factors in the products themselves; such products would include those with an excessive content of nitrogen compounds (N-nitro compounds, nitrates and nitrites) from chemical fertilizers. This particularly dangerous phenomenon concerns the reduction of intestinal nitrates to nitrites and oxides under the influence of intestinal bacteria, which may result in carcinogenic nitrosamines (*Hamra et al, 2015*). Improper processing of food products, as in processes of smoking, grilling or frying of relatively long duration, can be a source of carcinogenic heterocyclic amines and polycyclic aromatic hydrocarbons that easily penetrate into food (*Moorthy et al., 2015*). One of the great dietary errors is the consumption of stale foods. Such foods may contain shreds of mushrooms from the *Aspergillus* family that are the source of carcinogenic aflatoxins. Consumption of some products in excess may cause the development of many diseases, including cancers. One example of such products is alcohol, which in excess can destroy mucous membranes of the respiratory and digestive tracts, thus enabling the toxic effects of carcinogens to manifest themselves in the associated tissues (*Varela-Rey et al, 2013*). Excessive fat intake affects the proliferation of cells that have undergone cellular transformation, which speeds up the development of cancer (*Park et al, 2018*). The increased amount of

animal protein consumed, e.g. in red meat, which is subjected to thermal treatment, also contributes to the formation of carcinogenic changes and excessive amounts of free radicals (Yen et al, 2018). Consumption of excess table salt affects the mucous membrane of the stomach and intestines, which increases its permeability also for harmful substances (D'Elia et al, 2014). The study also suggests that total amount of fiber in the diet is a strong protecting factor against colorectal cancer. Moreover, soluble and insoluble fiber consumption is in inverse relationship to the incidence of colorectal and colon cancer (Song et al, 2015).

### NUTRIENTS REDUCING THE INCIDENCE OF CANCER

Natural factors that strengthen the body's immunity are physical activity, optimal sleep, and a proper diet. Such a diet should contain the right amount of high-value proteins, polyunsaturated fatty acids, vitamins with antioxidant activity, flavonoids, minerals and probiotics (Kaledkiewicz and Lange, 2013). Among the food ingredients that reduce the risk of cancer are those compounds with a strong antioxidant effect. However, it should be noted that too high a concentration of antioxidants in the diet may result in their role's being reversed, with the result that the protective substances become oxidants, thus contributing to serious disease symptoms (Bast and Haenen, 2002). Antioxidants behaving in this way include vitamins with properties that inactivate free radicals, e.g. vitamins C, E, D, B<sub>12</sub> and folic acid. The strongest antioxidant activity among these vitamins is obtained from ascorbic acid (vitamin C), which increases cellular immunity and thus reduces the incidence of cancer. It can also effectively inhibit the formation of carcinogens such as nitrosamines contained in nitrite-conserved foods. It inhibits nucleic acid oxidation, thus preventing DNA damage and providing genome stability (Kaput and Rodriguez, 2004). Vitamin E, as a component of phospholipids that build cell membranes and blood plasma lipoproteins, protects against the peroxidation of polyunsaturated fatty acids and interacts with vitamin C in inhibiting the formation of nitrosamines. It is a powerful antioxidant and, like vitamin C, inhibits the oxidation of nucleobases, thereby preventing DNA damage leading to, for example, the formation of colon cancer (Kaput and Rodriguez, 2004). An important role in inhibiting cancer cell proliferation, by regulating growth and differentiation, is played by vitamin D (Jacobs et al, 2005). Research by Peters et al. (2001) confirmed a reduction in the risk of colorectal cancer by 26% when there was an increase in vitamin D concentration in serum of 10 ng/ml. Vitamin D is also a stimulator of calcium binding protein biosynthesis,

thanks to which a larger amount of this element is absorbed in the intestine. Vitamin B<sub>12</sub> is involved in cell metabolic processes and protects against DNA strand damage (Xiao et al, 2014).

An important group of factors that reduce the incidence of cancer is the carotenoids, which include  $\beta$ -carotene, lycopene, lutein, canthaxanthin and zeaxanthin. It is a group of organic chemical compounds (unsaturated hydrocarbons) that occur in chloroplasts and chromatophores of plant cells, e.g. vegetables and fruits, giving them the colors yellow, red, and orange. Carotenoids are powerful antioxidants. They stimulate the immune system of the body, inhibit cell proliferation, capture free radicals, inhibit mutagenesis in bacterial cells, inhibit chemically induced neoplastic processes, protect cells from UV radiation, and protect cells against neoplastic transformation. In addition, they dissolve in fats, protecting unsaturated fatty acids against oxidation. The strongest antioxidant ability is demonstrated by lycopene. Its activity consists in preventing the oxidation of LDL lipoproteins. Lycopene also has antimutagenic and anti-cancer activity, especially with regard to lung cancer (Nguyen and Schwatz, 1999, Pouchieu et al, 2014). Another important group of plant compounds showing antioxidant activity is the polyphenols, which include flavonoids, isoflavones, catechin phytoestrogens, stilbene and lignin. Anti-cancer activity of these compounds in food products consists in removing heavy metals, enhancing the action of other antioxidants (vitamins A and E), inhibiting and strengthening the activity of some enzymes responsible for immunological functions, and inhibiting carcinogenesis and cell proliferation. Examples of polyphenols that effectively counteract cancer are anthocyanins that stimulate phase II antioxidants and the expression of detoxification genes such as reductase, peroxidase and glutathione S-transferase (Singletary et al, 2007). In addition, anthocyanins, like other polyphenols, influence regulatory proteins, thus controlling various stages of the cell cycle, which effectively inhibits the proliferation of cancer cells (Zhang et al, 2005). According to Feng et al. (2007), the extract obtained from black cranberries and grapes containing anthocyanins and anthocyanidins activates the process of programmed cell death (apoptosis). The phenolic acids constituting a group of plant chemopreventive compounds are also significant. These include coffee, chlorogenic, ferulic, elagic and gallic acids. The phenolic acids have the ability to block the carcinogens formed as a result of metabolic transformations of some carcinogenic substances such as 4 - nitroquinoline - 1 oxides. The health-promoting properties of phenolic acids are also associated with their antioxidant properties (Andreassen et al, 2001). Another group of glycoside

compounds of vegetable origin in consumed foods that act as cytotoxic to cancer cells is the saponins. These compounds stimulate the body's immunity and inhibit the proliferation of cancer cells (Sisto et al, 2012). In plant foods, phytosterols have an important role to play in reducing the incidence of some cancers. These compounds inhibit cell proliferation, inhibit metastasis, induce apoptosis and remove free radicals (Jarosz and Sajor 2010, Pieszka and Pietras 2010). Regularly taken as part of a diet they are effective in lowering cholesterol levels, and thus reducing the risk of atherosclerosis and heart attack, by acting against teratogen and being anti-inflammatory.

Among the phytochemicals that protect against cancer are sulforaphane, isothiocyanates, and glucosinolates, which also help to prevent heart disease. They affect all stages of the neoplastic process, the strongest effect being observed at the initiation stage. This was confirmed by Chung et al. (2000), who showed that dietary supplementation with sulforaphane and phenethyl isothiocyanate (PEITC) results in reduction of neoplastic changes during the initiation phase and promotion of carcinogenesis. The protective properties of sulforaphane have been observed in all stages of carcinogenesis. This compound has been shown to block the binding site of carcinogens to the DNA molecule and prevent the expansion of neoplastic cells by interfering with their cellular processes involving proliferation, differentiation and apoptosis (Hakama, 1998).

Two essential elements in the diet that reduce the incidence of cancer are calcium and selenium. An appropriate calcium content in the body effectively inhibits the proliferation of cancer cells (Platz and Giovannucci, 1999). According to Fenech et al. (2005), high levels of calcium protect the genome from damage, due to calcium's ability to inhibit chromosomal cracking [2]. Selenium is a component of many enzymes with antioxidant activity. The anticancer activity of this element consists in blocking the synthesis of DNA in neoplastic cells. In addition, it inhibits the oxidation of lipids and removes free radicals. According to Fenech et al. (2005), a deficiency of it may cause hypomethylation of DNA, which may lead to inappropriate gene expression and to genetic instability.

An important nutrient that indirectly protects against cancer is fiber, which contains such substances as hemicelluloses, pectin, cellulose and lignin. The protective mechanism of fiber activity manifests itself in a number of ways. First of all, fiber increases bulk stool and dilutes fecal carcinogens, as well as shortening fecal transit time in the colon. In these ways the amount of contact carcinogens have with the colon epithelium is reduced (Bingham, 1990, Schatzkin 2000). Moreover, fiber binds to the bile

acid by which it optimizes the pH inside the colon. Excess, non-binding bile acid, can be a carcinogenic factor (Wakai et al. 2007, Bermudez-Soto et al. 2007). It is well known that the fiber is fermented inside the gut to the short-chain fatty acids. Some of them inhibit carcinogenesis (Goncalves and Marteau, 2013). It was also observed that a bigger dose of fiber can reduce hyperinsulinemia (Hawk et al., 2002). In other studies Trepel (2004), Willett (2000) and Augenlicht (1999) demonstrated the contribution of fiber to maintaining the balance between proliferation, differentiation and apoptosis of colon epithelial cells. The presence in the gastrointestinal tract of bacteria of the genus *Lactobacillus*, *Escherichia* and *Bifidobacterium* inhibits the growth and development of carcinogenic pathogens. The sources of beneficial bacterial strains are probiotics. Lactic bacteria have the ability to bind and degrade potential carcinogens, as well as to induce the activity of enzymes involved in their metabolizing (Fotiadis et al., 2008).

The presence of polyunsaturated fatty acids in the diet reduces the risk of cancer. These acids are part of phospholipid cell membranes, and their anti-cancer character results from their participation in the growth and differentiation of cells and their influence on the course of inflammatory processes and the body's immune response.

### THE IMPACT OF DIET ON REDUCING THE RISK OF CANCER INCIDENCE IN POLAND

One of the most important components of lifestyle is diet, which is an important factor in the formation of malignant tumors. It is estimated that 20 to 30% of all malignant tumors are diet-dependent cancers, in which nutritional factors have played an important role. Among these are cancer of the breast, the large intestine, the esophagus, the stomach, and the pancreas (Pudlo et al., 2015). An ideal nutritional model that may be used in the prevention of cancer has been sought. According to Tantamango-Bartley et al. (2013), the sort of vegetarian diet that reduces the risk of colon, breast and prostate cancer deserves special attention. This diet contains a variety of nutrients with anti-carcinogenic properties, eliminates the eating of red meat, and is conducive to the maintenance of a proper body weight. The advantages and limitations of using a vegetarian diet in health prophylaxis are also described extensively in the Polish literature (Mitek et al. 2013, Pilis et al. 2014). Among the diets recommended in the prevention of cancer is the so-called Mediterranean diet, containing a large amount of polyunsaturated fatty acids, oleic acid and polyphenols (Turati et al. 2018, Robles-Almazan et al. 2018).

The risk of malignant tumors associated with the digestive system, e.g. oral cancer, and cancers of the larynx, esophagus, stomach, pancreas, colon, etc., can be reduced by certain nutrients. Among them are such compounds as vitamin C, lycopene,  $\beta$ -carotene, caffeic acid, acid chlorogenic, carotenoids, flavonoids, terpenes, limonoids, coumarin, antioxidants - glutathione, phytosterols, folates, which are present in plant products. In the case of colorectal cancer, important are both calcium as a compound and lactic acid bacteria, both of which are found in dairy products (Ciborowska and Rudnicka 2012, Jarosz and Sajor 2013).

The World Cancer Research Fund and the American Institute for Cancer Research (Report, 2007) presented recommendations in the report designed to prevent the development of cancer. These recommendations are concerned with lifestyle, including care for physical condition, avoiding stimulants, and using the right diet. Of the ten most important recommendations more than half are concerned with proper nutrition. These recommendations include avoiding the consumption of sweetened beverages and high-energy food, especially highly processed food with a high content of fat and sugar. An important aspect of a healthy lifestyle is the consumption of the right amount of food tailored to the needs of each body in five portions each day, with appropriate proportions of vegetarian foods such as fruits, vegetables, whole grain cereals and seeds of legumes. It is important that normal body weight should be maintained, avoiding being overweight as well as being obese. It is particularly important to limit the consumption of red meat in the diet, especially when it has been subjected to smoking or salting, or when it contains preservatives. Recommendations to prevent the development of cancer also include reducing the consumption of alcohol and table salt, and the avoidance of spoiled food and dietary supplements.

### **NUTRITIONAL PATTERN IN THE MOST COMMON CANCER DISEASES IN POLAND**

The highest incidence of malignant tumors in Poland is found in the categories of lung, colorectal, breast and prostate cancer.

Lung cancer is the cause of the highest number of deaths among oncological patients in highly developed countries. According to the latest data published by the International Agency for Research on Cancer (IARC), in 2012 there were 1.8 million cases of lung cancer in the world, which constitutes 13% of all cancers (Report 2015). In Poland, lung cancer is the most common malignancy both in terms of the number of cases and in terms of the number of deaths. In men, it accounts for about 21% of cases and in women 9%. Lung cancer

is generated by such factors as occupational exposure to asbestos, certain metals (lead, cadmium, arsenic, nickel), silica, and ionizing radiation. However, the most common cause of this disease is active smoking. In EU countries every fifth case of lung cancer is a so-called tobacco-dependent cancer. Gender also affects the risk of lung cancer, with the incidence of cases among men being three times higher than among women. The vast majority of cases of malignant lung cancer occur after the age of 50 (Szlitkus, 2018). The lung is one of the organs in which a tumor can develop for a very long time without there being any obvious symptoms. It is because of the lack of early symptoms that detection tends to be delayed. Furthermore, although lung cancer is one of the most common cancers, no screening for it is undertaken. Up to this point, only retrospective analysis of the causes and consequences of the disease by means of epidemiological studies has been possible.

Meta-analysis conducted by Koutsokera et al. (2013) confirmed the positive effect of eating fruit and vegetables in the fight against lung cancer. A beneficial effect was also noted with regard to the presence of black tea, fish, and cheese in the diet. Among food products that contribute to the development of lung cancer, the authors cite red meat. Similar conclusions were presented by Hosseini et al. (2014), who conducted a study on a group of 242 patients with lung cancer and a 484-person control group. The results indicated that vegetables, fruits, and sunflower oil may be protective factors against the occurrence of lung cancer, while food products that increase the risk of this cancer are non-wholegrain bread, white rice, beef, liver, and dairy products. Similar results were found in Poland by Hawrysz et al. (2015). They showed that people with lung cancer, compared to those without that disease, consumed significantly less often ( $p=0.008$ ) products such as vegetables, wholegrain bread, milk, sour milk drinks (yoghurt, kefir, etc.) and fish dishes. People with cancer more often ( $p=0.02$ ) consumed canned foods, such as meat, fish, vegetables and fruit, as well as powdered soups and pre-cooked soups.

Colorectal cancer is the third most common cancer in the world in men (660,000 cases, 10%) and the second in women (570,000 cases, 9%). Almost 60% of cases occur in economically developed countries. In Poland, the incidence of colorectal cancer in 2013 was approximately 17,000, and since 1980 there has been more than a four-fold increase in the number of these cases. Most cases occur after the age of 50 (94%), while in men they are about one and a half to two times more frequent than in women (Zyski et al., 2014). In most cases, colon or rectal cancer is formed on the basis of benign adenomas (polyps). As a result of genetic mutations occurring in individual cells, the adenoma is transformed into cancer. In the case of colorectal cancer, a relationship between morbidity and diet is

indicated. According to many researchers, the risk of developing cancer of the large intestine increases with the excessive consumption of red meat, carbohydrates and animal fats combined with too low a supply of dietary fiber. The above thesis is confirmed by the meta-study of *Gonzalez and Riboli* (2010), which was based on a total of 519,978 participants. These authors showed the positive effect of dietary fiber on reducing the risk of developing colorectal cancer, and also the anticancer effects of consuming fish, calcium, vegetables and fruit. Among the nutrients mentioned as effectively reducing the risk of developing colorectal cancer were probiotics and prebiotics, folic acid, methionine, vitamin D, selenium, vitamin E, anthocyanins, procyanidins, phytoestrogens, isothiocyanates, curcumin and resveratrol (*Trepel* 2004, *Kunnumakkara et al.* 2009, *Barone et al.* 2008, *Talalay et al.* 2003).

Prostate cancer is one of the most commonly diagnosed malignant tumors among men. The incidence of prostate cancer is increasing and becoming an increasingly serious medical problem in the world. The main risk factors for developing prostate cancer are old age, genetic determinants, a diet high in saturated fats, and heavy metal poisoning. The disease usually develops asymptotically, and the emerging symptoms indicate its advanced stage (*Twardak et al.* 2015). In Poland, prostate cancer is ranked second in terms of cancer incidence in men. The number of new cases is constantly increasing. In a recent year, about 10,900 new cases were diagnosed (*Torre et al.*, 2012). The increased risk of prostate cancer is positively correlated with a high intake of proteins contained in dairy products (35 g/day) and calcium from dairy products (*Gonzalez and Riboli* 2010, *Allen et al.* 2008). A food product that reduces the risk of prostate cancer is fish. It is recommended to consume it more often than three times a week (*Khan et al.*, 2010). Likely food products containing lycopene, belonging to the carotenoids, show a protective effect against prostate cancer. Food sources of lycopene are tomatoes, papaya, watermelons, pink grapefruits, peaches, wild rose and their preparations (pastes, purees, concentrates, juices) (*Wawrzyniak et al.* 2005).

Breast cancer is the most common malignant cancer in women in Poland. It is also the second highest, after lung cancer, as the cause of deaths attributed to malignant tumors among women. As reported by the National Cancer Registry, the number of cases exceeds 16,500 cases per year (*Jassem and Krzakowski*, 2014). The immediate cause of breast cancer is not known; however, a group of independent risk factors has been identified. These include age (80% of breast cancers occur after 50 years of age), geographical location (high-risk groups inhabit highly developed countries), increased exposure to endogenous and exogenous

estrogens (early menses before 11 years of age, menopause after age 54, childlessness), first birth after the age of 40), and genetic factors (*Dumitrescu and Cotarla* 2005, *Hulka and Moorman* 2001). Research shows that the consumption of excessive amounts of red meat (pork, beef and mutton) as well as of processed meat is associated with an increased risk of breast cancer, especially in postmenopausal women (*Taylor et al.* 2007, *Eunyoung et al.* 2006, *Ferrucci et al.* 2009). According to *Gonzalez and Riboli* (2010), there is a positive correlation between the incidence of breast cancer and a high content of saturated fat in the diet. Reducing the fat content by following a low-energetic diet serves to reduce the level of estrogens in the blood serum, the too high concentration of which may contribute to the development of breast cancer (*Yager and Davidson*, 2006). In addition, *Gonzalez and Riboli* (2010) are of the opinion that there are no reports that fruits and vegetables would reduce the risk of breast cancer. The observation carried out by *Kruk* (2006) contradicts this thesis. According to the author, the frequent eating of fruits and vegetables can reduce the risk of breast cancer. Of particular importance in cancer chemoprevention are cruciferous vegetables (white cabbage, red cabbage, Chinese broccoli, Italian cauliflower, broccoli, Brussels sprouts, radishes, rapeseed) (*Beliveau and Gingras*, 2011).

## CONCLUSIONS

Nowadays, neoplastic diseases are the most common diseases of civilization, affecting both women and men regardless of their age. The incidence of cancer in the world and in Poland is constantly growing. In Poland, neoplastic diseases currently account for approximately 20% of all deaths, including about 40% of deaths in women aged 45 to 65 and 30% of deaths in men in the same age range. The growth rate of the number of malignant tumors in Poland is much higher than the growth rate of the population and is among the highest in Europe (*Didkowska et al.* 2017). The increase in the number of these diseases and the deaths caused by them in Poland can be attributed to five main causes: population growth, changes in the age structure of the population consisting in an increase in the number of age groups with particularly high incidence, insufficiently fast changes in pro-health attitudes (e.g. with regard to smoking and alcohol consumption), poor quality of nutrition, and slow, and unsatisfactory improvement in the early diagnosis of cancer. Whereas the average cancer cure rate in Poland for both sexes is 30%, and in the Scandinavian and some West European countries it is 40%, in the USA it is 50% (<http://www.puo.pl/program-walki-z-rakiem/narodowy-program-zwalczania-chorob-nowotworowych/epidemiologia>).

Most of the tumors are the result of the effects of lifestyle and the state of the natural environment. Lifestyle means, among other things, but most importantly in this context, physical activity and a properly balanced diet. It is estimated that approximately 20 to 30% of all malignant tumors are diet-dependent cancers, in the development of which nutritional factors are significant (Kushi et al., 2006). Overeating is an extremely dangerous phenomenon that generates the risk of obesity, which is the main factor causing an increase in the incidence of malignant tumors. The number of obese people is increasing in Poland, especially in the 35 to 64 age group. Overweight and obesity are associated with an increased risk of developing many cancers, such as breast cancer in postmenopausal women, colon cancer, endometrial cancer, adenoma and esophageal cancer. Excessive supply of energy components and low physical activity cause an increase in body fat, which significantly affects the metabolism of estrogen in women, which may stimulate the development of breast cancer (Pudlo et al. 2015). Too much processed, high-calorie food, saturated with preservatives, first of all burdens the body's systems, particularly the digestive, circulatory and respiratory, and then leads to oncological disorders. It is reasonable to conclude that diet plays a major role in the development of more than a third of all cancer cases. There are several well-documented links between diet and the causes of cancer. One of the diets that reduce the risk of cancer is the Mediterranean diet. It is characterized by increased consumption of vegetables, fruits, oil, and fish and by limited consumption of red meat. The diet contains the majority of anti-inflammatory and antioxidant nutrients (phytochemicals and *omega-3* acids), which reduce the risk of cancer. The Mediterranean diet is particularly beneficial for reducing the incidence of prostate cancer and colorectal cancer (Pudlo et al., 2015).

Forecasts for the coming years, which show an increased incidence of cancer in Poland, demonstrate the need for an increased awareness of the role of diet in the prevention of morbidity. Among the types of cancer most commonly afflicting Poles are lung cancer, associated mainly with smoking, and colorectal cancer. Colon cancer is one of the cancers most highly affected by genetic factors, but its incidence is increased by inappropriate lifestyle choices, in particular a poor diet, especially when it contains very little fiber. Extremely important in the context of cancer prevention is awareness of the type of food consumed, its source, its processing, and its energy value. Research shows that people with a higher level of knowledge about the prevention of cancer are taking lifestyle decisions that are more beneficial to their health.

Lack of awareness regarding dietary cancer prevention is likely to be a major factor in the steady increase that has been predicted in the incidence of these diseases. Running programs of nutritional education especially for children and adolescents may help to reduce the incidence of food-dependent cancers in Poland.

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## FOOD GROUPS IN DIETARY PREVENTION OF TYPE 2 DIABETES

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### ABSTRACT

According to the World Health Organization diabetes will be the seventh leading cause of death worldwide in 2030. Majority of diabetic patients suffer from type 2 diabetes (T2DM), which is mostly avoidable. The most important modifiable risk factors of type 2 diabetes are: overweight and obesity, improper diet, sedentary lifestyle and tobacco smoking. Even in prediabetic state, improving diet and physical activity can slow down or even stop progression to diabetes. In the view of health burden of diabetes it is essential to thoroughly investigate the risk factors and develop more specific preventive strategies. Recently published studies focus on food groups rather than individual products to assess the link between nutrition and risk of type 2 diabetes. Identifying food groups of possible beneficial and deleterious effect on the risk of type 2 diabetes could facilitate the dietary counselling. The aim of the overview is to summarize the possible association between consumption of food groups on the risk of type 2 diabetes on the basis of available literature. Observations from studies and meta-analyses indicate on an inverse association between consumption of fresh vegetables and fruit, whole grains, lean dairy, fish, nuts and the risk of type 2 diabetes. Food groups that seemed to increase the risk of type 2 diabetes are: red and processed meat, refined grains, sugar-sweetened beverages. It is important to note, that no individual nutrients, but diverse dietary pattern, composed of every recommended food group in adequate amounts can contribute to healthy lifestyle and T2DM prevention.

**Key words:** *diabetes, diet, prevention, risk of diabetes, dietary prevention of diabetes*

### STRESZCZENIE

Według Światowej Organizacji Zdrowia (WHO) do 2030 roku cukrzyca stanie się siódmą z kolei przyczyną zgonów na świecie. Większość pacjentów cierpi na cukrzycę typu 2, której podłoże jest w dużej mierze modyfikowalne. Najważniejszymi modyfikowalnymi czynnikami ryzyka cukrzycy są: nadwaga i otyłość, nieprawidłowa dieta, brak aktywności fizycznej oraz palenie tytoniu. Wprowadzenie interwencji w zakresie poprawy sposobu żywienia oraz zwiększenia aktywności fizycznej wśród pacjentów ze stanem przedcukrzycowym może spowolnić lub nawet zatrzymać progresję do pełnoobjawowej cukrzycy typu 2. Z powodu ogromnego zagrożenia dla zdrowia publicznego, którego przyczyną jest stały wzrost zachorowań na cukrzycę, istnieje konieczność badania czynników ryzyka w celu opracowania skutecznych programów zdrowotnych. Niedawno publikowane badania analizujące związek pomiędzy żywieniem a cukrzycą typu 2, skupiają się na grupach produktów, a nie na pojedynczych składnikach pokarmowych. Identyfikacja korzystnych oraz potencjalnie szkodliwych grup produktów wpływających na ryzyko cukrzycy typu 2 może okazać się bardzo pomocna w poradnictwie zdrowotnym. Celem artykułu przeglądowego jest podsumowanie zależności pomiędzy spożywaniem poszczególnych grup produktów a ryzykiem cukrzycy typu 2 w świetle aktualnej literatury naukowej. Do grup produktów, które w badaniach oraz meta-analizach powiązane są z niższym ryzykiem cukrzycy typu 2 należą: warzywa i owoce, pełnoziarniste produkty zbożowe, chudy nabiał, ryby oraz orzechy. Do grup produktów, które powiązane są z wyższym ryzykiem cukrzycy typu 2 należą: czerwone oraz przetworzone mięso, produkty zbożowe z oczyszczonego ziarna, słodzone napoje. Należy zaznaczyć, że nie pojedyncze składniki pokarmowe lecz zróżnicowana dieta, składająca się z zalecanych grup produktów w odpowiednich ilościach przyczynia się do prewencji cukrzycy typu 2.

**Słowa kluczowe:** *cukrzyca, dieta, zapobieganie cukrzycy, ryzyko cukrzycy*

## INTRODUCTION

According to the World Health Organization (WHO), the most important modifiable risk factors of type 2 diabetes are: overweight and obesity, improper diet, sedentary lifestyle and tobacco smoking[1]. Recently published meta-analysis focus on food groups rather than individual products to assess the link between nutrition and risk of type 2 diabetes development[2]. According to the WHO improper diet is responsible for 4.6% of disability-adjusted life years (DALY), whereas overweight and sedentary lifestyle for next 3.7% and 1.4%, respectively[3]. Prevalence of diabetes increased over two-fold since the 80's of XX century, from 4.6% of adult population in 1980 to 8.5% in 2014 [1]. Diabetes caused approximately 1.6 mln deaths worldwide in 2015, but it is estimated that high blood glucose could contribute to next 2.2 mln deaths related to i.e. cardiovascular diseases[1]. Impaired fasting glucose and impaired glucose tolerance preceding full-symptomatic type II diabetes are regarded independent risk factors for cardiovascular diseases[4], although in recently published meta-analyses this association is not as strong as in the case of full-symptomatic diabetes[5]. The conditions of impaired fasting glucose or impaired glucose tolerance don't necessarily mean inevitable progression to type II diabetes. Despite present disorders of carbohydrate metabolism, improving diet and physical activity can slow down or even stop progression to diabetes[6]. In the view of health burden of diabetes it is essential to thoroughly investigate the risk factors and develop more specific preventive strategies. Identifying food groups of possible beneficial and deleterious effect on the risk of type 2 diabetes could facilitate the dietary counselling. Literature databases including Scopus (<https://www.scopus.com>) and PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/>) were searched. Search terms used: "type 2 diabetes" OR "diabetes" OR "hyperglycemia" and terms related to food groups ("cereals", "grain", "vegetables", "fruit", "dairy", "fish", "meat", "red meat", "processed meat", "eggs", "poultry", "fats", "oil", "nuts", "sugar-sweetened beverages"). Search was limited to the literature in English language. Additionally, the references of withdrawn articles were searched. If available, randomized studies, prospective and cohort studies in human population, published no earlier than in 2008 were prioritized. Well-conducted meta-analyses were also included in the search. The aim of hereby overview is to summarize the possible association between consumption of individual food groups on the risk of type 2 diabetes on the basis of available literature.

## Cereals

Dietary guidelines for diabetic patients [7], recommend increasing the consumption of whole grain products at the expense of refined grains. Whole grains in the contrary to refined grains are rich source of dietary fiber, resistant starch and various vitamins and minerals. Meta-analysis of 17 cohort studies performed by Yao et al. [8] indicates that increased consumption of dietary fiber decreases the risk of type 2 diabetes. According to Wirström et al.[9] consumption of whole-grain products decreases the risk of prediabetes. Chanson-Rolle et al.[10] in meta-analysis of prospective studies estimated that increasing the intake of whole-grain products up to 45 g/d would lower the risk of type 2 diabetes by 20%. As a matter of fact, the consumption of whole-grain products in so-called "western diet" is rather low: in the USA 72% of Americans, at the age of 19-50 years and 66% of those at the age of 50 years and older consume less than 0.6 serving (about 10.5g/d) of whole-grain products daily[11]. Meta-analysis conducted by Nettleton et al. [12] concluded that every additional serving of whole-grain products daily is associated with lower glucose concentration by 0.019 units and insulin concentration by 0.021 units. It is speculated that not only resistant starch and fiber present in whole-grain products are responsible for lowering the risk of type 2 diabetes, but also other compounds, such as: phytic acid, magnesium, zinc, calcium, selenium, tocopherols, phenolic acids, flavonoids, betaine, inositols and saponins[13]. It has been observed in human studies, that resistant starch improves glycemic control, but the exact mechanism is still an object of debate. Resistant starch, unlike regular starch, is not susceptible to digestion in stomach and small intestine, but is fermented by bacteria when it reaches large colon [14]. The main products of resistant starch's breakdown are short-chained fatty acids (SCFA), such as acetate, propionate and butyrate. Products containing resistant starch are not only slowly digested, which leads to slower glucose release, but it is speculated that also SCFA, as a product of fermentation, influence glucose homeostasis in liver and muscles[15].

Dietary carbohydrates have the largest effect on postprandial glucose among macronutrients. Several decades ago the concept of Glycemic Index (GI) was introduced to rank the foods according to their postprandial glucose response[16]. Glycemic response after glucose consumption is considered reference value and equals a GI of 100. Soon after the concept of Glycemic Load (GL) was established, which combines the GI and amount of carbohydrates in the product. Glycemic response after consumption of carbohydrate product can be differentiated i.a. by starch composition, content of dietary fiber, simple

sugars, protein and fat content, processing, time of storage and harvest[17]. Whole-grain cereals, like rye bread, oatmeal, durum pasta, brown rice have low GI (<55), which reflects also their slower rate of digestion and absorption; whereas products of refined wheat, white rice, confectionery have high GI (>70)[18], which reflects their rapid digestion and absorption. According to study by *Bhupathiraju* et al.[19], who analyzed data from three large prospective cohort studies, participants who consumed diets of high GI or GL and low cereal fiber had 40% higher risk of T2DM than those whose diets were characterized by low GI, GL and high fiber. On the other hand, results from other studies focusing on association between GI, GL and risk of type 2 diabetes are inconsistent. It is speculated that the association can be gender-specific. In studies in women, there was observed that low-GI diet was associated with lower risk of type 2 diabetes [20, 21], whereas in large randomized study in men GI or GL were not associated with type 2 diabetes risk [22]. Although there is no global consensus on dietary guidelines in diabetes management, there are evidence from randomized controlled trials that diabetic patients can benefit from low-GI diets. In study by *Jenkins* et al. [23] low-GI diet over 6-month period in type 2 diabetic participants resulted in lower HbA1c levels and higher HDL levels in blood. In randomized study by *Gomes* et al. [24], low-GI diet over 1-month period in type 2 diabetic participants resulted in slightly reduced inflammatory response (by lower levels of IL-6 mRNA and TNF- $\alpha$  mRNA expressions) and reduced body fat. Randomized study by *Ma* et al.[25] also indicates that low-GI diet can be an alternative to American Diabetic Association (ADA) dietary guidelines in diabetes management, as it was just as good in controlling HbA1c levels with concomitant less diabetic medication than in participants with ADA diet.

### Dairy products

Dairy is a vast group of products and diverse in composition and nutritional value. All dairy products derive from milk. According to the meta-analysis conducted by *Tong* et al. [26], participants, who were characterized by the highest consumption of milk and dairy products had lower risk of the development of type 2 diabetes by 14% in comparison to those participants, who consumed less dairy products. The same authors concluded that inverse correlation between consumption of dairy products and risk of type 2 diabetes, was only observed in the case of skimmed milk and low-fat dairy products – such association was not confirmed in the case of full-fat dairy products. It is speculated that high content of calcium and vitamin D are responsible for lowering the risk of type

2 diabetes in mechanism of modulating the function of pancreatic *beta*-cells, increasing insulin sensitivity and decreasing systematic inflammation by influencing cytokine excretion [27]. On the other hand, in Women's Health Study [28], the researchers observed the inverse association between the consumption of dairy products and risk of type 2 diabetes, independently from other factors, such as: intake of vitamin D, calcium and magnesium. It is speculated that not only vitamin D and calcium, but also other nutrients present in milk and dairy products play a role in regulation of carbohydrate metabolism, e.g. dairy proteins. There are some evidence, that whey protein can be associated with improved insulin sensitivity [29]. In study by *Ryan* et al., intraduodenal infusion of whey proteins, in loads resembling natural pace, resulted in increased release of cholecystokinin and glucagon-like peptide 1 (GLP-1) and increased pyloric motility[30]. According to the findings from Nurse's Health Study II [31], increased intake of dairy products in developmental age in women was associated with decreased risk of type 2 diabetes in middle age. In Epic-InterAct Study[32] the consumption of total dairy was not associated with risk of type 2 diabetes, but if adjusted for types of dairy products, the consumption of fermented dairy products (cheese, yoghurt, thick fermented milk) was in fact inversely associated with risk of type 2 diabetes. Similar association was observed in three large US cohort studies. Although the consumption of total dairy was not associated with risk of type 2 diabetes, there was observed a significant inverse association between consumption of yoghurt and risk of T2DM [33]. Same authors concluded that every additional serving of yoghurt per day was associated with 18% lower risk of T2DM. Yoghurt is abundant source not only of calcium, magnesium and vitamin D, but also conjugated linoleic acid and probiotics. In addition, fermentation increases dietary value of yoghurt in comparison to milk, as fermentation can improve the bioavailability of some micronutrients, like calcium, magnesium and vit. B12 [34]. It is speculated that probiotics can play an important role in modulating the risk of T2DM. In double-blind, randomized study by *Kassaian* et al.[35], the group supplemented with symbiotic (a mix of probiotic and prebiotic) in comparison to placebo, was characterized by improved fasting plasma glucose and insulin levels, improved glycated hemoglobin levels and insulin sensitivity (assessed by HOMA-IR index). The exact mechanism underlying the association between consumption of probiotics and glycemic control remain unclear. The composition of macro- and micronutrients vary from one dairy product to another. Analysis of impact of total dairy on the risk could be misleading. Dietary guidelines emphasizes that not only healthy people, but also diabetic patients should consume 2-3 servings

of low-fat dairy products, like skimmed milk, yoghurt and other fermented dairy products [7, 36, 37].

### **Meat, fish, eggs**

According to dietary guidelines, a food group including meat, fish and eggs (MF&E) shouldn't be consumed in amounts exceeding 1 serving per day (100-150 g) [36, 37]. Additionally, it is advised, that 1-2 times a week, a serving of MF&E should be replaced by a serving of legumes. MF&E are an abundant source of highly bioavailable protein, iron and vitamin B12 [36]. Dietary guidelines for management of adults with diabetes by American Diabetes Association (ADA) emphasizes, that recommendations for intake of MF&E for diabetic patients don't differ significantly from recommendations for general population. Diabetic patients are advised to choose leaner meats (e.g. poultry) over red meat and to choose leaner protein alternatives more often (e.g. legumes) [38]. In the study by *Ke et al.*, higher intake of protein from plant sources (e.g. legumes) was associated with decreased risk of T2DM, on the contrary to higher intake of protein from animal sources (e.g. red meat) [39]. Same authors emphasized the importance of focusing on dietary patterns, rather than individual macronutrients. According to *Feskens et al.* [40] the intake of red and processed meat significantly increases the risk of type 2 diabetes. In the randomized cross-over study conducted by *Kim et al.* [41] among overweight participants; participants with impaired fasting glucose or impaired glucose tolerance; the diet rich in red and processed meat and refined grains applied for 4 weeks, significantly increased insulin resistance in comparison to the diet rich in whole-grain products, skimmed dairy products, legumes and nuts. It was estimated that improving dietary habits by the patients at risk of developing of type 2 diabetes was associated with 50% increase of insulin sensitivity after merely the month of diet [41]. Researchers didn't observe changes in insulin sensitivity after implementing the diet in healthy subjects (without disorder of carbohydrate metabolism or insulin resistance). In the cross-sectional study by *Zelber-Sagi et al.* [42] total consumption of meat, but particularly red and processed meat was associated not only with increased risk of insulin resistance, but also non-alcoholic fatty liver disease, even after adjusting the analysis to Saturated Fatty Acids (SFA) and cholesterol content. Meat is a source of SFA and dietary cholesterol, but neither total dietary SFA [43], nor dietary cholesterol [44] have been associated with increased risk of T2DM in recent studies. Those conclusions were contrary to results obtained in the study by *Guess et al.* [45] in which researchers compared the intake of fatty acids between normoglycaemic participants,

prediabetes participants and participants with type 2 diabetes, and provided observation that increased consumption of saturated fatty acids was associated not only with higher risk of impaired fasting glucose and higher concentration of glucose after 2h in OGTT (Oral Glucose Tolerance Test), but also with insulin resistance. Moreover, higher consumption of trans-unsaturated fatty acids increases the risk of impaired glucose tolerance after 2 h in OGTT, while increased consumption of polyunsaturated fatty acids (regardless of type) improves glucose tolerance, as well as the peripheral insulin sensitivity. There is a possibility that not the individual types of fatty acids, but in fact their dietary sources and other components can play a major role in modulating the risk of T2DM. Study by *Wanders et al.* [46] provided no association between intake of SFA, MUFA, PUFA and trans unsaturated fatty acids (TFA) and markers of T2DM (fasting and postprandial blood glucose and insulin, HOMA-IR and HOMA-B). Interestingly, stratification by dietary sources revealed that fatty acids originating from meat were positively associated with insulin resistance and secretion, but no such association was observed in case of fatty acids originating from dairy and plant sources, providing a conclusion that association between fatty acids and risk of T2DM may be dependent on dietary sources [46]. Results from Framingham Offspring Study indicated, that although total dietary cholesterol was not associated with increased risk of T2DM or impaired fasting glucose, in contrast, higher intake of fish, whole-grain products and fiber were associated with lower risk of T2DM [44]. Red and processed meat are also a source of heme iron, heterocyclic amines (HCAs) and nitrates, the excess of which can play role in deterioration of glucose metabolism [47], though in case of HCAs and nitrates, the evidence come mostly from animal studies [48, 49]. The way, the meat is prepared also play a role in modulating the risk of T2DM. Processing meat (both red meat and chicken) on the open-flame and/or in high temperatures, like grilling/barbecuing/broiling was associated with increased risk of T2DM [50]. According to the findings from 25 years of observation in prospective study CARDIA [51] consumption of n-3 polyunsaturated fatty acids and fish (excluding fried fish) was associated with significantly lower risk of metabolic syndrome, impaired fasting glucose and impaired glucose tolerance. In Norwegian NOWAC study [52] researchers observed inverse association between consumption of lean fish and risk of type 2 diabetes. Interestingly, in literature, studies focused mostly on fatty saltwater fish, as richer source of n-3 polyunsaturated fatty acids than lean fish, and their protective role on the risk of metabolic syndrome. It is speculated, that lower content of contamination in lean fish, including heavy metals and higher content

of taurine (amino acid of potentially beneficial effect on the risk of metabolic syndrome and type 2 diabetes) than fatty saltwater fish can play role in understanding this association [52]. Interestingly, increasing fish consumption in the diet can be beneficial for management of T2DM complications. According to *Chua et al.* [53], increased fish consumption was inversely associated with severity of diabetic retinopathy, moreover, increased consumption of fish among diabetic patients without retinopathy was associated with wider retinal vascular caliber. Fish are an important dietary source of  $\omega$ -3 polyunsaturated fatty acids ( $\omega$ -3 PUFA) [36]. Increased consumption of  $\omega$ -3 PUFA with the diet, but also lower ratio of  $\omega$ -6/ $\omega$ -3 fatty acids in the diet has been associated with lower risk of T2DM [54]. Moreover, in meta-analysis of randomized controlled trials by *O'Mahoney et al.*, higher intake of  $\omega$ -3 PUFA was associated not only with lower HbA1c levels, but also with lower levels of TNF- $\alpha$  and IL-6, inflammatory cytokines, which can contribute to vascular complications in T2DM [55]. According to the mentioned CARDIA study [51], increased consumption of n-3 PUFA was associated with lower risk of impaired fasting glucose and impaired glucose tolerance. On the contrary, *Wu et al.* [56] in a meta-analysis of 16 observational studies did not confirm neither positive nor negative influence of  $\omega$ -3 PUFA (in this case combination of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) on the risk of T2DM. Similarly, more recent meta-analysis failed to provide significant association between consumption of  $\omega$ -3 PUFA and levels of HbA1c [57]. It is possible that influence of n-3 PUFA on risk of type 2 diabetes can be dependent of sex. According to a meta-analysis conducted by *Abbott et al.* [58], the consumption of n-3 PUFA was associated with lower risk of insulin resistance, but only in women, while in men such association was not observed.

Meta-analysis of prospective cohort studies conducted by *Tamez et al.* [59] concluded, that consumption of eggs is associated with higher risk of type 2 diabetes. On the other hand, the strongest correlation was observed in American cohort, but such association was not observed in other countries. Such observation could be explained by differences in composition of eggs between countries or other, country-specific factors in diet [59]. *Wallin et al.* [60] presented the same conclusion: during the Swedish cohort study (The Cohort of Swedish Men conducted in years 1998-2012 in group of 39 610 men) there was no association observed between consumption of eggs and risk of type 2 diabetes, but in conducted meta-analysis the association was observed only in cohorts from the USA.

## Fats/oils

Analyzing an influence of fat, as an independent food group, on carbohydrate metabolism is rather complicated, because of heterogeneity of fats and differences in metabolic effects of individual fatty acids. Dietary fats are defined as every lipid, of animal or plant origin, consumed with food [61]. Dietary fat can be introduced in visible form of oils, butter or lard or as a constituent of other products, like meat, dairy, eggs etc. Since the influence of fatty acids as constituents of meat, fish and eggs have been elaborated in previous paragraph, this section will be focusing on oils.

Vegetable oils, as a source of unsaturated fatty acids and vitamin E, are a recommended replacement for dietary sources of SFA, e.g. butter and lard, both in general population and diabetic patients [36–38]. Vegetable oils differ from one another regarding their composition and properties. Olive oil is a rich source not only of MUFA, but also bioactive compounds, like oleuropein and hydroxytyrosol, which have been hypothesized to have antihyperglycemic and antioxidant effect [62]. Oleuropein and hydroxytyrosol administered to diabetic rats were associated with decreased serum glucose and improvement of oxidative stress parameters [63]. Higher adherence to Mediterranean Diet, characteristic for high intake of olive oil, fish, fruit, vegetables and wholegrains has been associated with lower risk of metabolic syndrome, including impaired glucose metabolism [64]. Results from 22 years of observation in Nurses' Health Study indicate, that in women, increased consumption of olive oil was associated with lower risk of developing T2DM [65]. Rapeseed oil, which consists of 72.8% of MUFAs, 20.9% of PUFAs and only 6.3% of SFA [66], along with olive oil is recommended vegetable oil [36, 37]. In a small, but randomized study by *Nigam et al.* [67] in men with non-alcoholic fatty liver disease, participants were divided into three groups receiving daily over the period of 6-months: 1) olive oil; 2) rapeseed oil and 3) other commonly used oils (mostly safflower). Authors observed that in olive oil group in comparison to rapeseed oil group and control, fasting insulin levels and HOMA-IR were significantly lower. Moreover, while comparing the results pre- and post-intervention, authors observed that in rapeseed oil group, level of fasting blood glucose significantly decreased [67]. There are fewer studies focusing on association between risk of T2DM and consumption of n-3 PUFA from plant sources (predominantly with flaxseed oil) than from marine sources. According to *Wu et al.* [56] dietary consumption of  $\alpha$ -linolenic acid (ALA) is modestly associated with decreased risk of T2DM. The richest plant source of ALA is flaxseed oil [68]. In randomized, double-blind study by *Bloedon et*

al. [69], addition of flaxseed to the diet of participants, resulted in improved insulin sensitivity (HOMA-IR index lowered by 23.7%).

### Fruit and vegetables

Fruit and vegetables are considered some of the most healthy dietary products. Dietary guidelines recommend to consume at least 400 g of fruit and vegetables a day [37, 61]. Mediterranean diet, which is rich in mono- and polyunsaturated fatty acids, but also fruit and vegetables is considered highly effective in prevention of cardiovascular diseases and metabolic syndrome [64]. Both fruit and vegetables are not only the source of the dietary fiber, but also antioxidative vitamins, flavonoids and minerals, which can contribute to their beneficial effect [61]. In the study conducted by *Sotoudeh* et al. [70] dietary total antioxidant capacity (DTAC) was associated with lower risk of prediabetes and fruits and vegetables were the most prevalent sources of antioxidant compounds in the diet of analyzed participants. Oxidative stress is one of the possible factors contributing to deterioration of glucose metabolism. Diet rich in flavonoids and other polyphenols have been associated with decreased risk of T2DM [71]. According to meta-analysis conducted by *Wang* et al. [72], increased consumption of raw fruit and vegetables is associated with lower risk of type 2 diabetes. Other meta-analyses, such as one by *Shin* et al. [73] did not confirm the association between consumption of fruit and vegetables and fasting plasma glucose. In randomized study conducted by *Wallace* et al. [74] increased consumption of fruit and vegetables in diet of the obese patients did not significantly altered their insulin sensitivity (during the study the body mass of participants did not change). In the study by *Mamluk* et al. [75] overall data from NIH-AARP and EPIC Elderly studies showed no association between consumption of fruit and vegetables and incident T2DM. Same authors emphasize however, that there have been large discrepancies between results from cohorts, and in fact, when considering NIH-AARP study alone, there was a significant inverse association between increased intake of fruit and green leafy vegetables and risk of incident diabetes among elderly [75]. In a study by *Mursu* et al. [76] conducted in men, higher total consumption of fruit, vegetables and especially berries was associated with lower risk of T2DM after mean 19.2 years of follow-up. On the other hand, large prospective study conducted in Chinese women provided an observation, that high consumption of vegetables alone was associated with significantly lower risk of T2DM; for fruit authors found no such association [77]. Particular attention should be paid to legumes, like chickpeas, beans, soybean and lentils, which is a group of vegetables rich in protein and fiber, and characterized

by low GI. Evidence from PREDIMED Study [78] indicate, that participants characterized by highest consumption of legumes and lentils had significantly lower risk of developing type 2 diabetes after median 4.3 years of follow-up than participants, who were characterized by lowest consumption of legumes, even after adjusting the analysis for BMI and overall dietary pattern. In a meta-analysis by *Jia* et al. [79], higher consumption of cruciferous vegetables, but not citrus fruit was associated with significantly lower risk of T2DM. Authors speculated, that characteristic feature of cruciferous vegetables, content of isothiocyanates and indole-3-carbinol can play role in modulating risk of T2DM. As observed in animal studies, isothiocyanates may improve glucose tolerance and signaling [79].

### Sugar-sweetened beverages

According to *Singh* et al. [80] the consumption of sugar-sweetened beverages (SSB) in high- and upper middle income countries accounts for 0.51 and 0.80 serving/day, respectively (the average intake of SSB was the highest in the age groups of 20-39 years old exceeding 1 serving per/day). The availability of SSB between 1970 and 2005 increased by 19% in United States [81]. Meta-analysis of 11 prospective cohort studies performed by *Malik* et al. [82] indicates, that among participants who consumed beverages with added sugar in amounts of 1-2 servings per day, the risk of type 2 diabetes was higher by 26% in comparison to participants who consumed such beverages only occasionally (less than 1 serving per month). *Ma* et al. [83] in the analysis of 14 years of observations of Framingham Offspring Cohort study's participants, concluded that increased consumption of sweetened beverages was associated with an increased risk of prediabetes and insulin resistance by 46% on the contrary to participants, who did not consume such beverages. In the study conducted by *Anari* et al. [84] consumption of sugar-sweetened beverages was associated with 5-times greater risk of abdominal obesity in diabetic patients, which was associated with increased insulin resistance and increased risk of cardiovascular events. SSB are rich in sucrose or high-fructose corn syrup (HFCS). High consumption of fructose is associated with increased risk of metabolic disorders, increased deposition of fatty acids in the visceral tissue, insulin resistance and glucose metabolism disorders [85].

### Nuts

The association between consumption of nuts and seeds and the risk of type 2 diabetes is difficult to observe, as nuts and seeds differ from one another in terms of nutrients composition. Into this group we can

include tree nuts, like almonds, hazelnuts, walnuts, cashews, but also legume seeds, like peanuts.

Some studies found an inverse association between the consumption of nuts and risk of type 2 diabetes among adult women [86], but not men [87]. On the other hand, there are meta-analyses, which failed to find an association between nuts consumption and the risk of type 2 diabetes [88]. There are studies investigating the impact of nut consumption on the glycemic control. Meta-analysis of 12 randomized controlled trials [89] concluded that increased consumption of nuts was associated with better glycemic control in type 2 diabetic patients (median dose of 56g of nuts per day was associated with lower levels of HbA1c by 0.07% and lower fasting glucose level by 0.15 mmol/L). Consumption of nuts was associated with lower risk of cardiovascular diseases [90], presumably due to high content of beneficial mono- and polyunsaturated fatty acids as well as active non-nutritive compounds, like polyphenols, which improve oxidative stress and inflammation [91]. Since diabetes increases the risk of cardiovascular complications 2-4-fold [92], it is beneficial to include nuts in the diet. Results of NHANES study provided strong inverse association between consumption of walnuts and T2DM, but what's interesting, the effect was more profound in women than men [93]. Almonds are rich source of MUFA, PUFA, vit. E and minerals: magnesium, calcium, potassium [94]. Some studies show beneficial effect on glucose metabolism after the consumption of almonds: decrease in HbA1c levels [95], lower fasting insulin, fasting glucose and lower HOMA-IR index [96], whereas others fail to find an association between consumption of almonds and fasting glucose and insulin [97]. Walnuts, on the other hand, stand out from other nuts due to very high content of PUFAs (both n-6 and n-3 PUFAs). In two large prospective studies conducted in women in USA, consumption of walnuts was strongly inversely associated with the risk of T2DM, independently of BMI [98]. Peanuts are the richest source of protein among other nuts, they are also the source of MUFAs, PUFAs, potassium and magnesium [99]. In a study by Wien et al. [100] including peanuts into the diet of T2DM participants improved nutritional value of the diet, but did not significantly alter fasting glucose or HbA1c.

## CONCLUSION

There are observations from studies and meta-analyses of an inverse association between consumption of fresh vegetables and fruit, whole grains, lean dairy, fish, nuts and the risk of type 2 diabetes. Food groups that seemed to increase the risk of type 2 diabetes are: red and processed meat, refined grains, sugar-sweetened beverages. It is important to note, that no individual

nutrients, but diverse dietary pattern, composed of every recommended food group in adequate amounts can contribute to healthy lifestyle and T2DM prevention.

## List of abbreviations

**WHO**-World Health Organization; **DALY**-Disability Adjusted Life-Years; **T2DM**-Type 2 Diabetes Mellitus; **GI**-Glycemic Index; **GL**-Glycemic Load; **MF&E**- Meat, Fish and Eggs; **ADA**-American Diabetes Association; **OGTT**-Oral Glucose Tolerance Test; **SFA**-Saturated Fatty Acids; **MUFA**-Monounsaturated Fatty Acids; **PUFA**-Polyunsaturated Fatty Acids; **HCA**-Heterocyclic Amines; **SSB**-Sugar-sweetened beverages

## Ethics Approval and Consent for Participate

*Not applicable*

## Competing interest

*The authors declare no competing interest.*

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## QUANTITATIVE ASSESSMENT OF NUTRITION AND NUTRITIONAL STATUS OF PATIENTS WITH CELIAC DISEASE AGED 13–18

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### ABSTRACT

**Background.** Celiac disease is an autoimmune disease that affects about 1% of the European population and 0.3–1.3% of the world's population. The only method of treatment is introduction of a gluten-free diet.

**Objective.** The aim of the study was to assess the nutrition of adolescents with celiac disease and to assess their nutritional status.

**Materials and methods.** The study group comprised 24 patients with diagnosed celiac disease. The diagnosis was based on biopsy, serological tests and, in some cases, genetic tests. Anthropometric measurements included height, which was respectively 161.9 ±12.43 cm in boys and 163.6 ±9.03 cm in girls, and body weight oscillating between 56.55 ±16.24 kg for boys and 52.62 ±10.92 kg for girls. To assess the way of nutrition used an individually prepared questionnaire including an interview from the last 24 h. The menus were analyzed using the Dieta 5d program. The statistical analysis of the data was made using Statistica 12 program.

**Results.** Gluten-free diet contributes to the occurrence of caloric deficiencies up to 36%. It was found inadequate intake of dietary fiber, for girls 15.45 ±9.84 g and 14.41 ±4.73 g for boys. It has been observed too low intake of ingredients such as calcium (565.65 ±347.41 mg), magnesium (223.41 ±73.84 mg), vitamin D (1.34 ±1.28 µg) and E (5.05 ±2.32 mg) as well as potassium (2848.67 ±1132.07 mg), iron (7.62 ±2.05 mg), zinc (7.11 ±2.41 mg) and thiamine (0.87 ±0.38 mg). The ingredients such as riboflavin, niacin, pyridoxine, cobalamin, and vitamins C and A were consumed in the right amount.

**Conclusions.** Incorrectly used gluten-free diet may contribute to the recurrence of the disease. Chronic inadequate intake of fiber can lead to constipation. A deficiency of many nutrients can result in impaired development of the young organism such as anemia, growth retardation or osteoporosis.

**Key words:** celiac disease, gluten enteropathy, nutrition, nutritional status, teenagers, gluten-free diet

### STRESZCZENIE

**Wprowadzenie.** Celiakia należy do chorób autoimmunologicznych, która dotyka ok. 1% populacji Europy oraz 0,3–1,3% populacji światowej. Jedyną metodą leczenia jest zastosowanie diety bezglutenowej.

**Cel.** Celem badania była ocena sposobu żywienia nastolatków z chorobą trzewną oraz ocena ich stanu odżywienia.

**Materialy i metody.** Grupę badaną stanowiło 24 pacjentów ze zdiagnozowaną chorobą trzewną. Diagnozę postawiono na podstawie biopsji, badań serologicznych oraz w niektórych przypadkach badań genetycznych. Pomiar antropometryczny obejmowały wzrost, który wynosił odpowiednio 161,9 ±12,43 cm u chłopców oraz 163,6 ±9,03 cm u dziewcząt a także masę ciała oscylującą pomiędzy 56,55 ±16,24 kg u chłopców oraz 52,62 ±10,92 kg u dziewcząt. Do oceny sposobu żywienia wykorzystano indywidualnie przygotowaną ankietę obejmującą wywiad z ostatnich 24 godzin. Jadłospisy analizowano za pomocą programu dietetycznego Dieta 5d. Analizę statystyczną wykonano w programie Statistica 12.

**Wyniki.** Dieta bezglutenowa wprowadzała niedobory kaloryczne sięgające nawet 36%. Stwierdzono niedostateczne spożycie błonnika pokarmowego wynoszące dla dziewcząt 15,45 ±9,84 g oraz 14,41 ±4,73 g dla chłopców. Zaobserwowano zbyt niskie spożycie wapnia (565,65 ±347,41 mg), magnezu (223,41 ±73,84 mg), witamin D (1,34 ±1,28 µg) i E (5,05 ±2,32 mg) oraz kwasu foliowego (190,8 ±69,91 µg) a także potasu (2848,67 ±1132,07 mg), żelaza (7,62 ±2,05 mg), cynku (7,11 ±2,41 mg) i tiaminy (0,87 ±0,38 mg). W odpowiedniej ilości były spożywane takie składniki jak ryboflawina, niacyna, pirydoksyna, kobalamina oraz witaminy C i A.

**Wnioski.** Nieprawidłowo prowadzona dieta bezglutenowa może przyczynić się do wystąpienia nawrotów choroby. Przewlekłe niedostateczne spożycie błonnika może prowadzić do wystąpienia zaparć. Należałoby wdrożyć suplementację witaminy D, wapnia oraz magnezu a także wzbogacić dietę w foliany oraz witaminę E a także potas, żelazo i cynk. Niedobór wielu składników odżywczych może skutkować zaburzeniami rozwoju młodego organizmu takim jak niedokrwistość, zatrzymanie wzrostu czy osteoporoza.

**Słowa kluczowe:** celiakia, enteropatia glutenowa, żywienie, stan odżywienia, nastolatki, dieta bezglutenowa

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## INTRODUCTION

Celiac disease, also known as gluten enteropathy or celiac disease, is an autoimmune disorder of the small intestine with genetic background. It is associated with changes in the intestinal mucosa characterized by atrophy of the intestinal villi. This results in the occurrence of many deficiencies caused by a reduction in ability to absorb nutrients. The immune response is triggered in response to the protein - gluten fraction, and in particular to its prolamine - gliadin. Also prolamins contained in rye (secalins) and in barley (hordeins) and in oats (avenins) are responsible for causing an abnormal reaction. However, 90% oat is a safe crop for patients with celiac disease. Currently, the only treatment option is the introduction of a gluten-free diet [17, 40].

Celiac disease affects about 1% of the European population and the incidence is still increasing [18]. In Poland, no records of patients are kept, however, it is presumed that enteropathy may affect up to 1 in 100 people [21]. Over the years, celiac disease was considered a disease of childhood where the peak incidence at the age of 5, and today more often seen as a high incidence in adults aged 35-55 years [21]. Celiac disease twice as often occurs in women than in men [13]. Symptoms of the disease are closely related to both the patient's age and duration of the disease or symptoms from outside the digestive tract.

There are 4 types of celiac disease:

- Typical - especially in young children; villus atrophy is observed, whereas the symptoms mainly affect the gastrointestinal tract and are diarrhea and bloating [16];
- Atypical - it is diagnosed most often in adolescents, we also observe villus atrophy, and the prevailing symptoms are outside the gastrointestinal tract; often deficiencies of such elements as iron or vitamin B12 are noted, as well as co-occurring osteoporosis, chronic inflammation or infertility [35];
- Silent - characterized by asymptomatic course of the disease, however, as in the above forms, villus atrophy is also observed;
- Latent - normal intestinal mucosa and no symptoms of the disease, however, there is a probability of future celiac disease [16, 26].

In the course of enteropathy, symptoms such as growth deficiency or delayed development, as well as co-occurring liver diseases, are also observed. During the diagnosis of children, even 26-57% of them have an elevated level of aminotransferases [37]. Nonspecific symptoms also include neurological disorders and the occurrence of "brain fog", which is characterised by memory loss and decreased concentration [29].

Celiac diagnosis is based on specific serological tests, including antibodies against endomysium and anti-transglutaminase tissue [6, 15]. Serological tests are used not only for diagnosis but also for subsequent monitoring of compliance with a gluten-free diet [16]. The golden standard in the diagnosis of celiac disease is the biopsy [11]. During the biopsy, 4-5 samples are collected from several areas of the small intestine, thus determining the size of changes that have occurred in the mucosa. The severity of the symptoms will be the greater the larger intestinal area is affected. The *Marsh* scale is used for microscopic evaluation of collected specimens. This scale consists of 6 grades where 0 means no changes in the mucosa, while class 3 with subclasses abc associated with the presence of lesion [9]. Genetic tests for the presence of HLA DQ2 / 8 specific haplotypes for enteropathy are also used for diagnostics. Doing these tests, in certain cases, eg. the family load genotype, can prevent further tested [15]. Gluten-free diet counts as elimination diets. It mainly involves the conversion of common cereals - wheat, barley and rye to those that naturally do not contain harmful to the patients protein, which is gluten or to those from which it was removed through technological processes [24]. In the process of introducing a patient to a gluten-free diet, the patient should be appropriately educated as to preparing the dishes. Particular attention should be given to the possibility gluten contamination of the product during processing in the kitchen [17]. A gluten-free product is one in which the gluten content does not exceed 20 mg per kg of product or one that does not naturally contain this protein. A product with a very low gluten content is the one where the value of this protein does not exceed 100 mg per kg of product [4].

Recommendations regarding ingredients such as fats, carbohydrates and protein are consistent with those in a healthy diet model. Protein intake should be approx. 15% of the daily ration, and its main sources in the diet should be a dairy, meat, fish and legumes. The fat content in the diet should be up to 30%, while carbohydrates should be around 50%. To prevent possible deficiencies in the diet of patients, it is necessary to ensure the right amount of vegetables and fruits on the menu [34].

It was observed that inadequate consumption of vitamins, such as folic acid, cobalamin or pyridoxine is closely related to increased levels of homocysteine. Equating the state of intestinal mucosa, and the use of a gluten-free diet normalized homocysteine levels [22].

To enrich the diet of patients and prevent the occurrence of shortages, should include in the menu naturally gluten-free pseudo-grains, which include

amaranth, corn, millet, quinoa, tapioca, teff and rice. These cereals are the source, among others amino acids, calcium or B group vitamins [30].

Celiac disease is one of the most frequently occurring genetically determined diseases, current data suggest an increase in morbidity, especially among children and adolescents. The only method of treatment is the introduction of a strict gluten-free diet, which belongs to the elimination diets and if not properly carried out, can lead to numerous nutritional deficiencies. Children and adolescents are a group of patients in whom it is particularly important to ensure an adequate supply of nutrients to ensure adequate growth and development.

The aim of the work was to show through analysis of the nutrition and nutritional status of teenagers the biggest health risk that could result from the use of a diet eliminating gluten. In addition, the specific objectives included:

- analysis of the composition of menus and the way of feeding young people
- analysis of nutritional status by anthropometric methods

## MATERIAL AND METHODS

The study group consisted of 24 patients of the Gastroenterology Outpatient Clinic of the Independent Public Clinical Hospital No. 1. prof. *Tadeusz Sokolowski* of the Pomeranian Medical University in Szczecin. The inclusion criteria was based on disease-positive serology tests, intestinal biopsies (four-point) and in some cases genetic tests (DQ2 and DQ8 and DQ2.5). However, the exclusion criterion was age (below 10 and above 18 years of age). In the study group there were 14 girls and 10 boys. The average age of patients was  $15.3 \pm 1.45$  and  $14.6 \pm 1.43$ . Anthropometric measurements were also taken, including an increase of  $163.6 \pm 9.027$  cm in girls and  $161.9 \pm 12.43$  cm in boys, as well as a body weight of  $52.62 \pm 10.92$  kg for girls and  $56.55 \pm$  respectively.  $16.24$  kg for boys (Table 1). Anthropometric measurements were made by qualified hospital staff. The study was not a medical experiment, it was completely non-invasive, it was based on an interview, which was obtained by the approval of the PUM Bioethical Committee No. KB-0012/116/15. Interviews were carried out with the written consent and in the presence of parents.

Table 1. Characteristics of the studied group

	Girls (average +SD)	Boys (average +SD)	Average of the study group	p
Age (years)	$15.46 \pm 1.447$	$14.6 \pm 1.430$	$15.04 \pm 1.46$	0.217
Weight (kg)	$52.6 \pm 10.918$	$56.55 \pm 16.239$	$54.26 \pm 13.21$	0.485
Height (cm)	$163.6 \pm 9.027$	$161.9 \pm 12.432$	$162.92 \pm 10.36$	0.694
Body mass index (BMI)	$19.5 \pm 2.74$	$21.7 \pm 3.63$	$20.4 \pm 3.23$	0.575

The most frequently reported comorbidities include type 1 diabetes, hypothyroidism, reflux, anemia and asthma. A questionnaire including an interview on the last 24 hours of consumption, belonging to intelligence and quality-quantity methods was used to assess the diet. Anthropometric measurements: height, weight, age, were collected during the visit to the nearest 0.5 cm and 0.5 kg. The questionnaire included questions about the occurrence of allergies, food intolerances, medications and supplements, and physical activity of the child. In order to obtain precise information on the size of portions of meals consumed, the Photo Album of products and dishes which is recommended by the Institute of Food and

Nutrition (IŻŻ) [38]. The obtained anthropometric data such as height and body weight were analyzed using centiles of the OLA and OLAF project recommended by the Children's Memorial Health Institute (Figures 1 and 2). The analysis of menus was made in the Dieta 5d program recommended by the Food and Nutrition Institute. The obtained data was compared to Nutrition Standards for the Polish population, edited by *Jarosz* [12]. The results were interpreted on the basis of norms consistent with the average age of the entire group of 13-15 years. Data were statistically analyzed in the program Statistica 12.

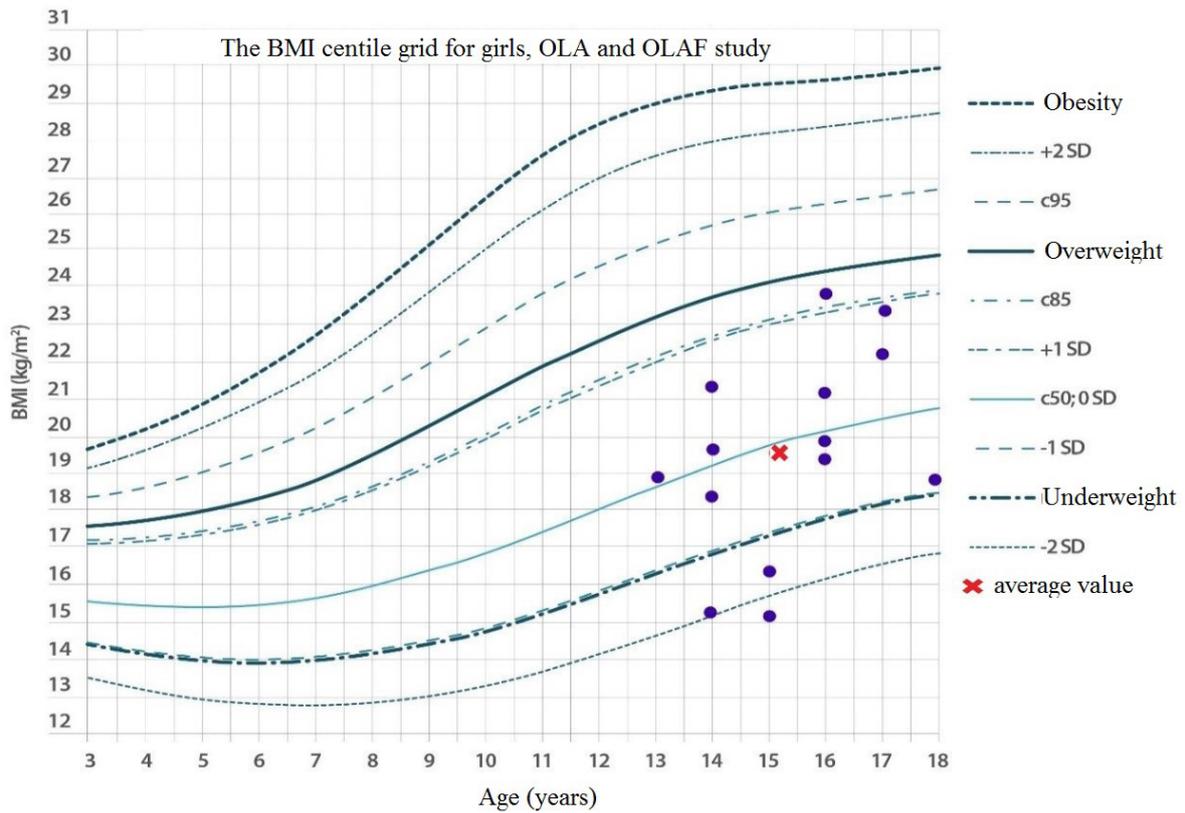


Figure 1. Body mass index (BMI) for girls

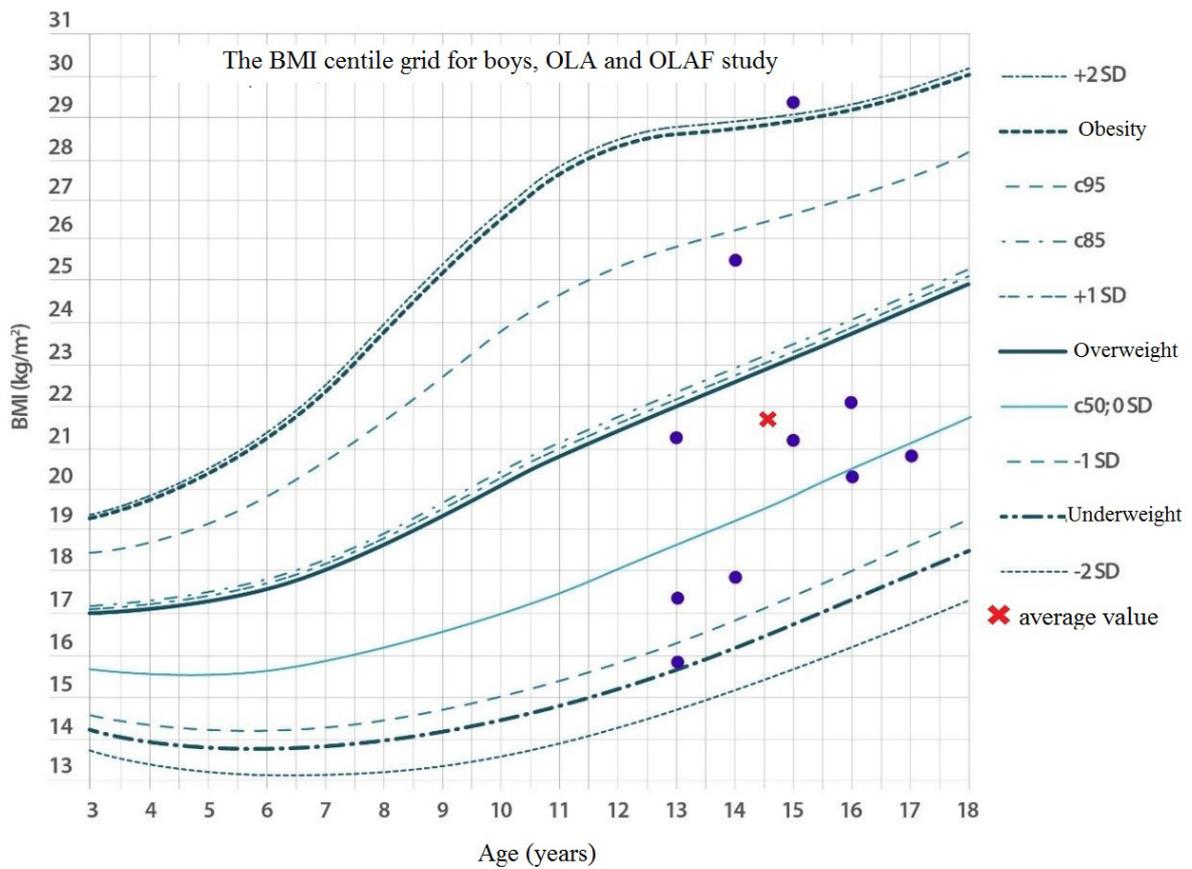


Figure 2. Body mass index (BMI) for boys

## RESULTS

Analysis of anthropometric data including body mass index (BMI) and age were related to the percentile charts separately for sex. 7 out of 14 girls were within accepted as the norm, and 7 were below the 50 percentile, of which 3 have extreme underweight. In the group of boys 7 were within 50 percentile, 1 was underweight while 2 boys were successively overweight and obese. Evaluation of nutritional status was related to the average age of the group, which was  $15.04 \pm 1.46$ . The level of the average demand for the group (estimated average requirement - EAR) was used for this purpose. For components for which this level has not been defined adopted adequate intake level (AI). For the total carbohydrate content, reference was made to the level of recommended RDA consumption. In relation to energy, fat, saturated fatty acids and cholesterol, the recommendations by the Institute of Food and Nutrition were used.

Both in the group of boys and in the group of girls, the energy consumption was lower than the daily demand, which was implemented at the level of 60-70% (Table 2). A significant excess was

observed for intakes of saturated fatty acids in the two groups, despite low intakes of total fat. There was also a relatively high cholesterol intake in the boys' group. In both groups, fiber intake was significantly below the recommended standards of consumption. Both minerals and vitamins in both groups were lower than the recommended value (Table 3). Daily demand for calcium was only 46% for girls and 59% for boys and for folates similarly 58% and 56%. Similarly, magnesium intake in both groups remained at the level of 70% in relation to the recommendations of the Institute of Food and Nutrition. Other components which are also present in quantities deficit is vitamin E, D and thiamine. In addition, a deficiency of components such as sodium, potassium, iron, zinc and iodine was also observed (Table 3). In boys, lower values of manganese and higher values of phosphorus were noted. A reverse relationship was observed in the group of girls. A statistically significant difference between the groups was recorded in the consumption of total protein and animal protein, with higher intakes of protein was observed in boys. The percentage of energy from both protein, fat and carbohydrates in both groups was correct (Table 4).

Table 2. Comparison of the mean energy intake, cholesterol, fiber and nutrients

Factor	EAR	Girls	Boys	p
Energy (kcal)	2450/3000*	1694.348	1928.268	NS
Lipids (g)	–	56.371	58.675	NS
SFA (g)	13.6–16.3/ 16.8–20.1*	24.518	23.917	NS
MUFA (g)	–	18.171	20.431	NS
PUFA (g)	–	5.871	5.735	NS
Cholesterol (mg)	max. 300	293.954	311.181	NS
Carbohydrates (g)	130 <sup>#</sup>	250.818	281.593	NS
Saccharose (g)	60	46.246	54.323	NS
Lactose (g)	–	7.393	5.635	NS
Dietary fibre (g)	19**	15.449	14.410	NS
Protein (g)	43/45*	59.237	79.819	0.032
Animal protein (g)	-	43.975	63.123	0.039
Plant protein (g)	-	13.621	14.230	NS

EAR – Estimate Average Requirement; NS - not statistically significant, \* - with gender and age distinction - girls / boys; \*\* - including guidelines for patients with celiac disease

Table 3. Comparison of the average consumption of minerals and vitamins

Factor	EAR	Girls	Boys	p
Na (mg)	2552/2944*	2062.815	2826.544	NS
K (mg)	3000	2756.099	2978.275	NS
Ca (mg)	1100	504.827	650.798	NS
P (mg)	1050	988.798	1238.091	NS
Mg (mg)	300/340*	210.653	241.268	NS
Fe (mg)	8	7.52	7.765	NS
Zn (mg)	7.3/8.5*	6.757	7.603	NS
Cu (mg)	0.7	0.786	0.807	NS
Mn (mg)	1.6/2.2*	2.22	2.017	NS
Iodine (µg)	95	75.953	87.634	NS
Vitamin A (µg)	490/630*	1326.444	1090.818	NS
Retinol (µg)	–	291.845	322.249	NS
Beta-carotene (µg)	–	6019.765	4412.423	NS
Vitamin E (mg)	8/10*	4.746	5.468	NS
Thiamine (mg)	0.9/1.0*	0.797	0.971	NS
Riboflavin (mg)	0.9/1.1*	1.198	1.311	NS
Niacin (mg)	11/12*	16.923	22.488	NS
Vitamin B6 (mg)	1/1.1*	1.727	2.115	NS
Vitamin C (mg)	55/65*	111.643	97.38	NS
Folate (µg)	330	193.528	186.97	NS
Vitamin B12 (µg)	2	2.191	3.116	NS
Vitamin D (µg)	15	1.185	1.563	NS

NS - not statistically significant

\* with a distinction between sex and age

Table 4. Comparison of the average percentage of energy from nutrients

Factor	Reference range (%)	Girls	Boys
Protein (%)	10–20	14.239	16.774
Lipids %	20–35	29.752	26.438
Carbohydrates %	45–65	56.009	56.788

## DISCUSSION

Celiac disease is an autoimmune disease affecting up to 1/100 of the world's population. This is one of the most common forms of malabsorption. The only form of treatment is the strict use of a gluten-free diet [1, 41]. *Alzaben et al.* [1] in study showed that the challenge for patients using a gluten-free diet is both its cost, which can be up to 50% higher than the costs of a traditional diet containing gluten and ensuring adequate nutritional value. Also, meals outside the home is a big problem for patients. In addition, there is

concern about contamination of naturally gluten-free products at each stage of the production process, which may contribute to the unconscious intake of harmful protein and thus to symptoms [8, 19]. *Ferster et al.* [8] noted in their study that the disadvantage reported by parents was the labeling of food and especially the presence of gluten in potentially gluten-free products. In products, gluten is used as a cheaper substitute for animal protein. A study conducted by *Rilley et al.* [32] involving 142 children between the age of 13 and 19 years of age showed in some patients the appearance of overweight and obesity, despite the normal values of body weight in the diagnosis of the disease. However, some patients with initially high body weight after using a gluten-free diet reduced or even achieved normal body weight.

In our own study it was shown that 70% of patients are around 50 percentile, which indicates a general good nutritional status. Similarly, in studies by *Radlovic et al.* [31] 70% of respondents showed a beneficial nutritional status after using a gluten-free diet. In the present study, the percentage of energy intake of

protein, fat and carbohydrates in both groups was within the norm. The opposite results were obtained in a study conducted by *Mariani* et al. [23] protein and fat were consumed in excessive amounts, which prevented malnutrition. However, as in our study, the diet was low in fiber, iron and calcium. As in the above study, patients consumed insufficient quantity of fiber. Its content in the diet did not exceed 16 g/d with recommendations for celiac disease of 20-35 g/d [39]. The results of these tests correspond to the results obtained by other authors [20]. Insufficient intake of calcium reported in the present study, confirmed the results of *Zuccotti* et al. [41] and *Alzaben* et al. [1], also be carried out in pediatric patients. *Ohlund* et al. [27] also observed low intake of this ingredient in the diet of patients, however, despite this, the intake was higher than in the healthy control group. Higher intakes may be caused by food fortification or calcium supplementation prescribed by a doctor.

The low intake of vitamin D observed in the study and hypocalcemia lead to increased bone resorption. Enteropathy predisposes to the appearance of osteoporosis in the future. However, the bone mineral density improves after the introduction of a gluten-free diet, also the bone growth processes normalize [3]. Therefore, early diagnosis in children and exclusion of gluten from the diet will enable them to achieve the correct peak bone mass [31].

Low magnesium intake may predispose to the development of behavioral disorders, growth retardation, as well as cardiovascular dysfunction [27]. The deficiencies of this element in the diet were observed by *Kautto* et al. [14], and *Balmatekin* et al. [2]. This study confirmed this relationship. *Rujner* et al. [33] showed that this unbalanced diet results from a deficiency of this element in both enteropathic and healthy people.

Insufficient iron intake observed in the own study may result in anemia with a deficiency of this element. A gluten-free diet, although it improves the absorption of nutrients, is still poor in iron. *Kautto* et al. found low iron consumption mainly in boys [14, 25]. It is believed that especially in the period of recovery in people with enteropathy, intake values should be interpreted referring to recommendations for healthy people. Therefore, most studies of interpretation based on the ratio of the EAR. Values for the content of protein, carbohydrate and fat recommended for patients are respectively 15%, 25-30% and 55% [10, 28].

The good sources of nutrients that are excluded from the diet of patients with celiac disease are pseudo-cereals. Teff can supplement the content of essential amino acids as well as calcium, iron or magnesium as well as dietary fiber [36]. Quinoa is a rich source of folic acid. Rich in fiber are amaranth and buckwheat.

They also contain unsaturated fatty acids that support the prevention of cardiovascular disease. A good source of thiamine, iron and zinc is oats. However, despite the lack of harm to patients, it is extremely important to check the product designation, as it is often contaminated with gluten on the production line [5, 28]. Buckwheat is a source of antioxidants, regulates blood cholesterol levels and is rich in many nutrients [7]. Unfortunately, in our study we observed little or no consumption of these products in the diet of patients. The menu was dominated by potatoes and white rice.

## CONCLUSIONS

1. Incorrectly used gluten-free diet may be the cause of recurrence of disease symptoms.
2. Celiac disease does not affect the occurrence of malnutrition but contributes to the occurrence of quality deficiencies.
3. Chronic insufficient intake of fiber may predispose to constipation and complications associated with it.
4. The study group is exposed to osteoporosis and growth disturbances due to calcium and vitamin D deficiency.
5. The demonstrated deficiency of magnesium, zinc, vitamin E and folic acid in food rations may affect the occurrence of multi-system abnormalities.

## Conflict of interest

*The authors declare no conflict of interest.*

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## RISK FACTORS OF EXCESSIVE BODY MASS IN CHILDREN AND ADOLESCENTS IN ŁÓDŹ

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### ABSTRACT

**Background.** Obesity and cardiovascular disease and metabolic disorders are an increasingly common problem worldwide, also in the developmental age population. Inhibiting this process requires identifying risk factors that can be modified.

**Objective.** The aim of the study was to identify the conditions of the occurrence of overweight and obesity in the Lodz youth at school age.

**Materials and methods.** The survey was conducted in 2008-2012 among school students attending primary and secondary schools in the four districts of Lodz (city in Poland). The study involved 622 students aged 12-18: 309 girls (49.7%) and 313 boys (50.3%). The BMI index was calculated based on anthropometric measurements (mass, body height) and was interpreted on the basis of centile charts of Lodz children (overweight  $\geq$  85-95 centile; obese  $\geq$  95 centile). Youth health behaviors were analyzed based on a questionnaire of an original interview modeled on the HBSC (Health Behavior in School-aged Children) study. The obtained results were subjected to statistical analysis (single- and multi-factorial logistic regression analysis).

**Results.** An excess of body weight was found in 23.5% of the examined youth. In multivariate logistic regression analysis, the factors significantly affecting the occurrence of overweight or obesity were: non-eating dinner (daily or sometimes, OR = 1.98); not eating fruit and vegetables every day (OR = 1.57), multi-hour passive relaxation time (use of TV, Internet, OR = 3.08) and low physical activity (OR = 1.76)

**Conclusions.** Intensive promotion of a healthy lifestyle - increasing the awareness and knowledge of schoolchildren, encouraging proper eating habits and active leisure activities - can significantly affect the reduction of obesity risk factors. Health education is required at school for children, as well as for parents and teachers.

**Key words:** *excessive body mass, risk factors, school youth, children, overweight*

### STRESZCZENIE

**Wprowadzenie.** Otyłość oraz choroby układu krążenia i zaburzenia metaboliczne są na całym świecie coraz częstszym problemem, również w populacji wieku rozwojowego. Zahamowanie tego procesu wymaga określenia czynników ryzyka, które można modyfikować.

**Cel badań.** Celem pracy była identyfikacja uwarunkowań występowania nadwagi i otyłości u młodzieży łódzkiej w wieku szkolnym.

**Materiał i metody.** Badanie przeprowadzono w latach 2008-2012 wśród młodzieży szkolnej uczęszczającej do szkół podstawowych i ponadpodstawowych na terenie 4 dzielnic Łodzi. W badaniach uczestniczyło 622 uczniów w wieku 12-18 lat: 309 dziewcząt (49,7%) i 313 chłopców (50,3%). Na podstawie pomiarów antropometrycznych (masy, wysokości ciała) obliczono wskaźnik BMI, który interpretowano w oparciu o siatki centylowe dzieci łódzkich (nadwaga  $\geq$  85-95 centyl; otyłość  $\geq$  95 centyla). Zachowania zdrowotne młodzieży, analizowano w oparciu o kwestionariusz autorskiego wywiadu wzorowanego na badaniu HBSC (Health Behaviour In School-aged Children). Uzyskane wyniki badań poddano analizie statystycznej (jedno- i wieloczynnikowa analiza regresji logistycznej).

**Wyniki.** Stwierdzono nadmiar masy ciała u 23,5% badanej młodzieży. W wieloczynnikowej analizie regresji logistycznej, czynnikami istotnie wpływającymi na występowanie nadwagi lub otyłości były: niespożywanie kolacji (codziennie lub czasami; OR=1,98); niespożywanie codziennie owoców i warzyw (OR=1,57), wielogodzinny czas wypoczynku biernego (korzystanie z telewizji, Internetu; OR=3,08) oraz mała aktywność fizyczna (OR=1,76).

**Wnioski.** Intensywne promowanie zdrowego stylu życia – zwiększanie świadomości i wiedzy młodzieży szkolnej, zachęcanie do prawidłowych nawyków żywieniowych oraz aktywnego spędzania wolnego czasu – może znacząco wpłynąć na redukcję czynników ryzyka otyłości. Konieczna jest edukacja zdrowotna prowadzona w szkole dla dzieci, a także dla rodziców i nauczycieli.

**Słowa kluczowe:** *nadmierna masa ciała, czynniki ryzyka, młodzież szkolna, dzieci, nadwaga*

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## INTRODUCTION

Currently, one of the biggest health problems of children and adolescents is excess body weight. Being aware of the seriousness of the physical and psychological consequences of obesity, many researchers are looking for conditions for its occurrence in children and adolescents [8, 36]. Obesity is a chronic disease, conditioned by both environmental and psychosocial factors as well as genetic predisposition [15, 22, 34].

According to *Oblacińska* et al. [25] and other authors among environmental and behavioral obesity conditions, we can distinguish:

- nutritional: unbalanced diet, irregularity of eating and leaving out meals, eating snacks with high energy value (fast food, chips, sweets, sweet carbonated drinks) between meals, low fiber intake (fruit and vegetables, whole grains); nutritional factors determine 20-40% obesity in children [27, 50];
- inadequate energy expenditure related to low physical activity (unwillingness to exercise activities) and preference for activities related to the sedentary lifestyle (television / computer);
- family: occurrence of obesity in closest family members, poor socio-economic situation, family lifestyle, low education of parents - especially mothers [28, 52];
- social: the influence of the environment favoring obesity (civilizational influences) - greater possibilities of food purchase, easy access and advertising of high-calorie food products, larger portions sold at a proportionally lower price, reduced opportunities for recreational activity, increased use of motorized transport, eg to school, barriers to physical activity (eg insufficient number of sports facilities, bicycle paths), prolonging recreation time in a sitting position [42];
- psycho-emotional factors: satisfying emotional needs through eating- eating foods can compensate for the failures and difficulties experienced, distracting the child from the difficult situation and the unpleasantness in the family, at school or in a peer group [27]; lack of ability to cope with stress [22];
- other physiological and psychological factors that may contribute to obesity include: eating too fast, low sensitivity to a "feedback" mechanism indicating being saturated [51], and short time sleep [23].

The aim of the study was to identify the conditions of the occurrence of overweight and obesity in the Lodz youth at school age.

## MATERIALS AND METHODS

The survey was conducted in 2008-2012 among school students attending primary and secondary schools in the four districts of Lodz (city in Poland).

The study involved 622 students aged 12-18: 309 girls (49.7%) and 313 boys (50.3%). Anthropometric measurements (mass, body height) were made and the BMI (Body Mass Index) was calculated. The results were interpreted on the basis of centile charts of Lodz children [30], using the following criteria: weight deficiency  $\leq 10$  percentile; correct body mass ratio in relation to the 10-85 percentile increase; overweight  $\geq 85-95$  percentile; obesity  $\geq 95$  percentile). Eating habits, school and out-of-school activities, passive spending of time by young people, were analyzed based on a questionnaire of an original interview modeled on the HBSC (Health Behavior in School-aged Children) study. Statistical program Statistica 9.0 was used for statistical analysis of the obtained results. In order to determine the relationship between adverse health behaviors of adolescents and the occurrence of excessive body weight, variables from the questionnaire were compared (favorable and unfavorable health behaviors) and logistic regression analysis was performed to identify those features that significantly increased the occurrence of overweight and obesity in the studied youth.

## RESULTS

Adolescents with normal nutritional status accounted for 70.3% of the study population, body mass deficiency occurred in 6.3% of students, while overweight and obesity was diagnosed in 23.5% of adolescents (Table 1).

Table 1. Nutrition status of adolescents according to BMI including centile grids (in %)

Nutritional status	Youth (n = 622)	
Underweight $\leq 10c$	n=39	6.3
Standard 10c-85c	n=437	70.3
Overweight 85c-95c	n=89	14.3
Obesity $\geq 95c$	n=57	9.2

In order to estimate the risk of overweight-obesity in the study, a univariate and multivariate logistic regression analysis was applied. In the univariate logistic regression analysis (Table 2), the factors significantly influencing the occurrence of overweight-obesity turned out to be 6 out of 27 features selected for this analysis. In comparison with people who eat supper regularly, those who do not eat it, are almost twice as often more obese or overweight (OR = 1.98,  $p < 0.05$ ). Not consuming fruit and vegetables every day increases this risk by 1.5 times (OR = 1.57,  $p < 0.05$ ). Passive rest of the respondents, measured by the number of hours of using television, Internet or computer games, increases the risk of overweight - obesity.

Table 2. Estimation of the influence of traits (risk) of overweight - obesity among adolescents based on a one-factor logistic regression analysis

Variable		Odds ratio	95%CI	P
Gender	Boys	1.13	0.78-1.63	p>0.05
	Girls	1.00	Reference group	
Age	12 years	1.54	0.96-2.47	p>0.05
	16 years	1.03	0.67-1.57	p>0.05
	18 years	1.00	Reference group	
First breakfast	No consumption	1.001	-	p>0.05
	Consumption	1.00	Reference group	
Second breakfast	No consumption	0.76	0.41-1.42	p>0.05
	Consumption	1.00	Reference group	
Diner	No consumption	0.59	0.23-1.17	p>0.05
	Consumption	1.00	Reference group	
Supper	No consumption	1.98	1.02-3.86	<b>p&lt;0.05</b>
	Consumption	1.00	Reference group	
Everyday consumption of milk	No	0.72	0.49-1.05	p>0.05
	Yes	1.00	Reference group	
Daily consumption of milk products	No	1.05	0.72-1.53	p>0.05
	Yes	1.00	Reference group	
Eating meat every day or several times a week	No	0.36	0.11-1.22	p>0.05
	Yes	1.00	Reference group	
Eating fish every day or several times a week	No	0.71	0.47-1.08	p>0.05
	Yes	1.00	Reference group	
Daily consumption of cereal products	No	1.19	0.79-1.77	p>0.05
	Yes	1.00	Reference group	
Daily consumption of whole meal bread	No	0.65	0.43-1.00	p>0.05
	Yes	1.00	Reference group	
Non-consumption of legumes	No	0.92	0.64-1.34	p>0.05
	Yes	1.00	Reference group	
Daily consumption of fruits and vegetables	No	1.57	1.07-2.29	<b>p&lt;0.05</b>
	Yes	1.00	Reference group	
Daily consumption of carbonated drinks	Yes	1.20	0.78-1.85	p>0.05
	No	1.00	Reference group	
Everyday eating junk food	Yes	0.75	0.51-1.08	p>0.05
	No	1.00	Reference group	
Hours of use of television, computer	Change by 1 hour	1.10	1.01-1.20	<b>p&lt;0.05</b>
	Change by entire range	3.08	1.06-8.91	
Physical activity after school	Little	1.76	1.11-2.79	<b>p&lt;0.05</b>
	High or medium	1.00	Reference group	
Exercise in physical education classes	No	0.90	0.50-1.63	p>0.05
	Yes	1.00	Reference group	
Mother's education	Basic/vocational	1.40	0.61-3.25	p>0.05
	Secondary education	1.29	0.69-2.43	p>0.05
	Higher education	1.00	Reference group	
Encouragement of physical activity by parents	No	1.32	0.86-2.04	p>0.05
	Yes	1.00	Reference group	
Watching TV over 2 h daily	Yes	0.95	0.62-1.37	p>0.05
	No	1.00	Reference group	
Using the Internet more than 4 hours daily	Yes	0.83	0.53-1.30	p>0.05
	No	1.00	Reference group	
Time for computer games longer than 2 h daily	Yes	1.04	0.67-1.63	p>0.05
	No	1.00	Reference group	
Night rest 5-6 hours	Yes	1.25	0.80-1.93	p>0.05
	No	1.00	Reference group	
Going to sleep not later than at 11 pm	Yes	0.49	0.33-0.71	<b>p&lt;0.001</b>
	No	1.00	Reference group	
More frequent snacking of fruit and vegetables than sweets and crisps	Yes	0.61	0.99-2.71	<b>p&lt;0.05</b>
	No	1.00	Reference group	

p - level of statistical significance

If the seating time increases by 1 hour, the risk increases by 10% (OR = 1.10,  $p < 0.05$ ), and if it increases by the whole range of variability, then the risk increases 3 times (OR = 3.08,  $p < 0.05$ ). In students who declared that in addition to physical education classes, they rarely take (or not at all) physical activity in their spare time (low physical activity) - the risk of overweight-obesity is almost twice as high as in adolescents who exercise at least 2-3 times more often in a week, min. 60 min. (average and high physical activity) (OR = 1.76,  $p$

$< 0.05$ ). Going to bed at no later than 11 pm reduces the risk of overweight- obesity twice (OR = 0.49,  $p < 0.001$ ). If snacking includes more frequently beneficial products (fruit and vegetables) than not beneficial to health (sweets, crisps) – it is a positive difference, the risk of overweight and obesity becomes almost twice as low (OR = 0.61,  $p < 0.05$ ). In the overweight and obesity group sweets and crisps were more often consumed than fruit and vegetables.

Table 3. Estimation of the influence of traits (risk) of overweight - obesity among adolescents based on multivariate logistic regression analysis

Variable		Odds ratio	95% CI	P
Supper	No consumption	2.75	1.03-7.31	<b>p&lt;0.05</b>
	Consumption	1.00	Reference group	
Everyday consumption of fruit and vegetables	No	1.86	1.01-3.44	<b>p&lt;0.05</b>
	Yes	1.00	Reference group	
Time watching TV, using computer (passive rest)	Change by 1 hour	1.21	1.08-1.42	<b>p&lt;0.01</b>
	Change by the entire range	3.41	2.57-62.02	
Physical activity	Little	1.82	1.03-3.21	<b>p&lt;0.05</b>
	High or medium	1.00	Reference group	
Going to sleep no later than at 11 pm	Yes	0.58	0.32-1.03	<b>p&lt;0.05</b>
	No	1.00	Reference group	
More frequent snacking of fruit and vegetables than sweets and crisps	Yes	0.55	0.30-1.03	<b>p=0.05</b>
	No	1.00		

In multivariate logistic regression analysis, (Table 3) in which important features in a univariate analysis were taken into account, the following were important: leaving out supper (those who do not eat, are obese or overweight almost three times more often (OR = 2.75;  $< 0.05$ ), not consuming fruit and vegetables every day increases this risk almost twice (OR = 1.86,  $p < 0.05$ ), similarly low physical activity (OR = 1.82,  $p < 0.05$ ); use of television and computer ( $p < 0.01$ ) - if the seating time increases by 1 hour, the risk increases by 20% (OR = 1.21), and if it increases by the entire range of volatility, then the risk increases over 3 times (OR = 3.41), going to bed not later than at 11 pm o'clock (OR = 0.58,  $p < 0.05$ ) and snacking – a positive difference – more often fruit and vegetables as snacks than sweets and crisps - the risk of overweight and obesity becomes almost twice as low (OR = 0.55,  $p = 0.05$ ).

## DISCUSSION

Too small number of meals and their irregular consumption increases the risk of overweight and obesity. Too long breaks between meals cause a feeling of hunger and the desire to eat sweet or fatty (high-calorie) products to quickly compensate for energy shortages. The body demands regular supply of the right amount of energy and nutrients. If meals are consumed

irregularly, the body begins to accumulate energy for periods of hunger in the form of adipose tissue [49]. Therefore, children who eat one or two large meals during the day are more likely to gain weight than those who have the same amount of food receive in 4-6 meals [32]. It is worth noting that, in the opinion of the young people, regular daily meals are of no importance for health and maintaining a healthy weight [47]. There is a widespread belief that reducing the number of meals consumed during the day is a good method of reducing the caloric intake of food [10]. Many studies indicate that children who are overweight and obese eat fewer meals during the day than their peers with normal body mass and they eat irregularly. They often erroneously treat giving up a meal (mostly breakfast) as a form of slimming diet [49].

In the own study, an important factor increasing the occurrence of excessive body weight was not eating supper. *Rampersand* et al. [37] observed a relationship between non-eating of breakfast and the occurrence of excessive body weight in the subjects. *Nicklas* et al. [24] noted that children who regularly eat breakfast, eat more cereal products, fruit and dairy products, which helps maintain a healthy weight. In addition, eating breakfast is associated with a lower consumption of high-fat and high-calorie snacks throughout the day [20, 41]. In the *Olszanecka-Glinianowicz* et al. study [29] in girls at prepubertal age, not eating breakfast

increased the risk of developing obesity, whereas in boys it was important to eat outside the home. 11-13 year-old children from Warsaw who were diagnosed with obesity, most often among the respondents (16.1%) declared consumption of less than 3 meals a day, than children with normal body weight (1.4%) [48]. Similar observations have been made in other studies. Children/adolescents with overweight and obesity consumed significantly less meals than children without excess body weight [11, 41]. On the other in the studies of *Gajda and Jeżewska-Zychowicz* [6], incorrect eating habits of adolescents regarding eating sapper were observed (especially among girls). According to the authors, this was most probably the result of an wrong way of maintaining a healthy body mass that could lead to eating disorders. However, in studies by *Ślawińska et al.* [39], a significant relationship was found between not eating a second breakfast and a more frequent use of a slimming diet in a group of 12-16 year old girls. The tendency to abandon supper, as well as leaving out breakfast, is often associated with a desire to reduce body mass [17]. Children/adolescents with excessive body mass may therefore attempt to control the amount of calories consumed by limiting the number of meals, which may have the opposite consequences to the intentions [1].

Another risk factor for overweight and obesity in the 12-18 year old population in the author's own work was not eating vegetables and fruit every day. Similar results were obtained by *Wolnicka and Jaczewska-Schuetz* [48]. The factors preventing excessive body weight may be the consumption of vegetables and fruit at least 1-2 times a day. A stronger protective factor can be eating fruit and vegetables even more often 3-5 times a day. *Oblacińska* study [25] also proved that middle-school students with overweight and obesity consumed products indispensable for health (fruit, vegetables, brown bread, milk and its products) at an unsatisfactory level. Similarly, in the study *Ledikwe et al.* [18] it was observed that obese people did not consume enough fruit and vegetables. The high proportion of vegetables and fruits, legumes, nuts and whole grains (high content of dietary fibers) in the diet have a preventive effect in relation to the development of excessive body weight [19, 44].

Just observing a low-energy diet and avoiding certain foods or leaving basic meals in itself does not guarantee due weight. The nutritional education of the child and his family in the aspect of proper eating habits is important, including the regular consumption of meals (preferably together with the family) and daily fruit and vegetable intake and appropriate physical activity [11, 25, 43, 52].

Systematic physical activity plays a key role in the prevention and treatment of overweight and obesity [5, 9]. The results of the author's own work have shown

that a significant factor increasing the risk of excessive body weight was low physical activity of the subjects. In the study of Silesian children - it was also found that in 7-9 year-old girls low physical activity increased the risk of developing obesity [29]. In other Polish studies [26], junior high school students with excess body mass compared to their peers with the correct weight, did less often take part in physical education lessons and participated in extracurricular physical activities or sport. Over 1/3 of obese adolescents did not participate regularly or did not take part in physical education classes (especially girls). A negative image of one's body, difficulties in its acceptance, fear of being ridiculed are an obstacle to physical activity, especially in the case of obese girls [12]. According to studies by *So et al.* [40], the smallest percentage of girls and boys with obesity participated in physical education lessons, compared to young people with deficiency and normal body mass. *Fenczyn et al.* [4] stated in their research that obese girls and boys more often than their peers did not take part in physical education lessons at school and did not exercise in their free time. After classes at school, adolescents with obesity more often chose reading books, talking with friends, watching TV. Similarly, other researchers showed that obese people were less active compared to peers with normal body weight [31, 33, 45]. In the population of 17-year-olds [35], physically active people had lower body mass, BMI and fat content in the body, in comparison with those who were not physically active. Similarly, in *Kasperczyk et al.* [14].

In some studies, there were no statistically significant differences between body weight or BMI and physical activity presented [16, 21].

Time spent in front of the TV or computer screen above 4.5 hours was a significant factor increasing the risk of overweight and obesity in the group of the studied youth. The obtained results in the own study are consistent with the observations of other authors [2, 38]. Among the children who spent 5 hours a day in front of the TV there were over 5 times more people with excess body weight than among peers who watched TV programs below 2 hours a day [7]. Based on NHANES - The National Health and Nutrition Examination Survey, the highest incidence of overweight and obesity in children who watched TV  $\geq 4$  hours and the lowest in those who watched  $\leq 1$  hours a day was demonstrated [3].

In the literature on the subject, you can also find works in which there is no significant impact of time spent in front of the TV/computer on the body mass of the tested youth [13, 35, 41, 46]. According to *Jodkowska et al.* [13] behaviors related to passive lifestyle are not competitive in relation to physical activity in Polish teenagers, while their relationship with abnormal nutritional behaviors (eating sweets, crisps, drinking carbonated beverages) may lead to the development of obesity.

## CONCLUSIONS

1. Intensive promotion of a healthy lifestyle - increasing the awareness and knowledge of schoolchildren, encouraging proper eating habits and active leisure activities - can significantly affect the reduction of obesity risk factors.
2. Health education is required at school for children, as well as for parents and teachers. Activities in nutrition education for children should be carried out by nutritionists and for parents and guardians, activities / workshops should be organized before obligatory monthly consultations.

### Conflict of interest

*The authors declare no conflict of interest.*

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## PRE-PREGNANCY NUTRITIONAL STATUS VERSUS MATERNAL WEIGHT GAIN AND NEONATAL SIZE

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### ABSTRACT

**Background.** Maternal weight during pregnancy may affect both, the course of pregnancy and the anthropometric parameters of the newborn. The steadily growing problem of excessive weight in reproductive-age women is associated with the risk for gestational obesity and its negative consequences for the infant.

**Objectives.** The aims of the study were to analyze the following: (i) maternal weight gain as compared to the pre-pregnancy BMI, and (ii) the link between maternal weight and other environmental factors versus neonatal size.

**Material and methods.** The study was conducted among 94 women in singleton term pregnancy, who delivered at the Department of Obstetrics, Gynecology and Oncology, Medical University of Warsaw. The American Institute of Medicine criteria for the recommended weight gain were followed. Multivariate logistic regression model and multiple regression analysis were used for statistical analysis.

**Results.** Normal weight gain was observed in only one-third of the subjects, while excess weight gain was detected in as many as 42.5% of the women. Active smokers were at a 4-fold higher risk for excess weight gain as compared to non-smokers (OR 4.13, 95% CI 1.19 - 14.34,  $p = 0.026$ ). Infants born to mothers with insufficient weight gain (24.5% of the mothers) were lighter by 302 g ( $p=0.0405$ ) and shorter by 2.4 cm ( $p=0.0025$ ) as compared to those born to mothers with normal weight gain.

**Conclusions.** Maternal weight gain in most of our subjects was not compliant with the current recommendations, regardless of the pre-pregnancy BMI. Inadequate pregnancy weight gain negatively affects the anthropometric parameters of the newborn.

**Key words:** pregnancy; body mass index; weight gain; anthropometric neonatal parameters

### STRESZCZENIE

**Wprowadzenie.** Masa ciała matki w okresie ciąży może mieć wpływ na przebieg ciąży i parametry antropometryczne noworodka. Narastający, już u kobiet w wieku rozrodczym problem nadmiernej masy ciała niesie ze sobą ryzyko otyłości ciężarnych i jej konsekwencji u dziecka.

**Cel.** Celem badania była analiza przyrostu masy ciała kobiet, w zależności od przedciążowego wskaźnika BMI oraz analiza związku, pomiędzy przyrostem masy ciała i innymi czynnikami środowiskowymi, a wielkością noworodków.

**Materiał i metody.** Badanie przeprowadzono wśród 94 kobiet w ciąży pojedynczej, które urodziły w terminie w Klinice Położnictwa, Chorób Kobięcych i Ginekologii Onkologicznej Warszawskiego Uniwersytetu Medycznego. Zalecany przyrost masy ciała przyjęto według kryteriów opracowanych przez amerykański Institute of Medicine. W analizie statystycznej wyników wykorzystano wielowymiarową analizę regresji logistycznej i wieloczynnikową analizę regresji.

**Wyniki.** Prawidłowy przyrost masy ciała miała tylko 1/3 pacjentek, a największy odsetek dotyczył przyrostu nadmiernego (42,5%). Kobiety palące w czasie ciąży miały ponad 4-krotnie większe ryzyko zbyt dużego przyrostu masy ciała, w porównaniu do kobiet ciężarnych niepalących (OR 4.13, 95% CI 1.19 - 14.34,  $p = 0,026$ ). Noworodki matek z małym przyrostem masy ciała (24,5% matek) były o 302 g lżejsze ( $p=0,0405$ ) i o 2,4 cm krótsze ( $p=0,0025$ ), niż noworodki matek z przyrostem prawidłowym.

**Wnioski.** Ciążowy przyrost masy ciała większości badanych kobiet odbiegał od aktualnych zaleceń, niezależnie od przedciążowego wskaźnika BMI. Negatywny wpływ na parametry antropometryczne noworodków miał zbyt mały przyrost masy ciała matek.

**Słowa kluczowe:** ciąża, masa ciała, parametry antropometryczne noworodków

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## INTRODUCTION

Pre-pregnancy weight and its gain during pregnancy are two factors which might significantly affect the course of pregnancy and neonatal health. Women who are too slim before conception are at a higher risk for delivering a low birth weight (LBW) or a small for gestational age (SGA) infant, while overweight or obese women are at risk for gestational diabetes, fetal macrosomia, or a large for gestational age (LGA) infant [13, 14, 18, 26, 34]. Inadequate and excess pregnancy weight gain may both have negative consequences but, in the era of global obesity, the research has visibly focused on the latter. Excess weight gain during pregnancy is associated with numerous complications, e.g. gestational diabetes, arterial hypertension [19, 23, 28], and fetal macrosomia [14, 29, 34]. Currently, it is believed that excess neonatal weight intensifies the problem of obesity both, in childhood and later in life [3-5, 10, 14].

As far as pregnancy weight gain is concerned, many countries – including Poland – follow the American guidelines which were designed to minimize the risk for delivering either an underweight or an overweight infant [21, 31]. In light of the guidelines in question, weight gain during pregnancy is determined by maternal pre-pregnancy body mass index (BMI). Noteworthy, lately the American criteria about nutritional status for reproductive-age women have been adjusted to the guidelines for the general population created by the WHO [31]. After nearly 20 years, the recommended BMI for such women has been lowered from  $\geq 19.8$  to  $\geq 18.5$ , which was caused by a dramatic increase in the number of American women with pre-pregnancy obesity, more advanced maternal age, and a higher number of multiple gestations.

In accordance with the standards of the medical care for pregnant women in Poland, patient BMI should be established at the first antenatal visit and patient weight must be monitored until pregnancy completion [17]. Also, it has been emphasized in the same document that maternal obesity is one of the risk factors for perinatal complications. UK belongs to the group of countries which question the validity of routine weigh-ins for pregnant women and maternal weight policies. The United Kingdom's National Institute for Health and Clinical Excellence firmly claims that data on the link between maternal weight gain and neonatal health are inconclusive and that the limits give rise to unnecessary concern among the mothers-to-be [21].

The aims of the study were to analyze the following: (i) maternal weight gain as compared to the pre-pregnancy BMI and (ii) the link between maternal weight and other environmental factors versus neonatal anthropometric parameters (weight, length, head and chest circumference).

## MATERIAL AND METHODS

### *Study Design*

The study included 94 pregnant women who delivered at the Department of Obstetrics, Gynecology and Oncology, Medical University of Warsaw, in 2014-2015. Only pregnant women of Polish nationality in singleton term ( $\geq 37$  gestational weeks) pregnancy, with no history of chronic diseases, were recruited. Written informed consent was obtained from all participants. Local Ethics Committee approved of the study (no. 10/162/KB/2014). Maternal characteristics are presented in Table 1.

### *Data Collection*

Direct interviewing (face-to-face) was used to collect data on maternal weight, pregnancy weight gain and lifestyle. In accordance with the American Institute of Medicine National Academy of Science guidelines, the following values of normal weight gain were accepted: 12.5–18 kg for underweight, 11.5–16 kg for normal weight, 7.0–11.5 kg for overweight, and 5–9 for obese women [31]. Values below or above recommendations were considered as insufficient or excessive, respectively. Nutritional status of women on admission was defined by the BMI, based on the either self-reported height and body weight or registered in the maternity notes. Due to a relatively small sample size, overweight and obese subjects were placed in one group (excess weight) and the ranges for overweight women were applied. Maternal weight gain was calculated as the difference between the body weight measured after admission to the delivery ward and the pre-pregnancy weight. As the study was a survey, pre-pregnancy weight and pregnancy weight gain were measured in kilograms (+/- 1kg accuracy).

Data on pregnancy duration and neonatal anthropometric measurements (weight, length, head and chest circumference) were obtained from the hospital medical records. The anthropometric measurements were taken by the midwives immediately upon delivery. Weight was measured using a physician beam scale. The remaining measurements were taken with the use of a tape measure. The total neonatal length was measured from the vertex of the head to the soles (with the feet kept vertical at 90 degrees). The occipital-frontal head circumference (tape was placed on the maximum protrusion of the occiput and supraorbital ridges) and the chest circumference (tape was placed horizontally on the sternum and lower tip of the shoulder blade) were measured.

The study considered also a few dietary factors which might affect neonatal size, in it maternal caffeine consumption (coffee, tea, and energy drinks), vitamin D (fish, eggs, butter, margarine, milk and dairy products), calcium (milk and dairy products) and vitamin/mineral supplementation during pregnancy.

The questionnaire, and the “Photo Album of Meals and Products” were used for data collection.

#### Statistical Analysis

Multivariate logistic regression model was used to analyze a possible relationship between selected variables (pre-pregnancy BMI, age, education, place of residence, gravidity, smoking, supplementation

with vitamin and mineral preparations) and maternal weight gain. Backward elimination ( $p=0.1$ ) was used to select statistically significant features. The level of statistical significance was set at 5%. The relationship between the investigated features and the matter in question was expressed using odds ratio (OR) and a 95% confidence interval.

Table 1. Maternal and neonatal characteristics

<b>Maternal characteristics</b>	
Number of women	94
Pre-pregnancy maternal BMI (mean $\pm$ SD )	22.9 $\pm$ 3.7
Pre-pregnancy underweight, n (%)	8 (8.5%)
normal, n (%)	63 (67.0%)
overweight/obesity, n (%)	23 (24.5%)
Age (in years) mean $\pm$ SD	29.9 $\pm$ 4.3
Education, n (%)	
higher	63 (67.0)
other	31 (33.0)
Gravidity, n (%)	
primiparas	40 (42.5)
multiparas	54 (57.5)
Gestational diabetes, n (%)	9 (9.5)
Smoking during pregnancy, n (%)	14 (15.0)
Professionally active during pregnancy, n (%)	54 (57.4)
Supplementation with vitamin/mineral preparations, n (%)	85 (90.4)
Daily vitamin D consumption – from diet ( $\mu$ g) median (min-max)	2.1 (0.2-11.5)
Daily calcium consumption – from milk and dairy products (mg) median (min-max)	596 (69-1872)
Daily caffeine consumption – from coffee, tea, and energy drinks (mg) mean $\pm$ SD	67 $\pm$ 51
<b>Neonatal characteristics</b>	
Number of newborns	94
Gestational age (weeks) mean $\pm$ SD	39.4 $\pm$ 1.0
Sex of the newborn	
male, n (%)	48 (51.0)
female, n (%)	46 (49.0)
Neonatal weight (g) mean $\pm$ SD	3515 $\pm$ 500
LBW neonates (<2500 g), n (%)	1 (1.1)
Macrosomia (>4000 g), n (%)	19 (20.2)
Neonatal length (cm) mean $\pm$ SD	55.4 $\pm$ 2.7
Neonatal head circumference (cm) mean $\pm$ SD	34.8 $\pm$ 1.4
Neonatal chest circumference (cm) mean $\pm$ SD	34.0 $\pm$ 1.9
Apgar score (points) mean $\pm$ SD	9.9 $\pm$ 0.1

Non-parametric *Spearman's* rank correlation coefficient was used to analyze the relationship between maternal pre-pregnancy weight (in kg) and pregnancy weight gain (in kg). A multiple regression analysis was used to investigate a possible relationship between selected baseline characteristics (pre-pregnancy BMI, weight gain during pregnancy, use of vitamin/mineral preparations, vitamin D

and calcium consumption, caffeine consumption, smoking, maternal age and education, gravidity, professional activity during pregnancy, gestational diabetes, and sex of the neonate) and neonatal weight, length, and head and chest circumference. The  $p$ -value of  $< 0.05$  was considered as statistically significant. Stata v. 14.1 was used for data analysis.

## RESULTS

### *Weight gain and the related factors*

Normal pre-pregnancy weight was observed in 67% of the investigated women, while 8.5% were underweight and 24.5% had excess weight – either

overweight or obese (Table 1). During pregnancy, excess weight gain was found in 42.5% of the subjects and normal weight gain was observed in only one-third of the women (Table 2).

Table 2. Pregnancy weight gain in comparison with pre-pregnancy BMI

Pre-pregnancy BMI	Gestational weight gain below recommendations n (%)	Gestational weight gain within recommendations n (%)	Gestational weight gain above recommendations (%)	Weight gain (kg) mean, (min-max)
underweight BMI <18.5	4 (50)	3 (37.5)	1 (12.5)	13.6 (9 – 20)
normal BMI 18.5–24.9	17 (27)	21 (33.3)	25 (39.7)	15.7 (6 – 32)
overweight/obesity BMI ≥25	2 (8.7)	7 (30.4)	14 (60.9)	13.8 (4 – 30)
total n (%)	23 (24.5)	31 (33)	40 (42.5)	15.0 (4 – 32)

No statistically significant relationship was found between pre-pregnancy BMI and pregnancy weight gain. However, we observed a tendency for underweight women to be at a lower risk for excess weight gain during pregnancy (Table 3). We found that smokers are at a 4-fold risk for excess weight gain as

compared to non-smokers (OR 4.13, 95% CI 1.19 - 14.34,  $p = 0.026$ ), as well as multiparas as compared to primiparas, although borderline statistical significance was detected in the latter case (OR 2.48, 95% CI 0.97 - 6.32,  $p = 0.058$ ) (Table 3).

Table 3. Analysis of the influence of pre-pregnancy maternal BMI and other factors on the risk for excess gestational weight gain

N=94	OR [95% CI]	p- value
pre-pregnancy BMI: underweight vs. normal overweight/obesity vs. normal	0.13 [0.01; 1.28]	0.081 >0.1
age (years): >30 vs. ≤30		>0.1
education: secondary vs. higher		>0.1
place of residence: Warsaw vs. other		>0.1
gravidity: multiparas vs. primiparas	2.48 [0.97; 6.32]	0.058
supplementation with vitamin/mineral preparations		>0.1
smoking during pregnancy	4.13 [1.19; 14.34]	0.026

No linear connection was found between pre-pregnancy maternal weight and pregnancy weight gain ( $\rho=0.0028$ ,  $p=0.9785$ ), although the highest weight gain (mean 15.7 kg) was detected among women with normal weight during the pre-conception period. Both, underweight and overweight women gained on average 2 kg less during pregnancy as compared to their normal-weight peers (Table 2).

### *Maternal weight gain and other environmental factors versus neonatal size*

As far as newborn anthropometric parameters were concerned, we found that children born to mothers whose weight gain in pregnancy was below recommendations were 302 g lighter ( $p=0.0405$ ), and 2.4 cm shorter ( $p=0.0025$ ), as compared to infants born to mothers with normal weight gain (Tables 4 and 5).

One case of LBW was observed in a patient with normal weight gain. Macrosomia (>4000 g) was found in 20% of the neonates but it proved to be unrelated to maternal BMI and pregnancy weight gain.

Table 4. Relationship between selected parameters and neonatal weight

Parameter	Regression beta coefficient (SE)	95% CI	p- value
Pre-pregnancy BMI: underweight	15.69 (199.141)	(-380.77; 412.15)	0.9374
overweight/obesity	70.77 (151.218)	(-230.28; 371.82)	0.6411
Low weight gain vs. normal gain	-301.77 (144.827)	(-590.10; -13.44)	0.0405
Excess weight gain vs. normal gain	55.03 (137.407)	(-218.52; 328.59)	0.6899
Supplementation with vitamin/mineral preparations	-232.65 (181.872)	(-594.73; 129.43)	0.2046
Vitamin D consumption	1.72 (2.951)	(-4.15; 7.59)	0.5616
Calcium consumption	5.90 (12.151)	(-18.29; 30.09)	0.6284
Caffeine consumption	-154.11 (138.210)	(-429.27; 121.04)	0.2683
Gestational diabetes	120.94 (176.572)	(-230.59; 472.47)	0.4954
Smoking	57.71 (159.212)	(-259.26; 374.67)	0.7180
Age	10.91 (13.953)	(-16.87; 38.69)	0.4365
Education	-144.76 (125.909)	(-395.43; 105.91)	0.2538
Gravidity	-57.38 (116.065)	(-288.44; 173.69)	0.6225
Professional activity during pregnancy	-60.90 (108.664)	(-277.24; 155.43)	0.5768
Neonatal sex	-28.27 (110.419)	(-248.10; 191.56)	0.7986

Table 5. Relationship between selected parameters and neonatal length

Parameter	Regression beta coefficient (SE)	95% CI	p- value
Pre-pregnancy BMI: underweight	-0.24 (1.078)	(-2.39; 1.91)	0.8247
overweight/obesity	-0.09 (0.82)	(-1.72; 1.55)	0.9176
Low weight gain vs. normal gain	-2.44 (0.784)	(-4.01; -0.88)	0.0025
Excess weight gain vs. normal gain	-0.29 (0.744)	(-1.77; 1.19)	0.6970
Supplement. with vitamin/mineral preparations	-0.99 (0.985)	(-2.95; 0.97)	0.3159
Vitamin D consumption	-0.01 (0.016)	(-0.04; 0.02)	0.5247
Calcium consumption	-0.04 (0.066)	(-0.17; 0.10)	0.5936
Caffeine consumption	-0.93 (0.748)	(-2.42; 0.56)	0.2189
Gestational diabetes	0.60 (0.956)	(-1.30; 2.51)	0.5295
Smoking	-0.14 (0.862)	(-1.85; 1.58)	0.8758
Age	-0.03 (0.076)	(-0.18; 0.12)	0.6666
Education	-0.68 (0.682)	(-2.04; 0.67)	0.3199
Gravidity	0.02 (0.629)	(-1.23; 1.27)	0.9740
Professional activity during pregnancy	0.26 (0.588)	(-0.91; 1.44)	0.6548
Neonatal sex	-0.07 (0.598)	(-1.26; 1.12)	0.9122

## DISCUSSION

According to our findings, which are consistent with reports – albeit scarce – from other Polish authors, pregnancy weight gain among most pregnant women is either below or above recommendations. Over 42% exceeded and one-fourth did not reach the recommended weight gain for the respective BMI values. *Suliga* and

*Adamczyk-Gruszka* reported similar results in their study: weight gain above and below recommendations was observed in 40% and 23% of their subjects, respectively [24]. *Wierzejska et al.*, found an even higher number of pregnant women who gained excess weight (48%), especially among subjects who were overweight or obese before conception (61%) [33].

Similar tendencies have been observed also in other regions of the world. In the USA, excess weight gain was reported for 50% of all pregnant women [8, 12], and as many as 64-66% for women with pre-pregnancy overweight or obesity [6, 19]. Weight gain below recommendations was found in 20% of the subjects [12]. In China, weight gain above and below recommendations was reported for 62% and 12% of the pregnant women, respectively [22], and in Australia for 41% and 33% of the pregnant women, respectively [20]. According to a recent meta-analysis of worldwide reports on the matter, including over 1 million pregnant women, weight gain above and below recommendations was detected in 47% and 23% of the subjects, respectively [7]. The abovementioned findings question the applicability and usefulness of weight gain guidelines, which for now seem rather theoretical. Some experts believe that routine weigh-ins for pregnant women during antenatal visits do not address the problem, others claim it still remains the simplest, cheapest and commonly accepted way of focusing public attention on the importance of maintaining healthy weight [16].

Excess maternal weight gain is difficult to explain because studies demonstrate that equally in Poland and in other countries, what is found is rather the insufficient supply of energy during pregnancy [2, 9, 11].

In our study, as in other reports from Poland [1, 15, 27, 33] mean pregnancy weight gain among overweight/obese women is lower than normal-weight women, which is a positive finding. Regardless, it is important to bear in mind that the recommended weight gain decreases with increasing BMI of the subjects in the pre-conception period [31]. The most rigorous weight limits are typically set for obese pregnant women as adipose tissue is a storage of fats which are necessary for proper fetal development and, later on, lactation, and need not be increased during pregnancy. The maximum recommended weight gain for obese women is 7 kg lower than for women with normal BMI. For that reason, most sources report that the percentage of women with pre-pregnancy obesity/overweight whose weight gain during pregnancy is above recommendations – even despite lower weight gain in kilograms – is higher than the percentage of women with normal pre-pregnancy BMI but excess gestational weight gain [1, 19, 33].

In our study, we found a 4-fold higher risk for excess weight gain among active smokers, which is yet another negative consequence of smoking, and the solution proves problematic because, according to the literature, quitting smoking after conception – which is recommended to pregnant women – is associated with a 7-fold higher risk for excess weight gain [25]. Despite the fact that the highest (61%) number of women with

weight gain above recommendations was observed among subjects with pre-pregnancy overweight and obesity, no statistically significant relationship between pre-pregnancy BMI and pregnancy weight gain was found, which might be due to a small sample size.

Maternal weight gain below recommendations had a negative impact on the newborn anthropometric parameters (weight, length). Infants born to those mothers were significantly smaller as compared to mothers with normal weight gain. *Szostak-Węgierek et al.*, reported similar relationship [27], in contrast to *Wdowiak et al.* [30] and *Berner-Trąbska et al.* [1], who found no correspondence between maternal weight gain and neonatal weight at birth. According to a meta-analysis of worldwide reports, maternal weight gain below recommendations increases the risk for small for gestational age newborn by 50% [7]. In our study there was no correlation between the anthropometric parameters of newborns and the estimated maternal nutrients intake, as well as supplementation with vitamin/mineral preparations during pregnancy.

It should also be emphasized that, a large percentage of neonatal macrosomia (20%) was found, which was not dependent on any of the factors under analysis. However, literature suggests that the risk of macrosomia is generally two to three times higher in women with excess weight gain [6, 7, 29, 33] and in women with gestational diabetes [10, 32].

Caution is advised when drawing final conclusions as our study was not without limitations, chief among them a small sample size and retrospective nature of the study, including self-reported pre-pregnancy weight. The latter might have affected the credibility of the BMI calculations and the later interpretation, although some authors claim that approximately 90% of pregnant women estimate their pre-pregnancy weight properly [20], which validates such methods of data collection.

## CONCLUSION

Pregnancy weight gain in the majority of the subjects was either below or above recommendations, regardless of their pre-pregnancy BMI. Infants born to mothers with insufficient weight gain were smaller than those born to mothers with normal weight gain.

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### Conflicts of interest

*The authors declare no conflict of interest.*

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## VARIATIONS IN EXPERIENCE OF SOCIAL SUPPORT AND PHYSICAL HEALTH AMONG ADULT RESIDENTS OF POLAND IN URBAN VERSUS RURAL AREAS

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### ABSTRACT

**Background.** A study reveals – against to common beliefs – less support between rural area residents in comparison to town-dwellers and significantly higher support for healthy, not for poor health research participants.

**Objectives.** The aim of our paper was comparing support from spouse/partner, relatives, friends and strangers among people with good and ill physical health. A next purpose was to find differences of social support and experience of social undermining in urban and rural residential settings.

**Material and methods.** The study “Epidemiology of Mental Disorders and Access to Mental Health Care, EZOP – Poland” was carried out on random sample of 24 000 of Poland residents and a 50,4% response rate, 10 081 computer-assisted personal interviews. Of those respondents, 4 000 constituted a sub-sample asked to complete the social networks and support section of the questionnaire. Data were analyzed by age, gender, residential setting and marital status for statistically significant differences in the percentage of functional and structural social support being reported, using the chi-squared test with a significance level of 0.05 used to reject the null hypothesis ( $H_0$  = lack of relationship between variables).

**Results.** A majority of respondents maintain that in difficult life situations, family and a close network of friends and acquaintances make it possible to openly discuss problems and obtain help. However, respondents who rate their health as “poor” or “very poor” significantly less often than healthy individuals experience support coming from their relatives, friends, or strangers.

In comparison to urban areas, the extent of social support in rural areas is significantly limited. The rural setting offers less support and even less opportunities for interaction with relatives, friends, acquaintances and strangers. Negative social factors – low levels of trust, isolation from friends and family, lack of a social life, lack of a helpful neighborhood – are conditions significantly more often found in the countryside than in urban areas.

**Conclusions.** Results obtained from the EZOP study shows that amount of social support received is higher in urban areas and among those who enjoy better physical health.

**Key words:** *relatives and friends support; residential setting; support and health; health status differences; gender differences; social undermining; cultural determinants.*

### STRESZCZENIE

**Wprowadzenie.** Praca odkrywa niezgodną z powszechnymi przekonaniem prawdę, że wieś jest mniej przyjaznym środowiskiem dla swoich mieszkańców niż miasto, a chorzy ludzie, najbardziej potrzebujący wsparcia, otrzymują go znacząco mniej niż zdrowi.

**Cel.** Celem niniejszej pracy jest porównanie wsparcia, jakie uzyskują osoby w dobrym i złym stanie zdrowia ze strony współmałżonka (partnera), rodziny, przyjaciół i obcych. Kolejnym celem jest ocena różnicy w uzyskiwanym wsparciu, a także przejawach zaprzeczenia wsparcia przez mieszkańców miast i wsi.

**Material i metody.** Badanie „Epidemiologia zaburzeń psychiatrycznych i dostęp do psychiatrycznej opieki zdrowotnej – EZOP Polska” zostało zrealizowane na próbie losowej 24 tysięcy mieszkańców Polski. Przy 50,4% poziomie realizacji wywiadów przeprowadzono 10 081 wywiadów indywidualnych wspomaganym komputerowo. Następnie

wyodrębniono 4 000 respondentów, którzy odpowiedzieli na pytania o relacje społeczne i wsparcie społeczne. W analizie uwzględniono podział według wieku, płci, środowiska zamieszkania i stanu cywilnego. Ustalono istotne statystycznie różnice w uzyskiwanym wsparciu strukturalnym i funkcjonalnym przy zastosowaniu testu chi-kwadrat, zakładając poziom ufności 0,05 do odrzucenia hipotezy zerowej ( $H_0$  = brak związku między zmiennymi).

**Wyniki.** Większość respondentów utrzymuje, że rodzina oraz krąg bliskich przyjaciół i znajomych - w trudnych sytuacjach życiowych - stwarza warunki do otwartego omówienia problemu i otrzymania pomocy. Niemniej respondenci, którzy oceniają swoje zdrowie jako „złe” i „bardzo złe” istotnie rzadziej doświadczają wsparcia, niż osoby zdrowe. Zakres wsparcia społecznego na terenach wiejskich jest znacząco ograniczony w porównaniu ze wsparciem wśród mieszkańców miast. W środowisku wiejskim stwierdzamy mniej wsparcia, a nawet mniej możliwości spotkania z członkami rodziny, przyjaciółmi, znajomymi lub obcymi. Również na wsi istotnie częściej niż na terenach zurbanizowanych obserwujemy działanie takich negatywnych czynników jak niski poziom zaufania społecznego, izolację wobec rodziny i przyjaciół, brak życia towarzyskiego, oraz brak pomocnego sąsiedztwa.

**Wnioski.** Wyniki badania EZOP wskazują, że zakres otrzymywanego wsparcia społecznego jest istotnie wyższy w środowiskach miejskich, oraz wśród osób cieszących się lepszym zdrowiem fizycznym.

**Słowa kluczowe:** *wsparcie w rodzinie; wsparcie przyjaciół; miejsce zamieszkania; wsparcie społeczne i zdrowie; różnice w stanie zdrowia; podział według płci; zaprzeczenia wsparcia; determinanty kulturowe.*

## INTRODUCTION

Susceptibility to illness, as well as the effects of illness and treatment outcomes may depend on the quality of social support provided by those nearest to the patient [1-8]. The study “Epidemiology of Mental Disorders and Access to Mental Health Care, EZOP – Poland” was carried out from 2010 to 2011 by the Institute of Psychiatry and Neurology (IPiN) in Warsaw, together with the National Institute of Public Health (NIZP-PZH) in Warsaw and the Psychiatry Department and Clinic at Wrocław Medical University [9]. Results obtained from the EZOP study shows that amount of social support received is higher in urban areas, for women and among those who enjoy better physical health.

The lengthy World Health Organization’s Composite International Diagnostic Interview (WHO-CIDI) questionnaire, translated into Polish and used for the study as the EZOP questionnaire, contained a section pertaining to social networks and support from family and close friends. The following were identified and studied as sources of social support in the EZOP Project: meetings and (phone) conversations engendering a sense of belonging – with one’s spouse/committed partner, with relatives (interactions and conversations), with friends and acquaintances (interactions and conversations), and with strangers/others (conversations). If the respondent had a serious problem or needed to talk to someone, he or she was asked how much she/he can rely on the support of a) spouse/partner, b) relatives not living with him/her, c) friends/acquaintances, d) other people. Questions asking the respondents to self-rate their symptoms and condition of physical health were used to gauge the state of their health.

## AIMS

Our paper aims to answer the following research questions:

Q1: Is the degree of social support in the two identified residential settings (urban vs. rural) the same or different?

Q2: Does *social undermining* occur in both settings equally often? Does the residential setting influence how social support is experienced or perceived? What about the experience of social undermining or denial of social support in the two settings [10]?

Q3: Who receives less social support from their spouse/partner, relatives, friends and strangers – those who are well or those who are ill in urban and rural areas?

## MATERIALS AND METHODS

Given a random sample of 24 000 of Poland’s residents, and a 50.4% response rate, 10 081 computer-assisted personal interviews were carried out. Of those respondents, 4 000 constitute a sub-sample asked to complete the social networks and support section of the questionnaire. The sub-sample consists in all respondents with mental disorders as well as their randomly selected counterparts.

The analysis presented in this paper is focused on functional and structural social support, based on answers that were given by 3 999 respondents of which 61.1% lived in the urban areas while 38.9% in rural areas.

*Measures of structural social support*, included answers to questions about the frequency of interactions with acquaintances, friends, family and spouse/partner, as well as demographic variables: the respondent’s residential setting, gender, education completed and marital status.

Measures of functional social support on the other hand, include how much the respondent can rely on help from family, friends and acquaintances in case of problems, how open he or she can be with them and how often he or she has conflicts or argues with them (reverse-coded) [11]. An example of such a reverse-coded question was: *Not including your (husband/wife, partner) how often do your relatives argue with you – (often, sometimes, rarely, or never)?* Another question, structured the same way, was asked about relatives placing too many demands on the respondent. Two analogous questions were asked about disagreements with and demands made by friends (see Annex).

Data were analyzed by age, gender, residential setting and marital status for statistically significant

differences in the percentage of functional and structural social support being reported, using the chi-squared test with a significance level of 0.05 used to reject the null hypothesis ( $H_0$  = lack of relationship between variables).

## RESULTS AND DISCUSSION

### SOCIAL SUPPORT ACCORDING TO RESIDENTIAL SETTING

As the tables illustrate, residents of rural areas receive significantly less support than residents of urban areas.

Table 1. Structural social support: Frequent interactions (conversations, meetings, phone calls) with the following people

Setting: Who:	Urban			Rural			Total		
	Percentages	95% CI		Percentages	95% CI		Percentages	95% CI	
Partner/spouse	71.7	69.1	74.2	76.5	73.4	79.4	73.6	71.6	75.5
Relatives living separately	81.6	81.5	84.9	78.6	78.8	83.3	80.4	81.1	83.8
Friends and acquaintances	88.1	86.5	89.5	82.9	80.6	85.0	86.1	84.8	87.3
Others	55.5	53.2	57.7	52.4	49.5	55.3	54.3	52.5	56.1

Table 2. Functional social support: Trust and degree of perceived help

Setting: Support:	Urban			Rural			Total		
	Percentages	95% CI		Percentages	95% CI		Percentages	95% CI	
Being open with relatives	70.8	68.7	72.8	67.0	64.2	69.7	69.3	67.7	70.9
Being open with friends and acquaintances	65.4	63.2	67.5	57.9	55.1	60.7	62.5	60.8	64.2
Perceived help from relatives	73.4	71.4	75.4	72.2	69.5	74.7	73.0	71.3	74.5
Perceived help from friends and acquaintances	20.3	18.5	22.2	15.0	13.1	17.1	18.2	16.9	19.7

### SOCIAL SUPPORT – STRUCTURAL VARIABLES

The EZOP study reveals that interactions with friends and acquaintances are more frequent than interactions with relatives who do not live with the respondent. In cities, the frequency of interactions (meetings in person, phone conversations) with acquaintances and friends is significantly higher than in the countryside. However, overall, Poles are more trusting and open towards their relatives than with friends; rural residents being

somewhat less open and trusting towards relatives than respondents living in cities.

When in need, in case of a serious problem, respondents indicated that they rely on their family for help [12, 13]. Friends and acquaintances were identified as a source of support four times less often than relatives living in a separate household. Rural residents less frequently expect direct help from friends and acquaintances than respondents living in urban areas [14].

## SOCIAL SUPPORT – FUNCTIONAL VARIABLES

Respondents who are equally open with family and friends/acquaintances are as often found in rural areas (9.6%) as in urban areas (10.5%) [15]. Men residing in cities (8.0%) reported being able to open up slightly more often in their interactions than their rural counterparts (7.3%). Likewise, female urban residents believe they can talk about their problems more often (12.8%) than do women living in rural areas (11.8%). The highest statistically significant difference in the ability to talk about one's problems was found between men in the countryside (7.3%) and women living in cities (12.8%).

One should ask whether respondents who are open towards friends and relatives are also equally open with their spouse or partner. Regardless of where they live, women are significantly more likely to talk openly with their partner/spouse (12.4%) than are men (7.7%). This difference between the sexes is also true

concerning conversations with relatives and friends. Women declare a greater willingness than men do to openly discuss their problems [16].

## DENIAL OF SOCIAL SUPPORT – CONFLICTS AND EXCESSIVE DEMANDS

*Social undermining*, the opposite of social support, is the intentional contestation of somebody's position, which is detrimental to self-esteem, social reputation and others' view of one's ability to maintain positive interpersonal relations [17].

The behavior of one's less-immediate family can be hostile or unfriendly at times. Still, those who live in the countryside report slightly less frequent overt denial of social support on the part of their relatives, when compared to respondents in cities. Rural residents indicate that their relatives argue/have conflicts with them slightly less often than do their counterparts living in urban areas – and this difference borders on being significant.

Table 3. Social undermining among relatives

Q: How often do your relatives argue with you?							
Social undermining:	Setting:	Urban		Rural		Total	
		Percentages	95%CI	Percentages	95%CI	Percentages	95%CI
Rarely, never		80.7	78.9-82.4	83.1	80.9-85.2	81.7	80.3-83.0
Often, sometimes		19.3	17.6-21.1	16.9	14.8-19.1	18.3	17.0-19.7

Table 4. Social undermining among friends

Q: How often do your friends make too many demands on you?							
Social undermining:	Setting:	Urban		Rural		Total	
		Percentages	95%CI	Percentages	95%CI	Percentages	95%CI
Rarely, never		84.3	82.6-85.9	88.1	86.1-89.8	85.8	84.5-87.0
Often, sometimes		15.7	14.1-17.4	11.9	10.2-13.9	14.2	13.0-15.5

The contrast between urban and rural settings when it comes to being subject to excessive demands of friends is as follows: 16.6% of respondents in cities compared to only 11.9% in the countryside report feeling that their friends' demands are excessive. This difference is statistically significant.

## SOCIAL SUPPORT AND PHYSICAL HEALTH

The social support network may play a crucial role in one's ability to cope with a serious illness [18-21]. We investigated whether in case of

illness the social network increases or denies its support, and whether this pattern is similar in cities and in the countryside.

### Relatives

Respondents who are ill and live in the country report being isolated from their relatives more often (24.3%) than their city-dwelling counterparts (21.6%). Similar results were obtained from healthy respondents, with 19.2% feeling isolated in the country and 16.7% in cities.

Respondents who reported that they do not receive help from their relatives constituted 28.1% of the whole sample. Among those who are ill, the percentage is higher: 35.1% in the countryside and 35.4% in urban areas. Thus, regardless of where they live, individuals in worse physical health count on help from relatives less often than do healthy individuals.

Worse physical health is also linked to lower levels of openness and trust towards relatives. 34.1% of ill respondents said they cannot be open with their relatives, compared to 31.6% of respondents whose health is satisfactory and 29.3% of respondents who are in perfect health. Isolation and lack of an open atmosphere among relatives is described by 34.0% of ill respondents in cities and by 34.2% in the country. This difference between residential settings is small and statistically insignificant.

About one third of ill respondents in urban areas feel their relatives demand too much from them while a corresponding figure in the countryside is about one fifth.

City residents in poor physical health report conflicts with relatives significantly more often (26.0%) while in the countryside only 12.4% of ill respondents mentioned family conflicts, which is suggestive of a rather agreeable environment.

### Friends and acquaintances

About 15% of all respondents, regardless of their health status, see their friends' expectations as excessive.

Nearly all healthy residents of urban areas (91.7%) mentioned frequent contact with their friends [22]. Healthy residents of rural areas maintaining frequent contact with friends and acquaintances constitute 87.8% of their group, which is less than in urban areas. The percentage of city-dwelling ill respondents maintaining such contacts is lower (80.4%), compared to even lower percentage of ill rural residents (71.9%).

16.7% of rural residents, who declare being in good health, are likely to receive help from their friends and acquaintances, compared to 13.4% of those who report that their health is bad. In urban areas, 23.2% of respondents who identify themselves as healthy count on the help of friends and acquaintances, but only 10.1% of ill individuals do. This difference is statistically significant.

Among healthy female respondents there is a clear difference depending on the place of residence. 25.5% of healthy women residing in cities say they can count on the help of friends, compared to only 14.5% of healthy female residents of rural areas.

The data used in this study reveal statistically significant differences in the situation of respondents, depending on whether they are in good or poor physical health. In general, ill respondents perceive less openness

in relations with their friends than do respondents who are healthy, regardless of whether they live in the city or in the country.

### Spouse/partner

Only in urban areas does illness play a role in how often personal problems are discussed with one's spouse or partner [23]. When compared to healthy city residents (73.7%), urban residents who are ill significantly less often count on the support of their spouse or partner (63.9%).

### Someone else

Poor health tends to significantly reduce trust [24] and the frequency of interactions with strangers and individuals with whom one is less acquainted. In urban areas, 58% of healthy respondents feel they can talk to strangers about their worries or problems, compared to only 46% of respondents who are ill. In the countryside, 55% of healthy respondents reported talking to strangers about their problems, while only 42.8% of respondents in poor health did the same. All of the above differences are statistically significant.

## CONCLUSIONS

1. A vast majority of respondents maintain that in difficult life situations, family and a close network of friends and acquaintances make it possible to openly discuss problems and obtain help. However, respondents who rate their health as "poor" or "very poor" significantly less often than healthy individuals experience support coming from their relatives, friends, or strangers.
2. In comparison to urban areas, the extent of social support in rural areas is significantly limited. The rural setting offers less support (in terms of functional variables) and even less opportunities for interaction (structural variables) with relatives, friends, acquaintances and strangers. Negative social factors – low levels of trust, isolation from friends and family, lack of a social life, lack of a helpful neighborhood – are conditions significantly more often found in the countryside than in urban areas.
3. Female respondents more frequently perceive that they are the recipients of social support. Likewise, respondents who are in a committed relationship, be it with a spouse or partner, also report receiving more support.

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### ANNEX SURVEY QUESTIONS

How often do you talk on the phone or get together with relatives who do not live with you – most every day, a few times a week, a few times a month, about once a month, or less than once a month?

MOST EVERY DAY.....	1
A FEW TIMES A WEEK.....	2
A FEW TIMES A MONTH.....	3
ONCE A MONTH.....	4
LESS THAN ONCE A MONTH.....	5
DON'T KNOW.....	8
REFUSED.....	9

How often do you talk on the phone or get together with friends – most every day, a few times a week, a few times a month, about once a month, or less than once a month?

MOST EVERY DAY.....	1
A FEW TIMES A WEEK.....	2
A FEW TIMES A MONTH.....	3
ONCE A MONTH.....	4
LESS THAN ONCE A MONTH.....	5
DON'T KNOW.....	8
REFUSED.....	9

How much can you rely on relatives who do not live with you for help if you have a serious problem – a lot, some, a little, or not at all?

A LOT.....	1
SOME.....	2
A LITTLE.....	3
NOT AT ALL.....	4
DON'T KNOW.....	8
REFUSED.....	9

How much can you rely on your friends for help if you have a serious problem – a lot, some, a little, or not at all?

A LOT.....	1
SOME.....	2
A LITTLE.....	3
NOT AT ALL.....	4
DON'T KNOW.....	8
REFUSED.....	9

How much can you open up to relatives who do not live with you if you need to talk about your worries – (a lot, some, a little, or not at all)?

A LOT.....	1
SOME.....	2
A LITTLE.....	3
NOT AT ALL.....	4
DON'T KNOW.....	8
REFUSED.....	9

How much can you open up to your friends if you need to talk about your worries – (a lot, some, a little, or not at all)?

A LOT.....	1
SOME.....	2
A LITTLE.....	3
NOT AT ALL.....	4
DON'T KNOW.....	8
REFUSED.....	9

How often do your relatives make too many demands on you – often, sometimes, rarely, or never?

OFTEN.....	1
SOMETIMES.....	2
RARELY.....	3
NEVER.....	4
DON'T KNOW.....	8
REFUSED.....	9

How often do your friends make too many demands on you – often, sometimes, rarely, or never?

OFTEN.....	1
SOMETIMES.....	2
RARELY.....	3
NEVER.....	4
DON'T KNOW.....	8
REFUSED.....	9

How often do your relatives argue with you – (often, sometimes, rarely, or never)?

OFTEN.....	1
SOMETIMES.....	2
RARELY.....	3
NEVER.....	4
DON'T KNOW.....	8
REFUSED.....	9

How often do your friends argue with you – (often, sometimes, rarely, or never)?

OFTEN.....	1
SOMETIMES.....	2
RARELY.....	3
NEVER.....	4
DON'T KNOW.....	8
REFUSED.....	9

When you have a problem or worry, how often do you let your (husband/wife/partner) know about it – always, most of the time, sometimes, rarely, or never?

ALWAYS .....	1
MSOT OF THE TIME .....	2
SOMETIMES .....	3
RARELY .....	4
NEVER .....	5
DON'T KNOW .....	8
REFUSED .....	9

When you have a problem or worry, how often do you let someone (else) know about it – always, most of the time, sometimes, rarely, or never?

ALWAYS .....	1
MSOT OF THE TIME .....	2
SOMETIMES .....	3
RARELY .....	4
NEVER .....	5
DON'T KNOW .....	8
REFUSED .....	9

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## FOOD AS A SOURCE OF EXPOSURE TO NICKEL

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### ABSTRACT

According to the European Food Safety Authority (EFSA), food is the main source of nickel intake by the general population. Based on the risk assessment, EFSA determined the tolerable daily intake of this element (TDI) from all sources at the level of 2.8 µg/kg body weight, which is for an adult 196 µg, while for a child 56 µg. The Benchmark Dose Lower Confidence Limit (BMDL<sub>10</sub>) associated with dermatitis at 1.1 µg/kg body weight was also determined as well as the Margin of Exposure (MOE). Nickel intake in the Member States varies and depends on consumption habits. CONTAM Panel of EFSA considered the unlikely possibility of developing cancers related to the intake of nickel with food. According to experts, other harmful effects on the human body are more often identified. An additional aspect requiring further investigations that will allow an actual estimation of exposure associated with intake of this element by various groups of population is the issue of nickel absorption in the human body. The review of the EFSA opinion on the request of the European Commission planned in the near future based on the collected data as part of the action of the Commission Recommendation (EU) 2016/1111 on monitoring the presence of nickel in food will contribute to taking appropriate actions related to consumer protection, including the most vulnerable groups of population.

**Key words:** *nickel/toxicity, foodstuffs, dietary exposure, sources of exposure*

### STRESZCZENIE

Według Europejskiego Urzędu ds. Bezpieczeństwa Żywności (EFSA), głównym źródłem pobrania niklu przez populację generalną jest żywność. Na podstawie dokonanej oceny ryzyka EFSA wyznaczył wartość tolerowanego dziennego pobrania tego pierwiastka (Tolerable Daily Intake TDI) ze wszystkich źródeł na poziomie 2,8 µg/kg masy ciała, co stanowi dla osoby dorosłej 196 µg, natomiast dla dziecka 56 µg. Określono również najniższą dawkę wyznaczającą (Benchmark Dose Lower Confidence Limit) – BMDL<sub>10</sub> związaną z występowaniem zapaleń skórnych na poziomie - 1,1 µg/kg masy ciała oraz wyznaczono wartość marginesu narażenia (Margin of Exposure – MOE). Pobranie niklu w państwach członkowskich jest zróżnicowane i zależne od nawyków żywieniowych. Panel CONTAM EFSA uznał za mało prawdopodobną możliwość powstawania nowotworów związanych z pobraniem niklu z żywnością. Zdaniem ekspertów znacznie częściej identyfikowane są inne efekty szkodliwe na organizm człowieka. Dodatkowym aspektem wymagającym dalszych badań, który pozwoli na rzeczywiste oszacowanie narażenia związanego z pobraniem tego pierwiastka przez różne grupy populacji, jest kwestia wchłaniania niklu w organizmie człowieka. Planowana w najbliższym czasie na wniosek Komisji Europejskiej rewizja opinii EFSA, w oparciu o zgromadzone dane w ramach zalecenia Komisji (UE) nr 2016/1111 w sprawie monitorowania obecności niklu w żywności, przyczyni się do podjęcia odpowiednich działań związanych z ochroną konsumentów, w tym najbardziej wrażliwych grup populacji.

**Słowa kluczowe:** *nikiel/toksyczność, środki spożywcze, żywność, narażenie człowieka z diety, źródła narażenia*

### INTRODUCTION

Nickel is an element widely distributed in nature and is present in water, soil, plants and animals [28, 30]. Its biological function in humans is not clear and there is no data indicating its essential role for humans [4, 28]. However for plants and some animals Ni is an essential micronutrient. In higher plants this element is an integral part of enzymes which participate in the

metabolism of nitrogen [31]. Higher concentrations could lead to several harmful alterations in plants. It was found that its optimal concentration in plants tissues should not exceed 3 mg/kg. The higher levels affect the development of plants in a degree depending on their sensitivity [15]. This element is also present in all animal tissues at levels up to several ppm. Due to its chemical properties, such as: hardness, high melting point, ductility, nickel is used as part of alloys.

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It imparts such desirable properties as corrosion resistance, heat resistance, hardness, and strength [14, 19].

Nickel containing stainless steel is widely preferable in the food industry because of its durability, lack of reactivity with foods and excellent conductivity [19]. Nickel alloys are also used for production of coins, jewelry while compounds of this element find application in ceramic production as pigments and in battery production [17, 28].

## SOURCES OF EXPOSURE TO NICKEL

Nickel can occur in the environment in the various form, generally occurs in the divalent form, as this is its most stable oxidation state [12, 28]. Plants are one of the major sources of exposure to nickel. The concentration of nickel in plants is dependent on the content of this element in the soil [25, 31]. Ni in agricultural soils has been reported at concentrations in the range from 3 mg/kg to 1000 mg/kg [28, 31]. According to monitoring data of Institute of Soil Science and Plant Cultivation – State Research Institute the average content of nickel in soils in Poland is 9.8 mg/kg. The highest nickel contamination is observed in the malopolskie voivodship, which is caused in large measure by industrial activity.

Significant sources of nickel contamination besides natural presence as an effect of volcanic eruptions, windblown dust, forest fires include anthropogenic activity, such as: coal burning processes, liquid fuels, primarily expelled by Diesel engines, the mining industry, production of paints, enamels and plastics [17, 20, 28, 30]. Nickel is commonly used as a raw material in metallurgical and electroplating industry is also used as a catalyst in chemical industry [17, 31] as well as in the fat industry, in the production of margarines and other food fats where nickel is used as a catalyst in the hydrogenation process. Occupational exposure to nickel is connected with elevated levels of this element in blood, urine and body tissues.

The main source of nickel exposure for general population is food and water [12, 17, 36, 37], other sources like dermal contact as well as air inhalation can contribute to exposure to this element. In the air, mainly its inorganic compounds occur such as sulfates, sulfides and nickel oxides. The levels found are usually much lower than those typically found in occupational situations. Nickel can also be released from food contact materials covered with nickel plated or containing this element as an alloy component. The research indicates that migration is higher in the presence of acidic food or food ingredients such as rhubarb and citric acid.

Foodstuffs that are the main contributors to the dietary exposure to nickel in case of general population are: grain and grain-based products, nonalcoholic

beverages (except milk-based beverages), sugar and confectionery, legumes, nuts and oilseeds, and vegetables and vegetable products (including fungi), milk and dairy products especially for the young population, in particular in toddlers. Chocolate and chocolate-based product as well as sugar and confectionery, non-alcoholic beverages are important contributors to nickel intake for children and adolescents [28].

## TOXICITY AND EFFECT ON HUMAN HEALTH

Toxicity of nickel is dependent on the chemical form, the route of exposure and solubility of nickel compounds. In 2012 compounds of this element were classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans (Group 1), while metallic nickel and nickel alloys as possibly carcinogenic to humans (Group 2B) [12, 14, 28]. For occupationally exposed population the respiratory tract and the skin are the major routes of exposure. Ni compounds are carcinogenic to humans after inhalation causing cancers of the lung, nasal cavity and paranasal sinuses [14]. Allergic contact dermatitis is the most frequent effect of Ni in the general population [17, 28, 37]. In humans, the non-carcinogenic effects of oral exposure to nickel include effects on the gastrointestinal, hematological, neurological and immune system [12, 17, 28].

Absorption of nickel from the gastrointestinal tract varies between 3-40 % depending on whether the nickel was in drinking water or food, with greater absorption occurring with drinking water. Fasting individuals have also been shown to absorb more nickel from the gastrointestinal tract than when food is present [12]. One of the factors that can influence, reducing the absorption of nickel from food is the co-ingestion of vitamin C and iron [26]. Most of the absorbed nickel is excreted in the urine, regardless of the route of exposure. About 20%-35% of the inhaled nickel that is retained in the lungs is absorbed into the blood [28].

The mechanism of nickel carcinogenic action is still the subject of numerous studies and still requires clarification, similar to the absorption from the gastrointestinal tract. It has been proved that this element causes disturbance of DNA synthesis, inhibition of its repair processes and loss of DNA sequence [1, 24, 30]. In 2008 WHO set a TDI of 0.012 mg/kg bw/day this value was confirmed in 2011. In 2005 the EFSA Scientific Panel on Dietetic Products, Nutrition and Allergies was not able to establish a tolerable upper intake level for intake of nickel from food due to inadequate data for dermal reactions [20].

Table 1. Contents of nickel in different categories of foodstuffs, ( $\mu\text{g}/\text{kg}$ ) [28]

Foodstuffs	n	LC (%)	LB/UB	Concentration ( $\mu\text{g}/\text{kg}$ )	
				Mean	P95
Grains and grain-based products	4291	26	LB	271	1069
			UB	321	1078
Vegetables and vegetable products (including fungi)	3738	26	LB	742	9250
			UB	753	9250
Starchy roots and tubers	664	24	LB	123	690
			UB	150	690
Legumes, nuts and oilseeds	1218	3	LB	1862	7000
			UB	1880	7000
Fruit and fruit products	966	31	LB	68	210
			UB	91	300
Meat and meat products (including edible offal)	2169	66	LB	191	310
			UB	239	500
Fish and other seafood	718	61	LB	77	330
			UB	112	390
Milk and dairy products	631	62	LB	71	435
			UB	93	488
Eggs and egg products	115	74	LB	38	179
			UB	57	179
Sugar and confectionery	1170	26	LB	1504	5170
			UB	1586	5170
Animal and vegetable fats and oils	363	58	LB	315	360
			UB	378	500
Fruit and vegetable juices	505	30	LB	35	102
			UB	58	120
Non-alcoholic beverages (excepting milk based beverages)	46	24	LB	32	-
			UB	35	-
Alcoholic beverages	892	69	LB	28	70
			UB	71	150
Drinking water	25700	89	LB	1	2
			UB	2	3
Herbs, spices and condiments	481	18	LB	1259	4640
			UB	1277	4640
Food for infants and small children	309	45	LB	126	500
			UB	152	500
Products for special nutritional use	471	26	LB	1999	9100
			UB	2051	9100
Composite food (including frozen products)	65	9	LB	181	490
			UB	184	490
Snacks, desserts, and other foods	73	62	LB	111	280
			UB	430	1200

n: number of samples; LC: left-censored data (percentage of analytical data below LOD/LOQ); LB: lower bound (results below the LOQ and LOD were replaced by zero in calculations); UB: upper bound (the results below the LOD were replaced by the LOD and those below the LOQ were replaced by the value reported as LOQ; mean; 95th percentile.

## EFSA OPINIONS ON NICKEL

In 2015 on request of Hellenic Food Safety Authority the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) published a scientific opinion on the risk to human health associated with the presence of nickel in food and drinking water. Based on available epidemiological data and occurrence data the EFSA established a tolerable daily intake (TDI) of  $2.8 \mu\text{g Ni}/\text{kg}$  body weight (b.w.) per day. The benchmark dose lower limit  $\text{BMDL}_{10}$  of  $1.1 \mu\text{g Ni}/\text{kg}$  b.w. associated with dermatitis following oral exposure to Ni based on

dose-response analysis was also determined. For risk characterization the CONTAM Panel decided not to establish an acute reference dose, but to adopt a margin of exposure (MOE) approach. Calculated value of MOE taking into account mean and 95th percentile acute exposure for all groups of population was below 10 which indicated to be of health concern. EFSA considered that it is unlikely that dietary exposure to Ni results in cancer in humans and only non-carcinogenic health effects of oral exposure to Ni include effects on the gastrointestinal, haematological, neurological and immune system can occur. Effects of acute exposure to nickel are connected

with gastrointestinal and neurological symptoms while exposure through skin or by inhalation may lead to Ni sensitization. Whereas oral exposure to Ni is not known to lead to sensitization, oral absorption of Ni is able to elicit eczematous flare-up reactions in the skin in Ni-sensitized individuals [28].

In 2015 EFSA also published scientific opinion concerning risk to animal, public health and the environment related to the presence of nickel in feed. This risk assessment was performed on a request of European Commission. EFSA assessed that any adverse impact of Ni via feed to animals is unlikely. Whereas risks from the presence of Ni in food of animal origin, might be of potential concern in the young population, in particular in toddlers, and other children taking into account chronic average exposure. In case of acute dietary exposure, in Ni-sensitized people different types of skin reactions associated with taking nickel from food of animal origin can occur [29].

### OCCURRENCE OF NICKEL IN FOOD

The average content of nickel in food is lower than 0.5 mg/kg, but there are foodstuffs with higher levels of this element [5, 26]. The highest mean concentrations of Ni have been measured in wild growing edible mushrooms, cocoa or cocoa-based products which contain above 10 mg/kg dry weight, beans, seeds, nuts and grains e.g. cocoa beans - 9.8 mg/kg; soybeans - 5.2 mg/kg; soya products - 5.1 mg/kg; walnuts - 3.6 mg/kg; peanuts - 2.8 mg/kg; oats - 2.3 mg/kg; buckwheat - 2.0 mg/kg; and oatmeal - 1.8 mg/kg [14, 27, 28]. Studies of total diet conducted in France indicate slightly lower average nickel contamination for nuts and oilseeds 1.15 mg/kg, chocolate - 0.63 mg/kg and breakfast cereals at 0.55 mg/kg and significantly lower for other groups of foodstuffs – much below 0.5 mg/kg [16]. Subsequent studies from 2012 indicate significantly higher contamination for chocolate and dried fruit, nuts and seeds and lower in case of for breakfast cereals [3].

Ni concentrations of about 30 µg/L and of 100 µg/L have been found in beer and wine; respectively [28]. Concentration of nickel in food is depending on different factors such as: the type of food, growing conditions (i.e. higher concentrations have been observed in food grown in areas of high environmental or soil contamination), and food preparation techniques (e.g. Ni content of cooking utensils, although the evidence for leaching from stainless steel cookware is somewhat mixed) [14, 26]. The nickel content in food also varies according to climate and season. Higher concentration of this element was observed in crops fruit and vegetables grown in spring and autumn in comparison to crops from summer. For above mentioned reasons content of nickel in foodstuffs very often appear to vary according to the sources, and differences are sometimes significant [26].

A total diet study conducted in Spain revealed nickel concentration between 2.35 mg/kg in nuts and 0.002 mg/l in drinking water [13].

Other studies on the nickel content in foods for infants and young children conducted in UK showed an average contamination of this group of foods at the level of 0.1 mg/kg (0.002 mg/kg - 1.4 mg/kg) [28]. Occurrence data collected by EFSA in 15 different European countries between 2003 and 2012 most of them in Germany (80 %) concerned mainly drinking water, food data were relatively scarce. Data collected by EFSA are presented in Table 1.

### INTAKE OF NICKEL WITH FOOD

Intake of nickel with food can vary widely not only among different population groups but also in a single individual in different seasons and different days. Factors which can may have influence on the intake are also national and regional dietary habits, diversity of foodstuffs consumed, contamination of drinking water, migration from food contact materials, preparation process of food, absorption in the gastrointestinal tract etc.

According to EFSA mean chronic dietary exposure to Ni across the different dietary surveys and age classes ranged from 2.0 µg/kg b.w. per day (elderly) to 13.1 µg/kg b.w. per day (toddlers). The 95th percentile dietary exposure ranged from 3.6 µg/kg b.w. per day (elderly) to 20.1 µg/kg b.w. per day (toddlers). The highest dietary exposure to Ni was observed in the age classes toddlers and other children. The adult population showed, in general, lower exposure than the young population (2.2 µg/kg b.w. per day ÷ 3.6 µg/kg b.w. per day). Similar results were obtained in investigation of daily diets led in Poland and covering Lublin province. The average daily intake of nickel was 99 µg - 133 µg and 130 µg - 178 µg in women and men diets [18]. Studies of total diet conducted in France indicate that the main contributors to the dietary exposure in children aged 13-36 months are chocolate-based products [2]. The main contributors to the dietary intake of this element by adults are: alcoholic beverages and fruits (9%), followed by water (8%) and vegetables excluding potatoes (7%) [3]. Assessed in other studies mean exposure of the French population to nickel was 2.33 µg/kg b.w. per day in adults and 3.83 µg/kg b.w. per day in children. At the 95th percentile, exposure was estimated 3.76 µg/kg b.w. per day in adults and 7.44 µg/kg b.w. per day in children and was higher than in the earlier investigations in this area about 25-50% [3].

Studies conducted in UK concerning intake of nickel with foodstuffs concluded that dietary exposure to nickel were unlikely to be of toxicological concern [11, 12].

## MIGRATION OF NICKEL FROM FOOD CONTACT MATERIALS

Food contact materials can be additional important source of human exposure to nickel by migration of this element into food or drinking water. Nickel is widely used in the production of high quality, corrosion resistant alloys with iron, copper, aluminum, chromium, zinc and molybdenum. Nickel containing stainless steels are very commonly used for production of e.g. process equipment, cook wares, milk and wine tanks. Nickel plated items are less durable and corrosion resistant than stainless steels and therefore not commonly used for articles in contact with food. EFSA in their opinion concluded that release of nickel may not be negligible for food contact materials made of poor quality stainless steel, or of other nickel containing metal alloys [28].

Other nickel compounds like nickel oxide is used for enamel frits and in ceramic glazes. Nickel carbonate is used for colouring ceramics and in glazes [34]. At present, as recommended by the Council of Europe, manufacturers of food preparation and handling tools and equipment made of stainless steel should respect the migration of Ni compliant with a specific release limit (SRL) of 0.14 mg/kg food [19].

Currently, mainly due to the lack of legal requirements in the EU legislation regarding the migration of nickel from food contact materials, Member States conduct such tests in a very limited scope.

## CONTACT ALLERGY TO NICKEL

The most frequently observed effects of nickel toxicity on the human body are different type skin allergic reactions [17, 26, 28, 32, 33]. Well known and described in literature are cases of sensitization caused by the use of kitchen utensils containing nickel and its alloys as well as use of jewelry covered with nickel. In recent years, quite common practices of piercing various parts of the body have paid special attention [26]. This type of treatments may also be associated with exposure to this allergen and the occurrence of various specific reactions. Studies confirm that rubbing the skin and sweating increase the release of nickel from jewelry and other everyday items therefore the intensification of contact hypersensitivity symptoms is mainly observed during the warm seasons [26].

Additional route of exposure to nickel and its compounds is iatrogenic exposure, which can result from implants and prostheses made from nickel containing alloys, from intravenous or dialysis fluids and from radiographic contrast media [30]. Scientific research confirms that about 20% of the general population in Europe suffering from nickel allergy [26].

## FOOD LEGISLATION

There are currently no maximum levels in the EU legislation for Ni in food. Also at the *Codex Alimentarius* level such requirements have not been established.

The highest acceptable levels of nickel in drinking water, natural mineral, spring and table waters at the level of 0.020 mg/l are regulated by the ordinances of the Minister of Health implementing Directives 98/83/EC and 2003/40/EC [22, 23]. Codex Standard for natural mineral water 108-1981 also set limit for nickel in waters at the level of 0.02 mg/l [6]. For food additives, nickel is included in the purity criteria in the range 1 mg/kg to 200 mg/kg.

In Poland, prior to accession to the EU, in accordance with national legislation, nickel content limits were applicable in such foodstuffs as hydrogenated fats and oils and margarine at the level 0.20 mg/kg [21].

There is also no regulatory limit for release of Ni from food contact materials in the EU except specific release limit (SRL) from metals and alloys used in food contact materials and articles, but this limit is not obligatory [19].

## EUROPEAN COMMISSION RECOMMENDATIONS

Due to the limited amount of representative data from the entire EU area in the scope of nickel contamination of food and feed, enabling appropriate actions in the area of risk management, the European Commission has decided to monitor the level of this contaminant during the years 2016-2018 [7, 8].

For food, the focus was first on data collection for those foodstuffs that have a significant contribution in dietary exposure and for which only limited occurrence data on the presence of nickel were available. Foodstuffs included in the monitoring were as follows: cereals, cereal-based products, infant formula, follow-on formula, processed cereal-based food for infants and young children, baby food, food for special medical purposes intended specifically for infants and young children, food supplements, legumes, nuts and oil seeds, milk and dairy products, alcoholic and non-alcoholic beverages, sugar and confectionery (including cocoa and chocolate), fruits, vegetables and vegetable products (including fungi), dry tea leaves, dry parts of other plants used for herbal infusions and bivalve molluscs.

The European Commission has extended the monitoring of levels of this element also to feed due to the use of metallic nickel as a catalyst in their production, although EFSA did not directly confirm that any adverse impact of Ni via feed to animals is possible.

Concerning the assessment of human health risks from the presence of Ni in food of animal origin, EFSA concluded that in the average population the current levels of chronic exposure to Ni, considering only foods of animal origin, might be of potential concern in the young population. In case of acute dietary exposure the Authority concluded that nickel-sensitized individuals are also at risk of developing eczematous flare-up skin reactions through the consumption of food of animal origin.

In order to ensure that the samples are representative for the sampled lot, Member States used procedure laid down in Commission Regulation (EC) No 152/2009 [9]. In case of food samples in order to ensure representatives for the sampled lot sampling was performed in accordance with the rules described in Commission Regulation (EC) No 333/2007 [10].

Member States were obligated to transmit data to EFSA according to reporting format as set by EFSA to enable evaluation of results and risk assessment.

Currently EFSA has been requested by the Commission to update the scientific opinion on the risk to public health related to the presence of nickel in food and drinking water taking into account the new occurrence data. This in view of possible future risk management measures.

## NOTIFICATIONS WITHIN THE RASFF

In the years 2010-2018, within the Rapid Alert System for Food and Feed (RASFF), there were a total of 204 notifications regarding high content or migration of nickel. 197 of them concerned the migration of nickel from food contact materials, among others: knives and kitchen utensils, grates, kitchen utensils (pots, pans) etc. mainly originated from China. The remaining few notifications were associated with the finding of high nickel content in dietary supplements. The highest value was detected in food supplement from India – 89 mg/kg [35]. A small number of food notifications are associated with a limited number of studies in this area.

## CONCLUSION

Due to the toxic effects of nickel and its compounds, the most sensitive population groups should be protected. For the purpose of proper risk management, it is appropriate to collect representative data on the contamination of various groups of foodstuffs with nickel taking into account different geographical area.

## Conflict of interest

*The authors declare no conflict of interest.*

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## EXPOSURE ASSESSMENT OF THE POPULATION IN POLAND TO THE TOXIC EFFECTS OF NICKEL FROM VEGETABLE AND THEIR PRODUCTS

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### ABSTRACT

**Background.** According to the European Food Safety Authority (EFSA), vegetable and vegetable products can significantly contribute to dietary nickel intake. Consumption of vegetable across European Union can vary significantly and depends on consumption habits in individual Member States. Toxicity of Ni is dependent on the chemical form, the route of exposure and solubility of nickel compounds.

**Objectives.** Determination of nickel content in commercially available vegetables and vegetable products and assessment of consumer exposure to Ni intake with these groups of foodstuffs.

**Materials and methods.** 66 samples of vegetables and their products were analysed for nickel content. Nickel was determined after microwave mineralization of samples by atomic absorption spectrometry with a graphite furnace atomization (GFAAS). Nitric acid and perhydrol were used for the mineralization of the samples. The estimated exposure for adults and children was compared with the tolerable daily intake (TDI -Tolerable Daily Intake) set by the European Food Safety Authority at 2.8 µg /kg body weight (b.w.) per day.

**Results.** Mean (MB-middle bound) Ni content from all investigated vegetable samples was 0.09 mg/kg (95th percentile MB 0.23 mg/kg). In vegetable products, mean Ni concentration was 0.191 mg/kg (95th percentile: 0.67 mg/kg). The highest nickel level was determined in the sample of roman lettuce (0.32 mg/kg), whereas lowest contamination was observed in the sample of onion (0.04 mg/kg). Contamination of investigated fruiting and leaf vegetable with nickel was slightly higher than root and bulb vegetables. The estimated average adults exposure to nickel from vegetable taking into account maximum absorption was 4.8% of TDI and 16.8% of TDI and does not pose a health risk. Exposure to nickel from vegetable products was 1.9% and 6.8% TDI, respectively.

**Conclusions.** Obtained results demonstrate that dietary nickel intake from vegetables and their products do not constitute a significant health threat to consumers in Poland.

**Key words:** *nickel, vegetable, vegetable products, exposure assessment, tolerable daily intake/nickel, TDI/nickel*

### STRESZCZENIE

**Wprowadzenie.** Warzywa i produkty warzywne należą do grupy środków spożywczych, które według Europejskiego Urzędu ds. Bezpieczeństwa Żywności (EFSA) mogą wносить istotny udział do pobrania niklu z diety. Spożycie warzyw w Unii Europejskiej może się znacznie różnić i zależy od nawyków konsumpcyjnych panujących w poszczególnych państwach członkowskich. Toksyczność niklu zależy od postaci chemicznej, drogi narażenia i rozpuszczalności związków niklu.

**Cel badań.** Oznaczenie zawartości niklu w warzywach i produktach warzywnych dostępnych w obrocie handlowym oraz ocena narażenia konsumentów na pobranie niklu z tymi grupami środków spożywczych.

**Material i metody.** Analizie na zawartość niklu poddano 66 próbek warzyw i ich produktów, pochodzących z obrotu handlowego. Zawartość niklu oznaczono po mineralizacji mikrofalowej próbek metodą absorpcyjnej spektrometrii atomowej z wykorzystaniem kuwety grafitowej (GFAAS). Do mineralizacji próbek wykorzystano kwas azotowy oraz perhydrol. Oszacowane narażenie w odniesieniu do osób dorosłych oraz dzieci porównano z wartością tolerowanego dziennego pobrania (TDI –*Tolerable Daily Intake*) ustaloną przez Europejski Urząd ds. Bezpieczeństwa Żywności ustaloną na poziomie 2,8 µg/kg m.c./dzień).

**Wyniki.** Średnia zawartość Ni (MB – middle bound) ze wszystkich badanych próbek warzyw wyniosła 0,09 mg/kg (95-percentyl MB 0,23 mg/kg). W produktach roślinnych średnie stężenie Ni wynosiło 0,191 mg/kg (95-percentyl: 0,67 mg/kg). Najwyższy poziom niklu oznaczono w próbce sałaty rzymskiej (0,32 mg/kg), natomiast najniższe zanieczyszczenie niklem zaobserwowano w próbce cebuli (0,04 mg/kg). Zanieczyszczenie badanych warzyw owocowych i liściastych niklem było nieco wyższe niż warzyw korzeniowych i cebulowych. Oszacowane średnie narażenie dla osób dorosłych na nikiel pocho-

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dający z warzyw, biorąc pod uwagę maksymalne wchłanianie, wyniosło 4,8% TDI i 16,8% TDI i nie stanowi zagrożenia dla zdrowia. Narażenie na nikiel z produktów warzywnych wyniosło odpowiednio: 1,9% i 6,8% TDI.

**Wnioski.** Uzyskane wyniki wskazują, że pobranie niklu w diecie z warzyw i ich produktów nie stanowi istotnego zagrożenia dla zdrowia konsumentów w Polsce.

**Słowa kluczowe:** *nikiel, warzywa, produkty warzywno, ocena narażenia, TDI/nikiel, tolerowane dzienne pobranie/nikiel*

## INTRODUCTION

Vegetables are important for human health because of their vitamins, minerals, phytochemical compounds, and dietary fiber content. Especially antioxidant vitamins (vitamin A, C and E), folic acid and dietary fiber content have important roles in human health. The naturally low fat and calorie content makes them especially recommended for a healthy diet. Adequate vegetable consumption can be protective some chronic diseases such as diabetes, cancer, obesity, metabolic syndrome, cardiovascular diseases, as well as improve risk factors. It has been estimated that every serving increase in vegetable consumption reduces the risk of cancer by 15%, cardiovascular disease by 30% and mortality by 20%, attributable to antioxidants such as ascorbic acid, vitamin E, carotenoids, lycopene, polyphenols [17, 20]. In addition to health aspects, consumption of vegetable may be associated with the intake of contaminants, i.e. heavy metals like lead, cadmium, mercury, nickel, arsenic as well as pesticides and nitrates. Risk and benefits analysis should be taking into account in case of vegetable before appropriate actions in area of risk management will be taken [19].

Such an analysis was carried out, among others, by European Food Safety Authority in case of nitrates in vegetable. Experts found that the health benefits of eating vegetables outweigh the risks associated with the presence of nitrates [20].

According to Central Office of Statistics mean monthly consumption of vegetable in Poland is 7.92 kg per capita including potatoes 2.97 kg, whilst dried vegetables and other processed vegetables 1.49 kg [7]. Rapid economic growth and transition makes that consumption habits change significantly and contribution of vegetables in our diets started to increasing.

Accumulation of nickel in vegetables is associated with the levels of this metal in soil and in the air. The main source of nickel contamination is anthropogenic activity [6, 23]. Increased nickel accumulation is observed in plants growing on acidic and wetland soils compared to other types of soil [10]. International Agency for Research on Cancer (IARC) has classified nickel compounds to Group I as substance carcinogenic to humans, while metallic nickel and nickel alloys to Group 2B as substance possibly carcinogenic to humans [8, 12, 21].

The EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) established a tolerable daily intake (TDI) of 2.8 µg Ni/kg body weight (b.w.) per day. The benchmark dose lower limit BMDL<sub>10</sub> of 1.1 µg Ni/kg b.w. associated with dermatitis following oral exposure to Ni based on dose-response analysis was also determined. For risk characterization the CONTAM Panel decided not to establish an acute reference dose, but to adopt a margin of exposure (MOE) approach [12, 21]. Calculated value of MOE taking into account mean and 95th percentile acute exposure for all groups of population was below 10 which indicated to be of health concern. Dietary exposure to Ni is associated mainly with non-carcinogenic health effects on the gastrointestinal, hematological, neurological and immune system. Dietary exposure and exposure via drinking water provide most of the intake of Ni [12, 13, 21, 27]. Ni absorption from the gastrointestinal tract in humans can vary significantly (between 1 and 40 %) depending on its chemical form, diet composition and fasting status [21].

According to EFSA vegetables and vegetable products are the main contributors to the dietary exposure to nickel similarly to grain and grain-based products, nonalcoholic beverages (except milk-based beverages), sugar and confectionery, legumes, nuts and oilseeds. In case of toddlers additional important contributors are milk and dairy products. Mean chronic dietary exposure to nickel, across EU countries, ranges from 2.0 (elderly) to 13.1 µg/kg body weight (b.w.) per day (toddlers). The 95th percentile dietary exposure ranges from 3.6 (elderly) to 20.1 µg/kg b.w. per day (toddlers) [21].

Currently, binding EU legislation does not place any limits for nickel contamination in foodstuffs. The national regulation of the Ministry of Health sets out the requirements for nickel in drinking water, natural mineral, spring and table waters at the level of 0.020 mg/l [15, 16]. Legislation on food additives gives purity criteria for nickel at 1 – 200 mg/kg [4].

Prior to accession to the EU in Poland, in accordance with national legislation, nickel content limits were set in a very limited groups of foodstuffs [14].

In order to determine the appropriate strategy for risk management, the European Commission has decided to develop recommendations for monitoring the level of nickel in food and feed in the years 2016-2018 [2, 3]. The results of these studies will contribute to the further work of the Commission in this area.

The study aims were to determine nickel content in vegetable and their products available on the market in Poland, along with estimating consumer exposure to nickel found in these products.

## MATERIALS AND METHODS

The test samples consisted of 66 vegetable and their products. Among the vegetable samples were root, tuber, bulb, fruiting vegetables, brassica and leaf vegetables as well as their products, that are available on the Polish market.

Nickel was measured by in-house adapted method based on manufacturer of apparatus guideline and was fully validated and accredited according to standard PN-EN ISO/IEC 17025:2018.

### *Apparatus and instrumentation*

An VARIAN SpectrAA 880Z atomic absorption spectrometer equipped with graphite furnace and Zeeman background correction was used. For graphite furnace measurements, argon was used as inert gas. Pyrolytic-coated graphite tubes (Agilent) without platform were used. The operating parameters for working conditions are presented in Table 1. Samples were injected into the graphite furnace using autosampler. The atomic absorption signal was measured as a peak surface mode against an analytical curve. Milestone MLS 1200 (Italy) microwave closed system at the stage of sample preparation was used.

### *Reagents*

All reagents used were of an appropriately high purity. Nitric acid (65%, Merck), hydrogen peroxide (for analysis 30% Merck), hydrochloric acid (pur p.a not less than 30%, Chempur), ascorbic acid (pure p.a. Poch), palladium matrix modifier for graphite furnace –  $10.0 \pm 0.2$  g/L ( $\text{Pd}(\text{NO}_3)_2 / \text{HNO}_3$  (Merck)), deionised water. The element standard solution used for calibration was produced by diluting a stock solution of 1g/L (GUM).

Recommended chemical matrix modifiers for measurement using flameless atomic absorption spectrometry should stabilize nickel compounds during the ashing stage among other a solution of palladium and a reducing agent such as ascorbic acid.

### *Quality Assurance*

The accuracy of the method was verified by analysis of certified reference materials: BCR-679 (White cabbage) and SRM-1515 (Apple leaves NIST).

### *Sample preparation – microwave digestion*

Samples of approx. 0.5 g to 1g were placed into mineralization vessels on the volume 100 mL. Then

5 mL of concentrated nitric acid and 1 mL hydrogen peroxide were added. After the reagents were added, the contents of the reaction vessel were mixed thoroughly to prevent clumping. After finished of the spontaneous reaction, the reaction vessels were quickly closed. The samples were then mineralized a pressure technique using microwave energy, in accordance with the guidelines of the microwave oven manufacturer. Digestion conditions for microwave system were as follows: 30 sec for 250W, 2 min for 0W, 5 min for 250W, 5 min for 400W and 5 min for 600W, ventilation 5 min.

The obtained solution, after quantitative transfer to a volumetric flask and filled with deionised water to a specific volume. Blanks as well as quality control samples were also prepared under analogous conditions.

### *Calibration curve*

Scope of calibration curve: from 0  $\mu\text{g/L}$  to 25  $\mu\text{g/L}$ .

*Instrument parameters:* Lamp Current 4mA, Slit 0.2 nm, Wavelength 232.0 nm

Table 1. Instrumental analytical conditions

Furnace Operating Conditions			
Step No.	Temperature (°C)	Time (sec)	Gas flow (L/min)
1	85	5	3.0
2	95	15	3.0
3	120	10	3.0
4	800	5	3.0
5	800	1	3.0
6	800	2	0
7	2400	1.1	0
8	2400	2	0
9	2600	2	3.0

### *Statistical evaluation*

Statistical assessment of results was performed according the substitution method used by EFSA for the treatment of left-censored data – LC (below limits of quantification (LOQ was 0.031 mg/kg). For results reported to be below the LOQ, the value equal to the LOQ (upper bound – UB), zero (lower bound – LB) or half the LOQ (medium or middle bound – MB) were used [22]. Left-censored data represented 33% of the analytical results.

## RESULTS AND DISCUSSION

Concentration of the nickel in the analyzed samples is presented in Table 2.

Table 2. Nickel content in vegetable available in the Polish market, mg/kg

Vegetable	Nickel content	
	Mean	P95
Root, tuber and bulb vegetable	LB: 0.08	LB: 0.22
	MB: 0.08	MB: 0.17
	UB: 0.09	UB: 0.22
Leaf and fruiting vegetables	LB: 0.10	LB: 0.27
	MB: 0.10	MB: 0.27
	UB: 0.11	UB: 0.27
All vegetables	LB: 0.09	LB: 0.23
	MB: 0.09	MB: 0.23
	UB: 0.09	UB: 0.23

LB – lower bound, MB – middle bound, UB – upper bound, P95 – 95th percentile

Mean (MB) nickel content from all investigated vegetable samples was 0.09 mg/kg (95th percentile MB 0.23 mg/kg). In vegetable products, mean nickel concentration was 0.19 mg/kg (95th percentile was 0.67 mg/kg). The highest nickel level was determined in the sample of roman lettuce - 0.32 mg/kg, whereas lowest contamination of nickel was observed in the sample of onion at 0.04 mg/kg. In case of vegetable products the highest result was obtained in a sample of dried beetroots – 0.74 mg/kg.

Nickel contamination of vegetables was significantly lower as compared with results collected by EFSA from EU Member States and comparable with mean contamination reported in France for vegetables except potatoes and for starchy vegetables which was: 0.08 mg/kg and 0.07 mg/kg respectively [11, 21].

According to EFSA, the mean (LB-UB) contamination was in the range: 0.742 - 0.753 mg/kg (P95 9.25÷9.25 mg/kg). In case of starchy roots and tubers obtained results were significantly lower (LB-UB was 0.123÷0.150 mg/kg; P95 0.690÷0.690 mg/kg) [21].

Contamination of investigated fruiting and leafy vegetable with nickel was: 0.10 mg/kg (mean MB) and 95th percentile 0.27 mg/kg, and was slightly higher than roots and bulb vegetables: 0.08 mg/kg (MB) 95th percentile 0.17 mg/kg respectively. The results reported in Pakistan indicate higher contamination of vegetables than in our studies, content of nickel in these studies was in the range 0.05 mg/kg - 1.8 mg/kg [9]. Other than above French study indicate also higher contamination than in these studies. The mean (MB) value of nickel contamination in vegetable excluding potatoes was 0.21 mg/kg (95th percentile 0.63 mg/kg), whilst for potatoes only mean value was 0.18 mg/kg (95th percentile 0.52 mg/kg) [1]. The survey conducted in Italy indicates comparable contamination of potatoes with results of these investigation, mean was in the range 0.076 mg/kg÷0.194 mg/kg. Similar to our results were for vegetable, 0.039 - 0.159 mg/kg [5].

In a study conducted in UK, it was found that mean nickel concentration in green vegetables was 0.11 mg/kg in other vegetables 0.09 mg/kg whilst in potatoes 0.10 mg/kg [24]. Similar results were obtained in the survey conducted by the Food Standards Agency (mean contamination of green vegetables was 0.086 mg/kg, potatoes 0.07 mg/kg, and other vegetables 0.079 mg/kg. Only contamination of canned vegetables was higher – mean 0.338 mg/kg [18].

Studies conducted in Iran indicated that the contamination of vegetables with Ni depends on seasons and the levels of nickel in vegetables. The higher contamination was observed in vegetables growing in spring than in vegetable growing in summer and autumn.

The mean concentrations of nickel in leafy vegetables obtained in this studies was  $0.775 \pm 0.043$  mg/kg and was comparable with results reported in these studies [25].

Due to the limited amount of research conducted on the contents of nickel in specific vegetable products, often being regional products, it is difficult to compare the results obtained in this research for this groups of foodstuffs with the results obtained by other authors.

To assess the dietary exposure to nickel from commercially available vegetable and their products mean and high contamination levels (P95), middle bound (MB), were taken into account.

Taking into account the data of the Central Statistical Office, along with the data of WHO, GEMS/Food Consumption Cluster Diets [26] on consumption of vegetables and their product, the intake of nickel from these foodstuffs was assessed and compared to the Tolerable Daily Intake (TDI) at 2.8 µg/kg body weight/ per day.

Mean (MB) intake of nickel by adult person from vegetables would be 12.1% TDI; at the P95 percentile contamination: 25.6% of TDI. Intake of nickel with vegetables by children taking into account mean MB contamination 42.2 % of TDI (95th percentile 89.6%).

Taking into account maximum absorption of nickel from the gastrointestinal tract in humans the mean intake would be 4.8 % of TDI (at the P95 percentile contamination 10.2 % of TDI) in adults and 16.8% of TDI (at the P95 percentile contamination 36% of TDI) and in both cases does not pose a health risk.

Mean intake of nickel with vegetable products by adults and children taking into account maximum absorption will be: 1.9% and 6.8% of TDI respectively which also does not pose a health threat.

Estimated of daily intake based on obtained results from investigated foodstuffs is slightly higher than that reported in France [11].

Assuming a much higher variant of vegetable consumption in accordance with the WHO data, which for

European countries is 478.7 g/ person/day, the nickel intake by adults will be at average contamination and maximum nickel absorption from the gastrointestinal tract 8.8% and 22.5% of TDI value. For children, respectively: 30.8% and 78.7% of TDI value.

This exposure assessment is fraught with uncertainty related to the contribution of vegetables in a diet and real consumption and the absorption of nickel from the human digestive tract.

## CONCLUSIONS

1. The content of nickel in the investigated samples of vegetable and their product is low and does not pose a health concern.
2. Levels of contamination found were mostly comparable to those reported in other countries
3. The obtained results will provide input to risk management in this area at UE level.
4. It is justified to continue a research on the content of nickel in other groups of foodstuffs that may make a significant contribution to intake of this element with a diet.

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## Conflict of interest

*The authors declare no conflict of interest.*

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## NATURAL MEDICINAL RESOURCES AND THEIR THERAPEUTIC APPLICATIONS

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### ABSTRACT

Natural medicinal resources are a country's natural wealth. Natural medicinal waters, medicinal gases, and peloids have many properties that enable their use in the treatment of gastrointestinal, circulatory, respiratory, bone and joint, and skin and soft tissue disorders. Balneotherapy can be also applicable in prevention of many diseases and rehabilitation. At present, because there are several chemicals of synthetic origin, there is a need to search for nonpharmacological approaches and explore natural healing sources, which better fit the human body. Compared to synthetic drugs, these resources rarely show side effects, which increases the comfort of therapy. The use of natural medicinal resources in the form of treatments in health resort medicine centers under the supervision of balneologists, combined with the healing properties of the climate, contributes not only to the reduction of treatment time for many diseases but also to improvement of therapy's results. The article discusses natural medicinal resources and some of their therapeutic applications.

**Keywords:** *natural medicinal waters, peloids, brines, balneology*

### STRESZCZENIE

Uzdrowiskowe surowce lecznicze stanowią naturalne bogactwo danego kraju. Naturalne wody lecznicze, gazy lecznicze oraz peloidy mają wiele właściwości wykorzystywanych w terapii schorzeń układu pokarmowego, krążenia, oddechowego, kostno-stawowego, a także skóry i tkanek miękkich. Balneoterapia może mieć również zastosowanie w profilaktyce, jak i rehabilitacji wielu chorób. W porównaniu do leków syntetycznych, naturalne surowce lecznicze bardzo rzadko wykazują działania niepożądane, co zwiększa komfort i bezpieczeństwo terapii. Wykorzystanie naturalnych surowców leczniczych w postaci zabiegów w uzdrowiskach pod nadzorem lekarzy balneologów, w połączeniu z leczniczymi właściwościami klimatu, przyczynia się nie tylko do skrócenia czasu terapii, ale także do poprawy wyników leczenia wielu schorzeń. W artykule omówiono naturalne surowce lecznicze i ich niektóre terapeutyczne zastosowania.

**Słowa kluczowe:** *naturalne wody lecznicze, peloidy, solanki, balneologia*

### INTRODUCTION

Balneological natural resources, which include natural medicinal waters (also named as healing waters or curative waters), natural gases, and peloids, are important elements of medical treatment and preventive physiotherapy worldwide [24]. Balneotherapy is a complex therapeutic intervention, which consists of various components including hydrothermal therapies, residential care in a specialized center (often called health resort medicine center), a beneficial climate, and rehabilitation and education of the patients [22]. Natural medicinal waters, gases and peloids can be used in different ways by internal and external application. The patients may either drink natural medicinal waters (crenotherapy); bath in natural medicinal water

(hydrotherapy), peloids or gases; inhale natural gases; or have some peloid packs or tampons with peloids [13].

Natural medicinal sources such as waters and peloids can play an important role in therapeutic procedures of different systems. The use of water for medicinal treatment is probably as old as mankind. However, its popularity dropped with the development of effective analgesics and other synthetic medicines. Chemical drugs are reported to cause adverse reactions, including life-threatening ones [2]. At present, because there are several chemicals of synthetic origin, there is a need to search for nonpharmacological approaches and explore natural healing sources, which better fit the human body and cause less adverse effects.

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In this review, the authors describe the characteristics of chosen natural medicinal resources such as waters and peloids and provide their some therapeutic properties.

### CHARACTERISTICS OF NATURAL MEDICINAL WATERS

In the past, various nomenclature and characteristics were used to describe natural medicinal waters and natural mineral waters. They were differentiated for the first time during the International Balneological Congress in Nauheim in 1911 with further changes in Salzuflen in 1934. The first European classification of medicinal waters defined them as natural waters with at least

1 g/l of dissolved minerals. Some of the medicinal waters were distinguished by minimum concentrations of components with a specific biochemical effect on the human body including for fluoride, sulfur (II) compounds, iodides, bromides, iron (II), arsenic, radon, and metasilicic acid (Table 1). These criteria still vary in different European countries owing to the lack of unambiguous clinical data for accepted specific substance concentrations, mainly regarding their pharmacodynamics and toxic properties as well as the local tradition of the country [16]. Compared with natural medicinal waters, natural mineral waters (bottled waters) are defined as food and their labeling has to abstain from anything that may be interpreted as medical advertising.

Table 1. Classification of medicinal waters according to the International Balneological Congress in Nauheim in 1911 with further changes in Salzuflen in 1934 and the Polish Ministry of Health Regulation from April 13, 2006 [16]

Specific water components (water type)	Minimum contents of water components according to the Nauheim/Salzuflen medicinal water classification	Minimum contents of water components according to the Polish classification of natural medicinal waters
Iodine I <sup>-</sup> (iodide water)	1.0*/5.0*/10.0* mg/l	1.0 mg/l
Bromine Br (bromide water)	5.0/25.0 mg/l	-
Fluoride F <sup>-</sup> (fluoride water)	2.0/20.0 mg/l	2.0 mg/l
Ferrum Fe <sup>2+</sup> (ferric water)	10.0/20.0 mg/l	10.0 mg/l
Metasilicic acid H <sub>2</sub> SiO <sub>3</sub> (metasilicic water)	50.0*/75.0*/100.0* mg/l	70.0 mg/l
Arsenic As(III) (arsenic water)	0.2/0.7 mg/l	-
Boric acid HBO <sub>2</sub> (boric water)	5.0/50.0 mg/l	-
Sulfur S <sup>2-</sup> (sulfide water)	1.0/10.0 mg/l	1.0 mg/l
Radon Rn (radon water)	1/100 nCi	2nCi
Temperature (thermal water)	20°C	20°C
Carbon dioxide (CO <sub>2</sub> ) (carbonic acid water)	-	250 mg/l
	-	1000 mg/l

\*Minimum contents of water components in various European countries.

From a balneological point of view, natural medicinal water is subterranean water that is chemically pure and exhibits slight fluctuations in chemical and physical properties [24]. Its composition depends on the type and structure of the rocks with which it comes into contact, hydrogeochemical processes (such as sorption, oxidation and reduction, leaching, weathering, hydrolysis), and physical parameters (temperature, pressure) and others [6]. The main criteria in the assessment of these waters are not only the confirmation of their original chemical and microbiological purity and quality but also their beneficial effects on human health.

The current Polish version of the classification of natural medicinal waters includes the actual research data on the properties of water elements (e.g. arsenic and boron) that can be potentially harmful to human health and therefore does not mention those elements as specific ones. According to the basic criteria of balneochemical classification, natural medicinal waters are classified as mineral medicinal waters (waters containing more than 1 g/l of dissolved mineral components), low-mineralized

medicinal waters (waters containing less than 1 g/l of dissolved components, but distinguished by the content of one or several specific components at a concentration that exert pharmacodynamic effects), and mineral specific medicinal waters (waters meeting the criteria for mineral water and specific water) [17].

The content and type of minerals in a given medicinal water depend on local geological conditions. In groundwater, which is of natural origin, more than 50 elements of the periodic table were determined, which were divided into macronutrients, rare elements, and trace elements. The dominating macronutrients in groundwater include sodium, potassium, calcium, magnesium, chlorides, sulfates, and bicarbonates [17].

Sodium has a high waterbinding capacity, and together with carbonates and bicarbonates, it constitutes an alkaline reserve of the body. For per os use, water with a sodium content usually not exceeding 1 g/l is used. Sodium chloride saline waters up to 15 g/l and brine (15–50 g/l) are mainly used for bathing and after dilution for inhalation.

Calcium is found in medicinal waters mainly in combination with bicarbonates or chlorides. At a concentration of 500–700 mg/l, calcium is found in bicarbonate–calcium–magnesium waters. These waters supplement the body's need for calcium and magnesium and normalize heart function. At higher concentrations of about 1000–7800 mg/l, calcium is present in brine as calcium chloride. Waters of this type are mainly useful for bathing and in appropriate concentrations for inhalation and rinsing of body cavities. Magnesium is co-present with calcium in medicinal groundwater, but in concentrations generally lower than calcium (by about 50%). Magnesium participates in many enzymatic reactions, reduces myocardial sensitivity to hypoxia, has anti-arrhythmic properties, regulates blood pressure, and reduces nerve tension [26].

In addition to sodium, chlorides are the main component of sodium chloride waters, and their content in water reaches up to several dozen grams per liter (brines). The effects of chlorides on the body during bath (osmotic) or inhalation (increasing the secretion and fluidity of mucus) are because of their reaction with sodium ions [17]. Brines are concentrated salt (sodium chloride waters) solutions, which occur widely in natural forms such as coastal lagoons, salt or soda lakes, deep-sea brines, groundwater, and salterns or saltworks of anthropogenic origin [14]. A graduation tower is a unique structure that is used to produce salt; it removes water from a saline solution by evaporation, thereby increasing the concentration of mineral salts. It is constructed using natural materials (usually wood, branches of blackthorn). Effective brine concentrations are 5–7% solutions with sodium chloride as the main constituent. Other elements present in lower concentrations are calcium, magnesium, and potassium chloride. Inhalation with the use of the salt aerosol formed on brine graduation towers is one of the methods used in the treatment of respiratory diseases [8].

Sulfur (II) compounds occur in medicinal waters as hydrogen sulfide, sulfides, and bisulfides (depending on the pH of the water) and have keratolytic, keratoplastic, and bactericidal effects on the skin. Because hydrogen sulfide and sulfides bind heavy metals, they detoxify and desensitize when administered per os.

Sulphates (VI) occur in groundwater in combination with calcium, sodium, and magnesium. Waters containing significant amounts of magnesium sulfate are barely absorbed by the intestine and have a laxative effect after per os administration [17, 26].

## CHARACTERISTICS OF PELOIDS

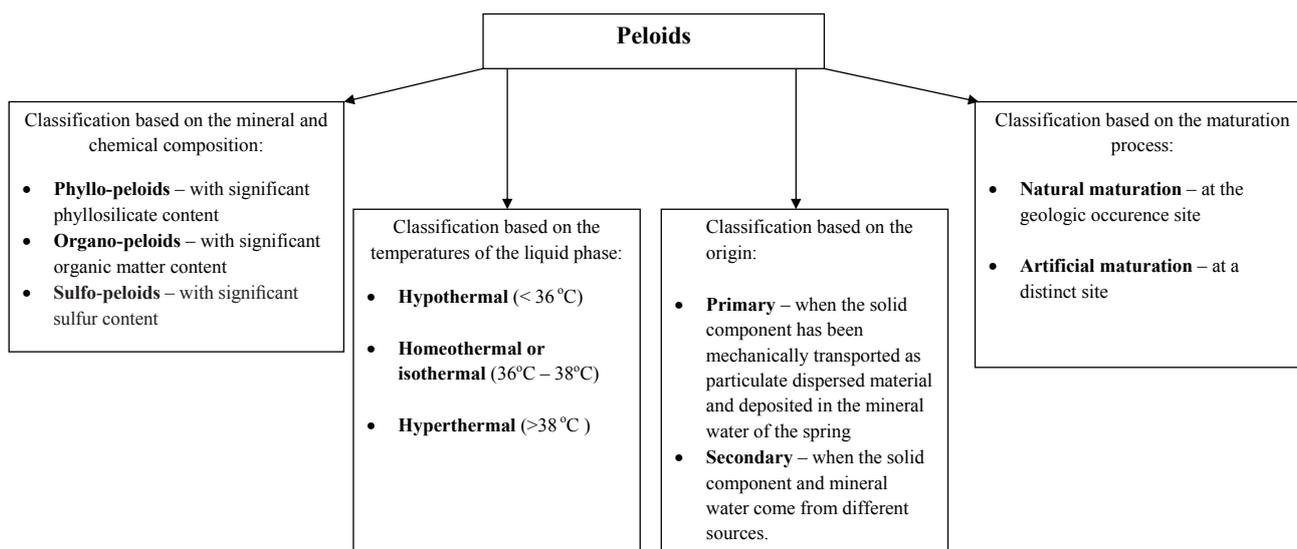
Peloids consist of humus and minerals formed over a very long period of time by physical, chemical, biological, and geological processes [3]. The properties of peloids also depend on the humified material and the regional rock.

One of the first definitions of peloids was established by *Lewis* [18] in 1933. According to him, peloid was any natural product composed of a uniform mixture of finely divided organic and inorganic matter with water and applicable in medical practice as cataplasm for external treatment.

Peloids can be classified based on their mineral and chemical composition (phyllo-peloids, organo-peloids, sulfo-peloids), temperature of their liquid phase (hypothermal, homeothermal or isothermal, hyperthermal), their maturation process (natural, artificial), and their origin (primary, secondary) [12]. The classification of peloids is presented in Scheme 1. Peloids can also be classified into eupeloids (original, undressed), parapeloids (crushed, milled, dressed), and peloids apogones (peloidic substances produced by adding liquid carriers). Based on the applications and properties of peloids, we can distinguish them into medical and cosmetic peloids. Medical peloids are recognized and evaluated by proper national authorities, which indicate their possible therapeutic applications. Medical peloids can be applied under medical prescription and supervision. Cosmetic peloids can be used in cosmetology and dermocosmetics as moisturizers, cleansers, and anti-wrinkle or anti-cellulite factors [12].

Therapeutic effects of peloids include stimulatory, antiphlogistic, and analgesic activities. In the maturation process of peloids with high organic content, new bioactive compounds can be biosynthesized by microorganisms. Fangotherapy is usually used to treat rheumatic diseases (arthrosis, arthritis, and fibromyalgia) and skin diseases (acne, psoriasis, and seborrhea). The term “fango,” which originated in Italy, means the mud deposited from the thermal springs of sulfur-bearing sulfurous or sulfated water.

Another natural resource is named *gyttja* (also known as “nekron” mud, *sapropel*, or *dy*). *Gyttja* is a Swedish term for organic-rich freshwater mud, which is a mixed organic-rich mud that is rapidly accumulated in eutrophic lakes; the organic component that makes up to 40% of the dry mass results from the partially anaerobic putrefaction of plankton. It is a unique geological formation occurring at the bottom of water bodies (mostly in overgrowing, eutrophic lakes) [28]. According to *Korde* [15], *gyttja* contains not less than 15% and up to 90% of organic matter. However, *gyttja* is also known for its high mineral content. For example, in *gyttja* samples derived from lakes of eastern Latvia, minerals such as Ca, Fe, Mg, K, Mn, Na, Zn, and Ba were detected at concentrations above 50 mg/kg [28]. Sr, Cu, Cr, Ni, Pb, V, As, Co, Rb, Li, Se, and Cd were found at concentrations below 50 mg/kg. Because metal elements are incorporated in organic substances, it is important to evaluate the concentration of potentially toxic microelements such as As, Cd, Cr, and Pb [28].



Scheme 1. Classification of peloids

Depending on the origin, sediments can be classified as gytija attributed to autochthonous sediments and dy attributed to allochthonous sediments.

Pelotherapy, which is a term usually used in southern and central European countries, is defined as the external application of peloids in both therapeutic and skin care indications.

### THERAPEUTIC PROPERTIES OF NATURAL MEDICINAL RESOURCES

There are numerous therapeutic effects of natural medicinal waters and peloids. Bicarbonate mineral waters demonstrate positive effects on the digestive tract. Their consumption may neutralize acid secretion, increase the pH level in the gastric lumen, accelerate gastric emptying, and stimulate the release of digestive hormones. Bicarbonate waters create an alkaline environment and decrease bone resorption. They also have some benefits in reducing total cholesterol, LDL cholesterol, and fasting glucose [23].

Sulfate mineral waters are characterized by the presence of sulfate anions with different cations. Magnesium sulfate and sodium sulfate mineral waters have beneficial effects in the treatment of gastrointestinal disorders such as constipation. They improve bowel movements and stool consistency. Chloride waters contain chloride as the predominant element and sodium, calcium, and magnesium as the most abundant ones.

There are a few key therapeutic directions in which natural medicinal waters and peloids are successfully applied. Balneological treatments in health resort medicine centers are one of the most commonly used nonpharmacological approaches for rheumatologic diseases. The mechanisms by which immersion in medicinal or thermal water or the application of mud al-

leviates suffering in rheumatic diseases are not fully understood. The overall benefit is probably the result of the combination of various factors, mostly mechanical, thermal, and chemical effects. Baths in thermal water may influence muscle tone and pain intensity and may help to reduce muscle spasm and to increase the pain threshold. Mud-bath therapy increases plasma  $\beta$ -endorphin levels and secretion of corticotrophin, cortisol, growth hormone, and prolactin. Thermal mud-pack therapy reduces the circulating levels of important mediators of inflammation and pain, such as prostaglandin E2 (PGE2), leukotriene B4 (LTB4), interleukin-1  $\beta$  (IL-1 $\beta$ ), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) [9].

Balneotherapy has also been proved to have beneficial effects on patients with osteoarthritis. Osteoarthritis is a degenerative musculoskeletal disease and leading cause of pain, disability, and impaired quality of life [4,10,11]. It affects synovial joints (mainly hips and knees), in which cartilage destruction, subchondral bone remodeling, osteophyte formation, and synovial inflammation are found, thereby leading to joint stiffness [11]. Osteoarthritis usually affects approximately 10% of people over 60 years of age [10]. Different clinical trials were conducted to evaluate the effectiveness of balneotherapy in patients with osteoarthritis. In one such study conducted by Branco et al., patients of both genders aged  $64.8 \pm 8.9$  years were diagnosed with osteoarthritis of the knee. They were randomized into three groups: sulfurous water (SW) group (47 patients), nonsulfurous water (NSW) group (50 patients), and control group (43 patients). Patients in the SW and NSW groups received a 10-week treatment consisting of 30 individual thermal baths (three baths a week, each bath lasting 20 minutes) in either sulfurous water or nonsulfurous water (tap water) at temperatures ranging from  $37^{\circ}\text{C}$  to  $39^{\circ}\text{C}$ . The patients in the con-

trol group did not receive any treatment. The results showed that at the end of treatment, hot SW baths were effective in reducing pain during movement, and their overall effects lasted longer than those of heated NSW baths [4]. In another clinical study, 42 patients (aged  $\geq 60$  years) diagnosed with knee osteoarthritis received mud therapy for 10 days. Mud therapy included the whole-body application of the combination of mineral medicinal water (with bicarbonate and calcium as predominant ions) and mud, which consisted mainly of silt, clay, sand, phyllosilicates, quartz, and calcite. The results showed that mud therapy significantly improved osteoarthritis-related pain, stiffness, and physical function. It also increased knee flexion and extension angle [11].

Balneotherapy has short- and long-term effects on patients with low back pain-another noninflammatory musculoskeletal disease. In a study by *Balogh et al.*, a group of 60 patients with low back pain were assigned to balneotherapy and control groups. Balneotherapy was provided in the form of 30-minute baths in tubs filled with warm water (36°C), 6 days per week, for a total of 12 sessions in 15 consecutive days. The same procedures were applied to the control group with tap water as a placebo. Water used in balneotherapy was natural sulfur water with 2.4 mg/l  $S^{2-}$  concentration containing relatively high amounts of metasilicic acid (37 mg/l). Clinical improvements were found in the group of patients treated with balneotherapy and persisted for 3 months after the therapy [1].

As balneotherapy has been proved to be effective in the treatment of chronic pain, a randomized clinical trial on patients with fibromyalgia was designed and conducted. Fibromyalgia is a syndrome characterized by generalized skeletal muscle pain accompanied by diverse symptoms, such as fatigue, sleep disturbance, and anxiety/depression. In the study by *Pérez-Fernández*, a sample of 50 patients was divided into group A and group B. In phase 1, the patients in group A took 14 baths, 30-minute long, for a month, in bicarbonate sodium water of medium mineralization, alkalinity, lithic content, fluorine content, and silicate content at a temperature of 38°C in As Burgas, (Ourense), a thermal and public pool, and underwent the treatment prescribed by their doctor. Group B was treated only with the pharmacological treatment prescribed by their doctor. In phase 2, the groups were crossed. Immersion in mineral medicinal water caused a significant improvement in the impact caused by fibromyalgia. Balneotherapy has been proved to cause physiological effects both locally and generally, exerted by physical, chemical, and biological mechanisms. Hydrostatic pressure caused by thermal baths can produce analgesia. Bathing in mineral medicinal water can reduce certain mediators of inflammation, and this may be because of the presence of chemical components in the water [21].

Sulfurous medicinal waters have been used in medical hydrology as treatment for skin, respiratory, and musculoskeletal disorders [5]. Sulphur-rich water is effective in the treatment of dermatological disorders. The sulfur that penetrates the skin is oxidized and induces various physiological responses in the skin, such as vasodilation in microcirculation, analgesic influence on the pain receptors, and inhibition of the immune response. Sulfur also interacts with oxygen radicals present in deeper layers of the epidermis, producing sulfur and disulfur hydrogen, which may be transformed to pentathionic acid and may serve as the source of antibacterial and antifungal activities of sulfur water [20]. Moreover, if sulfurous medicinal water is applied to the skin in the form of maturated mud or peloid, its effect may be potentiated. The beneficial effects of sulfurous waters and sulfurous mud have been attributed to the presence of sulfur mainly in the form of hydrogen sulfide ( $H_2S$ ). This form is largely available at acidic pH.

Subterranean therapy is based on exposing patients to the synergic effects of physical, chemical, and biological stimuli present in underground excavations such as Wieliczka salt mine [19]. Its microclimate affects the whole organism stimuli and has a local effect in the respiratory tract as it isolates it from allergens, irritants, and harmful substances. High concentration of sodium chloride present in the underground aerosol stimulates the motor and secretory function of the respiratory tract epithelium, thus improving its cleaning and moisturizing effects [25].

## CONCLUSION

Balneotherapy is officially recognized in many countries such as Italy, France, Spain, Hungary, Poland, Germany and Russia and is dependent on some specific geological, geographic, and meteorological preconditions [13]. The therapeutic activity of natural medicinal resources such as natural medicinal waters and peloids is widely known. In many disorders such as chronic pain, the use of balneotherapy is a safe therapeutic option with little adverse reactions and is usually well tolerated by patients; moreover, it provides analgesic, sedative, and muscular rejuvenative effects, which are quite important to achieve relief from these disorders. However, there are still not too many clinical studies to explain the mode of action of natural resources. *Varga* [27] explained that the therapeutic activity of these natural resources is linked with the inorganic content of water, brines, and peloids. However, he assumed that many experimental balneological studies were not designed properly, and they needed more treated groups, including negative controls. Reflecting the effects of balneotherapy in health resort medicine, it is important to consider other

environmental factors. The final therapeutic effect on the patient is the combination of many factors, such as the use of natural medicinal resources (hydrotherapy, pelotherapy), climate, outdoor activities, diet, health education, psychotherapy, and/or physiotherapy.

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### Conflict of interest

The authors declare no conflict of interest.

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## DEVELOPMENT OF LAND TRANSPORT CONNECTIONS BETWEEN ASIA AND EUROPE AND THEIR POSSIBLE IMPACT ON VECTOR INTRODUCTION INTO EUROPEAN COUNTRIES

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### ABSTRACT

The possibility of transfer of several organisms – disease vectors by land transportation Asia – Europe corridors into European countries is discussed. In Europe most alien species are of Asiatic origin. Trade and exchange of goods have developed very intensively for the beginning of the XXI century between Asia and European Union countries both by sea and land routes. Road and railway connections shorten the time of goods' transport from China to Europe to 10,5 – 12 days. Shorter travel time and increased intensity of trade can increase the risk of introducing vector organisms from Asian countries to Europe. Existing legal international regulations (International Health Regulations, IHR) provide procedures to protect goods and persons against the carriage of organisms – vectors at every stage of transport and travel. Mass passenger and car traffic at border crossing points increase the likelihood of vector organisms entering as random stowaways; therefore it is proposed to intensify educational activities to make people aware of the danger posed by the transport of alien species of arthropods and what preventive actions to take. Unloading goods in a transit country (such as Poland) may take place at a transshipment center located near the border or inland. It is postulated to introduce a 400 m vector monitoring zone around both.

**Key words:** *disease vectors, New Silk Road, Asia-Europe trade exchange*

### STRESZCZENIE

Przedstawiono możliwości przenikania organizmów - wektorów chorób poprzez lądowe korytarze transportowe łączące Azję z Europą do państw europejskich. W Europie większość gatunków obcych jest pochodzenia azjatyckiego. Wymiana handlowa pomiędzy krajami Azji i Unii Europejskiej od początku XXI w zaczęła się intensywnie rozwijać. System połączeń kolejowych i drogowych skrócił czas transportu towarów z Chin do Europy do 10,5 – 12 dni. Skrócenie czasu podróży i intensyfikacja wymiany towarowej może wpłynąć na zwiększenie ryzyka introdukcji organizmów wektorowych przenoszących choroby. Aktualne międzynarodowe przepisy prawne (International Health Regulations, IHR) zapewniają ochronę towarów i osób przed możliwościami przeniesienia wektorów na każdym etapie transportu towarów i podróży. Intensywny ruch osobowy i samochodowy na lądowych przejściach granicznych może zwiększyć prawdopodobieństwo przeniesienia organizmów wektorowych jako przypadkowych „pasażerów na gapę”. Dlatego też proponuje się zintensyfikowanie edukacji, aby ludzie byli świadomi niebezpieczeństwa, jakie niesie za sobą przeniesienie obcego gatunku stawonoga i jakie należy przedsięwziąć środki zaradcze. Przeładowywanie towarów w kraju tranzytowym (tak jak np. w Polsce) może odbywać się w centrach przeładunkowych zlokalizowanych na granicy lub wewnątrz kraju. Proponuje się wyznaczenie 400 m strefy monitoringu wektorów wokół obu rodzajów centrów.

**Słowa kluczowe:** *wektory chorób, Nowy Jedwabny Szlak, wymiana handlowa Azja – Europa*

### INTRODUCTION

Conquering new areas is an evolutionary phenomenon of many species. Humans have played a significant role in this process. When people changed the place of their residence, together with them and their belongings moved all organisms on their bodies,

clothes, and movables. This process become more dynamic in the years of globalization, when more and more people moved because of economic, touristic and safety reasons, and also goods exchange become more intensive [13, 38]. According to Roques et al. [26] in the pre-industrial era in the Europe appeared 1-2- new species of invertebrates/year; in the period 1900 – 1950

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there were about 6 new species; in the years 1975 – 2000 – there were 13 new invertebrate species per one year, respectively. Increase of prosperity influences positively a development of transport infrastructure: building national and international roads, railway connections, water channels. They can create gates for invasive species to grasp new territories. It was found, that increase of Gross Domestic Product Brutto (influenced by international trade and exchange of goods) was correlated with richer fauna of spiders, plants, birds and mammals which colonize these countries [16]. In Europe the most alien species are of Asiatic origin – 29.3% [26, 38]. It was stated that 45% of them are pests of medical, veterinary or economic importance.

Because trade and exchange of goods have developed very intensively since the beginning of the XXIst century between Asia and European Union countries, it would be interesting to analyze capabilities of transfer of several organisms – disease vectors by land transportation routes (railway or car transport).

### EUROPA – CHINA TRADE PAST AND PRESENT

Overland trade between China and Europe dates back more than two millennia. The Silk Road carried not only silk and could be highly profitable. At different times, oases along the routes – for example Khiva, Bukhara, Samarkand – were amongst the largest cities in the world. The destruction of the overland trade was caused in times when Portuguese sailors discovered the sea routes from Europe to Asia round the Cape of Good Hope around 1500. For the next 500 years, sea was the dominant mode of transport between Europe and East Asia. In the 20th century several rail links were constructed in Asia, but none was a significant carrier of China–Europe freight. The most important was the Trans-Siberian railway built by Russia between 1891 and 1905 [22].

Economic growth in countries of Europa and Asia in XX and XXI century has been accompanied by an increase in goods exchange and in demand for transport services by air, sea, rail and road. Air transport is the most expensive; on the other hand maritime transport is much cheaper but it takes long time (35 – 45 days). Development a rail and road links from China and other Asiatic countries aims to construct transport cheaper than by planes and faster than by sea way [10, 22].

The value of goods transported by rail from China to European Union increased between 2011 and 2016 up to 194.6%, while decreased by maritime and air transport. Since 2011 regular services were established on railway routes between several Chinese and European cities (Table 1) [33].

Table 1. Transport connections developed in recent years between China and Europe

Route	Length (km)	Duration (days)	Rail/road
Souhou - Warsaw	11,200	18	rail
Chengdu - Łódź	9,826	10.5	rail
Zhengzhou - Hamburg	10,124	19 - 20	rail
Xianmen - Warsaw	8,500	12	road

Source: Euro-Asian trade flows, in: Euro-Asian Transport Linkages, Operationalisation of inland transport between Europe and Asia: 32 – 101, UNECE, New York and Geneva 2019, modified

In 2017 China and 68 countries signed the agreement about renewal a land transport route called “New Silk Road”. It will pass through Middle Asiatic countries, Kazakhstan, Russia, Belarus, Poland to West Europa countries [28, 39]. It is planned that in 2020 about 5,000 container trains will run on the route Europa – China – Europa per year. In October 2019 socio – economic media [21] informed about opening a road connection between China and Poland. The time for a 24-tonnes truck to pass this rout is about 12 days (Table 1). In Table 2 there are listed several categories of commodity in Europe – Asia trade exchange; many of them were transported by rail and road routes because of short time of journey.

Table 2. Selected categories of goods in Europe – Asia trade exchange. Relative intensity of transport of good category in the direction Europe – Asia or Asia – Europe is showed by number of “+”

Category of commodity	Europe – Asia direction	Asia – Europe direction
Live animals	+++	+
Animal originated products	++	+++
Trees, plants, ornamental plants	+++	+
Vegetables, roots, edible	++	+++
Fruits and nuts, citrus, melons	+	+++
Coffee, tea, spices	++	+++
Oil seeds, grains, medicinal plants	++	+++
Prepared animal fodder, residues, wastes	++	++
Rubber, rubber products	+	++
Miscellaneous manufactured articles	+	+++
Textiles clothing	+	+++
Textiles, tapestries, woven fibers	+	+++
Stone, plaster, cement, asbestos	++	+++
Aluminum, nickel, zinc, tin	+	++
Electronic articles	+	+++

Source: Trade flows between Europe and Asia, in: Euro-Asian Transport Linkages, Operationalisation of inland transport between Europe and Asia: 197 - 287, UNECE, New York and Geneva 2019, modified

## RISK OF “UNEXPECTED PASSENGERS” – DISEASE VECTORS TRANSFER THROUGH LAND TRANSPORT CONNECTIONS FROM ASIA TO EUROPE

The majority of important disease vectors are active vectors – they can insert pathogen into human organism by direct damage of human skin by biting, stinging, because a pathogenic organism can be present or develop inside the vector. Important features of active vectors are: possibility of changing the host, anthro/zoophily, sucking blood several times. Mosquitoes and ticks are examples of active vectors.

The other group are passive (or mechanical) vectors – they carry pathogens on surface of their bodies or in digestive tract. Their presence in the environment close to people and mobility can pose a threat to human health. Non-bloodsucking flies and cockroaches appearing in mass numbers close to people, penetrating different environments, having wide spectrum of food can mechanically contaminate food or surfaces by pathogenic microorganisms.

### Mosquitoes

Although trade and travel are important in the introduction and subsequent dispersion of mosquitoes, climate suitability is also believed to have been an important factor. Warm seasonal and annual temperatures and ample rainfall in Europe offer conducive climatic conditions for *Aedes albopictus* – one of the world’s most invasive vector. The introduction and geographical expansion of the vector has coincided with favorable climatic conditions in France, the Balkans, the eastern coasts of Spain and the Adriatic Sea, the Benelux countries and western Germany [27, 29]. Considering transport corridors Asia – Europe, the freight exchange between countries of these two continents is growing from year to year. There are existed and planned great hubs on ground crossings where containerized goods had been reloaded to transport further by trans-European routes [22, 28]. As Thomas et al. [32] simulated, there can be an increasing risk of introducing of *Aedes albopictus* mosquito when climatic suitability is higher and freight via train is increasing. Such a situation can be created on hubs at South – East EU border, where ground crossings (with intensive commodity flow: Bulgaria – Turkey, Romania - Ukraine) lay in suitable for *Ae. albopictus* climatic zone. However, some other parts of Europe that have not yet been invaded by this vector can be climatically suitable for *A. albopictus* and lay on the main transport routes from East to West. Several localities in Poland along the

transportation corridors from East to West could be an example of regions where suitable conditions for a Tiger Mosquito could be considered; in such towns as: Wrocław, Katowice, Łódź, Poznań average summer months temperature could be high enough to allow development of 2 generations of *Aedes albopictus* mosquitoes and winter temperatures in these towns in recent years oscillated around 2-3°C, which could be enough to overwintering eggs of this mosquito [29]. Figure 1. shows a system of international and national roads and railway connections in Poland important for transit goods in East – West direction. The main logistic centres are: Brest/Terespol and Malaszewicze on the Poland – Belarus border; Medyka/Żurawica on the Poland – Ukraine border; inland logistic centers are: Warsaw, Łódź, Sławków (Katowice nearby), Wrocław, Poznań.

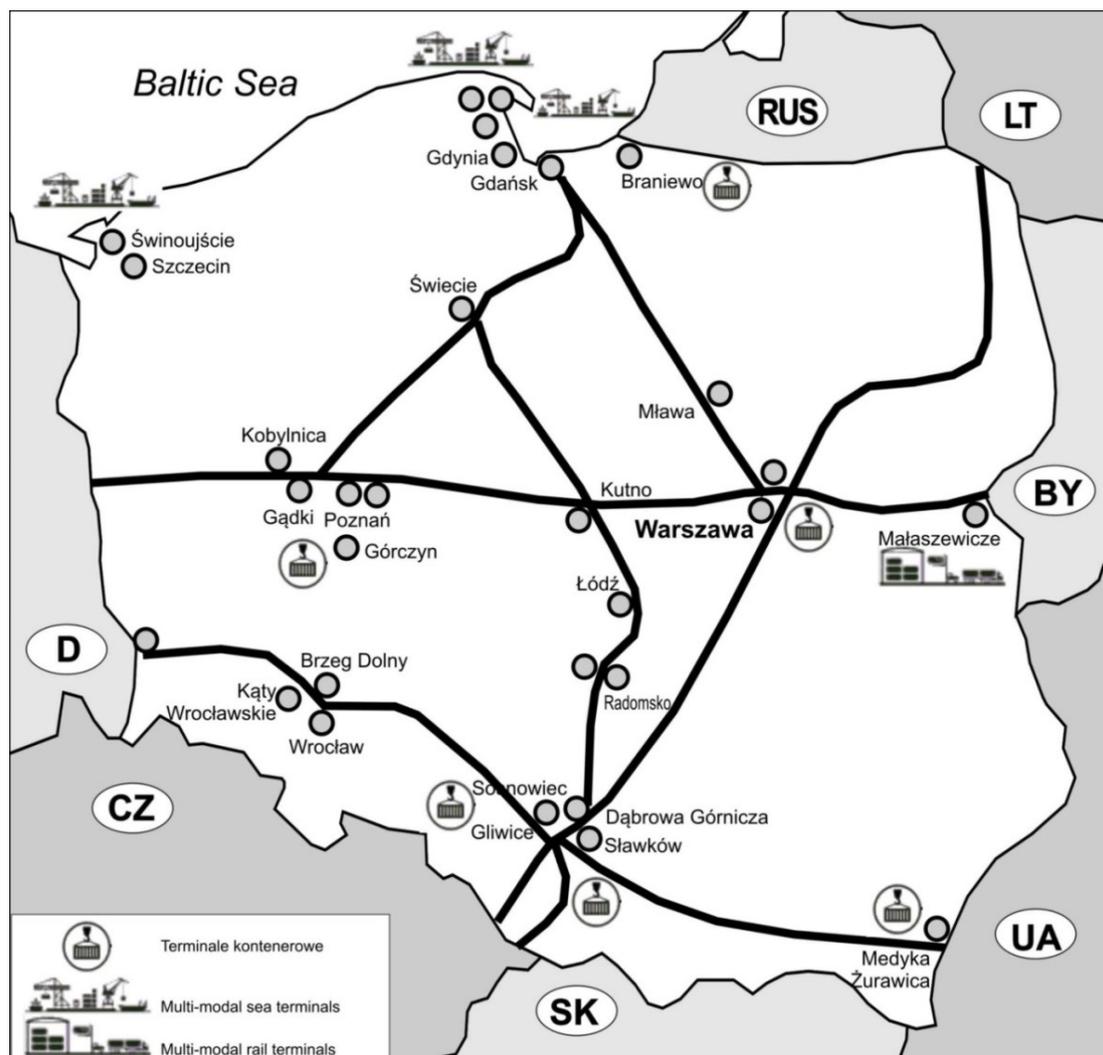
Trade companies work on shorten time of delivery goods from Asia – now it is between 10.5 and 21 days (Table 1). In this time adults mosquitoes can survive and immature stages can develop in appropriate conditions (humidity and temperature).

Table 2 presents categories of commodities transported from China to Europe - among them are plans – several of them are transported in water or moist substrate. This enhance the probability of transportation of eggs or larvae of mosquitoes. One of the way of introducing *Aedes albopictus* to European region (Benelux countries) was an import of Lucky Bamboo plants which were transported in small containers with water (larvae of mosquitoes were developed in them). Different way was export of used tires and then transported from sea ports via car transport across West European countries [29].

To sum up, considering trade routes and conditions, the freight transport way from Asia to Europe could play a role in introduction *Ae. albopictus* into several European territories, both where this mosquito is establish by now and also new territories with suitable climatic conditions.

Data from the literature [14, 15, 27] showed that other invasive *Aedes* species in North and Central Europe do not find suitable environmental conditions to expand till now, even the introduction cases have taken place. *Anopheles* mosquitoes could accompanied mostly living beings: travelling people or transported animals. Generally, the inflow of alien mosquito species must be continuous or at least multiple to establish population in a new area [17]. However, the changing climatic conditions should be taken into account: several too cold territories now can be warmer and more suitable in the future for mosquitoes.

Figure 1. A system of international and national roads and railway connections in Poland important for transit trade in East – West direction.



(Source: [www.agatstudio.waw.pl](http://www.agatstudio.waw.pl))

### Ticks

Most of ticks can reach new territories on their host bodies. Migratory birds can be the source of introducing ticks; but mostly these arthropods do not build stable populations when are transported long distance – between continents. Bigger chance to establish in a new environment have ticks who were transported on birds at shorter distances – for example moving from East to West or South to North Europe on bird of one species changing the territory in Autumn or Spring [11, 14]. The tick *Ixodes ricinus*, effective vector of Lyme borreliosis is present almost in the whole Europe [20].

Livestock transported into Europa countries from East – South territories (South Europe and Asia) could be infested by *Hyalomma* ticks [15]. Living animals is one of the commodity category transported from Asia to Europe and there is a possibility to transport ticks on them as well. - Despite of a danger to introduce new tick species animal transports should be carefully inspected and veterinary checked before transportation.

People coming back from holidays and their pets can be the carriers of ticks living in south and east-south territories of Europe: *Hyalomma spp.*, *Ripicephalus spp.* [11, 19]. *Ripicephalus sanguineus* tick is of Mediterranean and Black Seas Basins origin. It was found on dogs which had been taken for holidays in south and then carried ticks when they returned back to their homes [14, 19].

### Fleas

Fleas can extend territory with their hosts together. Many of them live on specific animal species and occur where they live. The changing of living area by an animal specimen causes that all external parasites go with him. This is true for people and their belongings – they can be also carriers of external parasites [12, 37, 38].

Several flea species, among them the oriental rat flea - *Xenopsylla cheopis* (which is the vector of *Yersinia pestis*, a plague causative agent) parasitize on

rats, so the ratproofing and rat control of transported goods are important actions which ought to be undertaken to prevent dissemination of fleas.

### Cockroaches

Cockroaches are common in the whole world except arctic areas. There are species present at human dwellings and lived outside. They can invade means of transport like ships, aircraft, trains and are present everywhere they can find food and water. Many categories of transported commodities can serve as appropriate food and harborage for cockroaches of several species – they can travel between continents [2]. Exotic tropical species were found in Sweden (in heated greenhouses *Pyenoscellus surinamensis* was established), but *Periplaneta australasiae*, and *Supella longipalpa* were recorded from Czech Republic [15]. Transported goods should be carefully controlled if they are cockroach free, because these insects can survive and develop during long journey in hidden places.

### Flies

There is no part of world free from flies. They are common around human settings, animal farms, food processing plants, restaurants, hotels, e.t.c. Housefly is elsewhere, so it is difficult to consider it as an invader. Many fly species are called “synantropic flies” as they are present in antropogenic environment, close to people [30].

Flies can accompany living animals in transport. Where are living animal there is manure. In this medium many species of flies can develop, so it is necessary to clean regularly animal containers and to use IGR (Insect Growth Regulators) agents for prevent development of flies. Transported animals can carry in their bodies larvae of fly species which develop in living organisms and are aliens in the new area. Such invasions can occur among tourists coming back from tropical or subtropical climatic zones as well. Among species recorded as larvae in human and animal bodies, alien in Europe, were: *Cordylobia anthropophaga* (Africa, Arabian Peninsula), *Wohlfartia magnifica* (Mediterranean area, Russia, China) [13, 15].

The procedures of insect proofing and insect control should be applied during preparing goods to transport and veterinary procedures when living animals will be transported.

## DISCUSSION

Hazard of diseases caused by pathogens transported by arthropod vectors which can arise at ground crossings at East and South – East EU border should be considered taking into account the following aspects [17, 38]:

1. Presence of vectors infected by pathogens in the place of loading goods or starting point of journey of people.
2. Transport or journey conditions – if they allow to survive some of development form of vector.
3. Transport of vector - incidentally (little chance of introduction) or multiple (greater chance of introduction).
4. Conditions - suitable by vector organism to survive at the point of entry or not.
5. Environmental conditions in the target area - suitable for surviving or development of vector or not.

Actions undertaken to stop the invasion of alien species - vectors to the new territories according to above list of problems should be carried out at starting point of loading goods (or starting point of passenger journey), during transport, on crossing point at the border and at the terminus where commodities were unloaded. Such operations are regulated by International Health Regulations [19] and European Union [1, 4, 5, 6, 7, 8, 9, 23, 24, 25] and state laws [34, 35, 36].

Vector organisms, as well as others, change and expand their area of occurrence in time. This process accelerated in the 20th and 21st centuries. This may be related to:

- globalization - intensifying trade in goods and increasing the travel of people between continents and various climate zones;
- climate change: many species find favourable conditions for living in new areas that are not yet climatically accessible to them, while the others leave areas that are becoming inappropriate for them;
- urbanization of the environment, which is associated with higher temperatures in cities resulting from the intensive human economy [38].

In Western, South and lately Central Europe, the expansion of the *Aedes albopictus* mosquito, a vector of dengue and Chikungunya virus has been observed from the 70s. This mosquito gradually takes over areas located in France, Germany, Italy, Spain, Switzerland, Croatia, Austria and the Czech Republic. Also other mosquitoes of the genus *Aedes* spp., having the ability to expand beyond their original limits of occurrence colonize new areas in Europe (e.g. *Aedes aegypti* was the vector of Dengue causative agent DENV-1 in Madeira island in 2012) [29].

Ticks from the genera *Hyalomma* spp., and *Rhipicephalus* spp., that were found in the past in the Mediterranean and Eurasian forest-steppe areas are also noted more north [11, 19]. Exotic species of cockroaches are brought to the countries of Europe along with transported goods (there are cases of their survival in heated greenhouses and hotels) [15].

Travelers, returning from tropical countries infected with fly larvae developing in human and animal tissues, report to doctors [13].

Existing regulations governing the exchange of goods and the movement of persons between countries are accurate and cover all aspects from the preparation of the goods to dispatch / commencement of travel by people, to reaching the final destination by the goods and people [20, 39].

Crossing the border between states (in this aspect - the state border between a country bordering on the west or south-west side and a country of the European Union) is one of the stages included in legal regulations. It should be emphasized that the goods are not always unloaded at transshipment centers on the border; in Poland such centers exist in the interior of the country (Warsaw, Poznań, Łódź and Sławków near Katowice) or containers are only opened at the destination. In addition to border controls, those that take place in customs warehouses in transshipment centers play a significant role in the control of transported goods. Therefore, the proper preparation of goods for transport is even more important in the aspect of preventing arthropods - vectors from infesting them and protecting the container and goods against rodents. These types of activities are recorded in the transport documents controlled at the border crossing [4, 5].

Customs and sanitary regulations regarding the flow of people across borders clearly specify the control in situations of threat to public health [18, 25]. It should be stated that actions aimed at limiting the accidental invasion of an arthropod - vector are difficult to carry out by sanitary and border services and can be burdensome for travelers. Some, despite the assumed effectiveness, cannot be carried out (e.g. passenger car, luggage, clothes). Therefore, it should be assumed that the source of vectors - stowaways at the border crossing may be passenger transport vehicles and people traveling with them. This route was confirmed in the case of the spread of the mosquito *Aedes albopictus* through ferry communication between the islands in the Mediterranean Sea and in places along the Sun Highway on its European coast [29]. Since it is not possible to carry out intensive eradication activities at border crossing points in passenger traffic, it would be necessary to strengthen public education so that people increase their knowledge about vector organisms and their role in transmitting diseases, their occurrence, possibilities of accidental transport and means of protection against them.

At border crossing points with significant passenger traffic or where goods are transshipped, it is reasonable to create a 400-meter vector monitoring zone, as proposed in the International Health

Regulations [18]. Such zones should also be created in customs warehouses and transshipment centers within transit countries (e.g. in Poland). Existing provisions of law do not provide for this; one should therefore consider the legitimacy of their changes in this respect. The provisions of international law [18] and national regulations since 2005 regulate every stage of the international flow of goods and people. However, it should be taken into account that the presence of alien arthropod vectors has been signaled in many European countries since the 90s of the XX century [29, 31]. Existing legal regulations provide control over the introduction of organisms - disease vectors into European Union countries from countries bordering it. However, the problem is the spread of vectors in areas within the European Union. Control of these processes could be ensured by adequate monitoring. This requires the involvement of human resources and measures, which is why it is currently carried out at random, in some areas and only in some countries. It would be particularly needed in countries with a high transit flow of goods, such as Poland. Due to the epidemiological significance, at least the mosquito fauna should be monitored around the transshipment centers of goods on the eastern border and within the country (perhaps also here appropriate legal regulations are needed).

## CONCLUSIONS

1. Vector organisms can enter new areas along with goods, in luggage or clothing of travelers, as well as a result of the expansion of acreage occurring in natural evolutionary processes.
2. Existing legal regulations provide procedures to protect goods and persons against the transport of organisms - vectors at every stage of transport and travel.
3. Expansion of Asia-Europe transport routes and shortening travel time can increase the risk of introducing vector organisms from Asian countries to Europe
4. Mass passenger and car traffic at border crossing points increases the likelihood of vector organisms entering as random stowaways, therefore it is proposed to intensify educational activities to make people aware of the dangers posed by the transport of alien species of arthropods and what preventive actions to take.
5. Unloading goods in a transit country (such as Poland) may take place at a transshipment center located near the border or inland. It is postulated to introduce a 400m vector monitoring zone around both.
6. Such a zone should also be taken into account at border crossings with heavy passenger and car traffic.

## Vectors do not respect political borders!

### Conflict of interest

*The author declares no conflict of interest.*

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## STATE SCHOOL OF HYGIENE AS A DEPARTMENT OF EDUCATION IN THE NATIONAL INSTITUTE OF HYGIENE IN WARSAW\*

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### ABSTRACT

The article presents the history of the establishment of the State School of Hygiene (PSH) in Poland after the First World War. The difficulties faced by the public health service in a country destroyed by war and created after the reunification of the lands, which for over 150 years remained under the control of three powers, were pointed out. It discusses how the foundations of modern teaching in the field of public health were created in the National Institute of Hygiene (PZH) in Warsaw, an institution to which the Ministry of Public Health entrusted tasks related to health education in the country. The State School of Hygiene was built by the Polish Government with a significant financial contribution from the *John Davison Rockefeller* Foundation. The official opening ceremony took place on 20 April 1926. The State School of Hygiene in Warsaw was the first such school in Europe. It educated professional staff for the health service in Poland, especially sanitary physicians, sanitary inspectors, nurses and staff to work in health offices. The importance and scope of influence of the State School of Hygiene as the Department of Education in the National Institute of Hygiene was constantly increasing, as evidenced by the number of students (about 800 per year) participating in courses, especially in the first years after its establishment. By the end of 1935, 6,389 students had completed the courses, including 1,900 physicians. Apart from the teaching activities, the State School of Hygiene also carried out research work. The State School of Hygiene was supported by the Rockefeller Foundation, which funded scholarships for the employees of the National Institute of Hygiene at university centers in the USA.

**Key words:** *State School of Hygiene (PSH), National Institute of Hygiene (PZH), public health service, education, Rockefeller Foundation, Poland*

### STRESZCZENIE

W artykule przedstawiono historię utworzenia Państwowej Szkoły Higieny (PSH) w Polsce po I Wojnie Światowej. Wskazano na trudności, z jakimi borykała się publiczna służba zdrowia w kraju wyniszczonym wojną i powstałym po zjednoczeniu ziem, które przez ponad 150 lat pozostawały pod zaborem trzech mocarstw. Omówiono jak powstawały podstawy nowoczesnego nauczania w dziedzinie zdrowia publicznego w Państwowym Zakładzie Higieny (PZH) w Warszawie, instytucji, której Ministerstwo Zdrowia Publicznego powierzyło zadania związane z edukacją zdrowotną w kraju. Państwowa Szkoła Higieny wybudowana została przez Rząd Polski z wydatną pomocą finansową Fundacji *Johna Davisona Rockefellera*. Uroczyste jej otwarcie odbyło się 20 kwietnia 1926 r. Państwowa Szkoła Higieny w Warszawie była pierwszą tego typu szkołą higieny w Europie. Kształciła personel fachowy dla służby zdrowia w kraju, a w szczególności lekarzy sanitarnych, inspektorów sanitarnych, pielęgniarki i personel do pracy w urzędach zdrowia. Znaczenie i zakres oddziaływania Państwowej Szkoły Higieny jako Działu Nauczania w Państwowym Zakładzie Higieny, stale wzrastał, o czym świadczyła liczba studentów (około 800 rocznie) uczestniczących w kursach, zwłaszcza w pierwszych latach po jej utworzeniu. Do końca 1935 r. kursy ukończyło 6389 słuchaczy, w tym 1900 lekarzy. Niezależnie od działalności dydaktycznej w Państwowej Szkole Higieny wykonywane były także prace badawcze. Państwową Szkołę Higieny wspierała Fundacja Rockefellera fundując stypendia naukowe pracownikom Państwowego Zakładu Higieny w ośrodkach uniwersyteckich w USA.

**Słowa kluczowe:** *Państwowa Szkoła Higieny, PSH, Państwowy Zakład Higieny, PZH, szkolenia, publiczna służba zdrowia, Fundacja Rockefellera, Polska*

### INTRODUCTION

In the initial period of Poland being reborn after World War I, one of the most acute shortages was the lack of staff in the public health service. This was due not only to the lack of physicians, pharmacists

and sanitary staff, but also to the different level of education of these personnel, who came from three different partitions of Poland and the poor sanitary condition of the country.

At that time, the National Institute of Hygiene (PZH) in Warsaw, established in 1918, was the most

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important health-related institution in Poland, to which the Ministry of Public Health entrusted tasks related to health education in the country, including the training of medical and auxiliary health care personnel [3, 5]. Therefore it turned out to be necessary to establish a hygiene school in Poland, which would be responsible for theoretical and practical training in public health [5]. Already at that time, it was well known that not only the quality of disease treatment, but also health prevention supported by education and dissemination of knowledge throughout the country contributes to the health of the society.

### BEGINNINGS OF THE STATE SCHOOL OF HYGIENE

In order to meet these needs, the Council of Ministers adopted a resolution of 19 June 1922 on the establishment of the State School of Hygiene (PSH) as a new department in the National Institute of Hygiene [6]. An Inter-ministerial Committee for the Creation of the School was setup and started to work as early as September 1922. This was made possible by an agreement between the Polish Ministry of Public Health and the *J. D. Rockefeller* Foundation on July 10, 1922, under which the Foundation allocated \$ 292,500 for the construction of the State School of Hygiene in Warsaw. However, this amount turned out to be insufficient and therefore the Polish Government, for its part, allocated PLN 500 000 (and also a building lot) for the finishing of the School and its equipment. At the same time, the government undertook to maintain the School [3].

The school was to educate specialist personnel for health care, in particular sanitary physicians, sanitary inspectors, nurses and office staff dedicated to work in health offices operating at the provincial level throughout Poland.

The building of the School, designed by architect *Czesław Przybylski*, was to be completed in 1924. At that time the director of the National Institute of Hygiene was Dr. *Ludwik Rajchman*, who held this position in 1918-1930.

The Polish authorities at that time understood perfectly well how important for the proper development of society and the functioning of the state will be the establishment of such a training centre, which was intended to radiate knowledge throughout Poland [6].

At that time, the National Institute of Hygiene was the only institution in Poland that was able cope with the tasks imposed on the State School of Hygiene.

The establishment of the State School of Hygiene as an Department of Education in the National Institute of Hygiene made it possible to use many outstanding scientists to conduct training activities. Thanks to

this, the students of the School of Hygiene could learn from the most eminent specialists who usually combine research passion with practice in the field of bacteriology, immunology, epidemiology, food safety, proper nutrition and hygiene.

The State School of Hygiene was established two years before its official opening on 20 April 1926 [7].

In 1926, the State School of Hygiene, whose director was Dr. *Witold Chodźko*, consisted of the following divisions [6].

- Biochemistry – Head, Dr *Kazimierz Funk*
- Epidemiology and Statistics – Head, Dr *Marcin Kacprzak*
- Sanitary Technology – Head, Eng. *Aleksander Szniolis*
- Occupational Hygiene – Head, Dr *Brunon Nowakowski*
- Social Hygiene – Head, Dr *Jerzy Lubczyński*
- and Museum of Hygiene

The State School of Hygiene also owned the Amelin estate with the Health Centre and Bursa. Some of these branches had already been operating in the National Institute of Hygiene before [1].

It is worth noting that the State School of Hygiene in the National Institute of Hygiene in Warsaw was the first such school of hygiene in Europe. Similar schools of hygiene were soon opened in Zagreb and Budapest [2].

It was recognized that the programme for hygiene schools had to be developed through international cooperation with the participation of both professors with knowledge of teaching and health officials with knowledge of practical hygiene needs.

The official opening of the State School of Hygiene in Warsaw became an opportunity to organize a meeting of the Section of Hygiene of the League of Nations, whose director was Dr *Ludwik Rajchman*. It was attended by members of this Section - representatives of universities and state administration from Berlin, Budapest, Lisbon, London, Paris, Warsaw and Zagreb. The opening ceremony was attended by *Aleksander Skrzyński* - Prime Minister. *Witold Chodźko*, Director of the State School of Hygiene, gave a lecture presenting the curriculum of the School. He was later invited to give a lecture on the occasion of the opening of the School of Hygiene in Budapest [2, 7].

### ORGANISATION AND TASK OF THE SCHOOL

The National Institute of Hygiene was located in a complex of buildings at 24 Chocimska Street in Warsaw. The State School of Hygiene occupied a separate, four-story building located at the front of Chocimska Street. On the ground floor there were offices, a library and a laboratory for bacteriological trainings for 50 people. The Museum of Hygiene also played an important role. It occupied a significant part

of the first floor, the remaining part was occupied by the Laboratory of Occupational Hygiene. The Museum had the character of a permanent exhibition and occupied an important place in the process of education and dissemination of knowledge on the epidemiology of infectious diseases and public hygiene. The Museum had the following sections: food hygiene, village hygiene, sanitary engineering and others. It also had a section named "Health and Disease", where examples were used to explain what are epidemics, what are the conditions for their spread, what is immunity and how external conditions can affect human susceptibility to disease. The museum was visited by more than 5,000 people a year [3].

On the second floor of the State School of Hygiene there were two lecture rooms (small and large), seminar room and rooms for professional staff. The third floor was occupied by the Department of Biochemistry. There were rooms for chemical exercises and separate rooms for assistants and academics. In addition, there was also a room for experimental animals in the building. The fourth floor was used for housing for the employees of the State School of Hygiene [6].

The Amelin property at 91 Puławska street in Warsaw was an auxiliary institution for the State School of Hygiene. The Amelin estate was purchased by the Government in 1922 thanks to the help of the American "Joint Distribution Committee". In two buildings standing there was a bursa of the State School of Hygiene, whose rooms could accommodate 50 students. The next two buildings were occupied by the Health Centre with many outpatient clinics serving as didactic facilities for the School's students. A separate building was also erected in this area, in which disinfecting and insect control devices used for practical exercises were placed [3]. The Health Centre in Amelin had a tuberculosis clinic with a children's sanatorium, an anti-venereal diseases clinic, a maternal and child care station, a milk station, an anti-trachoma clinic, a mental hygiene clinic, an anti-alcoholic and a dental clinics [6, 7]. Apart from treating and spreading sanitary knowledge among the population, doctors gained there practical experience and became acquainted with many issues of social medicine.

The significant step in the development of the State School of Hygiene was to put at its disposal an experimental station to study the methods of wastewater treatment in Kaskada Park<sup>1</sup>, which enabled

the introduction of practical classes in this important area of sanitary engineering. Regardless of the training, the access to the experimental station on the Cascade made it possible to investigate the level of pollution of the Vistula river and developing wastewater treatment methods. Studies on the effectiveness of chlorinating drinking water were also carried out there [7].

The importance and scope of the impact of the State School of Hygiene was constantly increasing, which is indicated by the growing number of students participating in the courses.

The number of students in the first years after the establishment of the School of Hygiene is shown in Table 1.

Table 1. The number of students in the first years of the State School of Hygiene [7]

Years	1924	1925	1926	1927
Number of students	76	258	478	806

## DIDACTIC AND RESEARCH ACTIVITY

The National Institute of Hygiene was the only research and development institution in Poland at that time that trained hygiene physicians and auxiliary staff [3], and the State School of Hygiene operating there conducted basic courses for specific groups of employees (i.e. candidate physicians in the public health service or sanitary inspectors) and information courses of a more general nature.

The scope of training was consistent with the requirements of the Act on the State Civil Service, according to which each provincial physician should undergo one-year training completed with a passed state examination in the field of epidemiology, medical statistics, social hygiene, sanitary administration, sanitary legislation and forensic medicine. Each participant of the course acquired theoretical knowledge in the State School of Hygiene for 6 months, and for the remaining part (3 months) of the nine-months training he completed practical exercises in health centres and sanitary administration offices.

The regulations concerning obligatory studies at the State School of Hygiene covered only provincial physicians but not city physicians. Nevertheless, the high level of graduates of the State School of Hygiene resulted in the fact that they were also employed as hygienists in the cities [3].

<sup>1</sup> Kaskada Park - at the junction of Kolektorska Street and Trószczyńskiego Street in Warsaw. In the years 1913-1915, the Experimental Station for Sewage Treatment was built here, designed by *Rafał Gomółski* with the main sewerage system of the city existing since the 1880s. Works on the construction of the station, interrupted during World War I, resumed in 1927. The official address of the institute was Marymoncka 16, where research was conducted in the field of sewage treatment methods, next to the station, on the collector, there was also an aqueduct on the Rudawka river. [https://warszawa.wikia.org/wiki/Miejsc\\_pami%C4%99ci\\_w\\_Parku\\_Kaskada](https://warszawa.wikia.org/wiki/Miejsc_pami%C4%99ci_w_Parku_Kaskada)



Figure 1. Training for provincial physicians in 1929.

Sitting in the first row from the left: Prof. *Ludwik Hirszfeld* (first) director of the National Institute of Hygiene (PZH), Dr. *Witold Chodźko* - director of the State School of Hygiene (sixth from the left).

(Photo from the collection of the National Institute of Hygiene, Warsaw).

Training was also organised for medical auxiliaries, including sanitary inspectors. They constituted the future staff of the Voivodship Sanitary and Epidemiological Stations established after World War II. The main objective of these trainings was to improve the sanitary condition of the country and to transfer appropriate knowledge and skills in the field of environmental hygiene, supervision of food products, water intakes and, what was then extremely important, disinfection treatments of the homes of people suffering from infectious diseases.

The State School of Hygiene educated health care staff and provided many other trainings and courses on its own initiative or at the request of the authorities, such as [6]:

- 1) Training of public health personnel, at the initiative of the General Directorate for Health Services and the State School of Hygiene itself. In 1924, 76 students and in 1925, 83 students were trained;
- 2) Courses run by the public authorities in consultation with the State School of Hygiene. The aim of these courses was to train staff in public hygiene. In 1925, 95 students were trained;
- 3) Lectures and courses conducted by scientific organisations and social associations with the participation of PSH staff in order to teach and promote hygiene and preventive medicine to different groups of people. In 1925, 80 students were trained and 32 lectures were given.

For the duration of the training, the course participants were housed in the dormitory of the School of Hygiene in Amelin, where they also received full board for a moderate fee [6].

The School of Hygiene during the economic crisis (1932-1933) was financially supported by the Rockefeller Foundation. It also funded scholarships for employees of the National Institute of Hygiene (PZH) to enable them to undergo training at scientific universities in the USA (International Health Division, *John Hopkins* University in Baltimore and Cambridge University in Boston).

Scholarship holders of the *J. D. Rockefeller* Foundation from the National Institute of Hygiene in honor of *John Davison Rockefeller* funded a commemorative plaque. Unveiling of the plaque signed: "*Rockefellerczycy Polskiej Służby Zdrowia*" took place on 6 January 1938 in the hall of the State School of Hygiene. Unfortunately, this plaque disappeared during the German occupation during the World War II. There is only a photograph of it. However, a plaque commemorating the establishment of the State School of Hygiene, which is located nearby the entrance to the main auditorium of the National Institute of Hygiene, has been preserved. On the photograph (Figure 2) a plaque commemorating the establishment of the State School of Hygiene in Warsaw is visible in the foreground, and in the background one can see the lost memorial plaque funded by the Rockefeller Foundation scholarship holders.



Figure 2. The plaque commemorating the establishment of the State School of Hygiene in Warsaw by the Polish Government with the significant financial support of the *J.D. Rockefeller* Foundation. Lost memorial plaque funded by Rockefeller Foundation scholarship holders in the background.

In 1935, the State School of Hygiene acting as the Department of Education, after the organisational changes that took place in the National Institute of Hygiene, constantly grew and eventually consisted of the following Departments [3].

- Statistics, Social Hygiene and Epidemiology
- Occupational Hygiene
- Nutrition Hygiene and Biochemistry
- Control of Biological Products
- Sanitary Engineering (Administration)
- Institute of Mental Hygiene
- Museum of Hygiene
- Library
- Bursa (in Amelin)

Regardless of the didactic activity in 1938, the departments carried out the following research [3]:

*The Department of Statistics, Social Hygiene and Epidemiology* conducted research on rural hygiene, organization of general medical care, infectious diseases and population issues. The latter, carried out in cooperation with the Polish Institute for Population Research, allowed to demonstrate that in reality infant mortality in the eastern provinces was much higher than the official statistics. As a result of these studies 23 papers were published.

*The Department of Occupational Health* carried out field and laboratory tests of workers. The methods for the determination of lead in blood, urine and faeces, benzene, hydrogen sulphide, sulphur dioxide, carbon disulphide and chlorinated hydrocarbons in the air, free silica dust were developed there. Besides the research on dust and ionization of air the study were conducted in the ventilation chamber. There were also led modern field studies in factories concerning the importance of active rest for female workers. As a result of these activities 5 papers were published.

*The Department of Nutrition Hygiene and Biochemistry* dealt with, among others, the study of the biological values of cereal and vegetable proteins, the study of the influence of storage on the content of vitamin C in cranberries, the influence of alcohol on adrenal function, the study of biological values of vitamin preparations. 10 papers have been published on these issues.

*The Department of Control of Biological Products* conducted pharmacological and biological tests of 415 hormonal and vitamin preparations from the Polish market. There have been also conducted numerous scientific studies in the field of endocrinology (e.g. iodine content from thyroxine in thyroid preparations), pharmacology and vitamin sciences, including the mechanisms of their action, calibration of vitamin E in different products, vitamin B1 content in yeast preparations. Since 1935, pregnancy tests in urine have been performed. 4 papers were published.

*The Department of Sanitary Administration* was responsible for the retrospective examination of the progression of measles for several dozen years, defining the characteristics and factors influencing the development of the epidemic. The results of diphtheria vaccination in the years 1935-1938 and health indicators in the Central Industrial District were also examined. Surveys on the development and care of infants and organizing nursing competitions for mothers were also conducted. 3 papers were published.

The location of scientific departments in the structure of the State School of Hygiene, whose scientific employees were obliged, apart from teaching, to conduct scientific work and publish its results, was a solution ensuring the highest possible level of education under given conditions. Direct contact between course participants and lecturers allowed to get acquainted with current health care problems and enabled students to access the latest scientific achievements.

The Institute of Mental Hygiene was also incorporated into the structure of the State School of Hygiene from 1935 [9]. Its task was to organise scientific research and normative works, to teach and disseminate knowledge in the field of mental hygiene, and first of all to organize and run clinical facilities in this area, which could serve

as a model in the emerging state health service. Within the framework of these activities, 5 outpatient clinics for children and youth were opened. In 1937, the turnout at outpatient clinics for children was 1,839 and the number of visits to outpatient clinics for adults was 302. Independently of outpatient care, the Institute, through the Social Welfare Department, organized the placement of children with mental disorders in foster families in rural areas and organized courses for social nurses and educators, as well as lectures for parents [3, 10].

By the end of 1935, the State School of Hygiene had organized 122 courses, training 6389 students, including 1900 physicians. By the end of 1938, 8614 students had completed their courses. This indicates that around 800 students completed the courses annually [4, 8, 11].

The subject matter of the courses was very diverse and included a wide range of social medicine. For example, the courses organized in 1935 included the following topics [8]:

- Public hygiene training for physicians applying for public health service positions
- Training for sanitary inspectors
- Trachomatology training for physicians
- Instructional training for doctors of Health Centres
- Hygiene training for primary school teachers
- Sports rescue training
- Alcohol counselling and training centre
- Course in eugenics and prenuptial counselling for physicians
- Information course on school hygiene for teachers of Primary Schools
- Course for physicians of industrial adoption camps.

Some of these courses were repeated in the subsequent following years, but there were new issues and so between 1937 and 1938, in addition to the courses mentioned above, the following courses were included [10, 11]:

- Course in medical microbiology for the sanitary cadets of the reserve
- A 3-month course in mental hygiene for nurses and educators
- Theoretical and practical course on blood group science for reserve physicians
- Course in the field of population issues
- Course on prevention, diagnosis and treatment of venereal diseases for social insurance physicians.

## ACTIVITIES AFTER THE WORLD WAR II

In 1946 the State School of Hygiene resumed its teaching activity and started training social health service personnel, who were to take up new tasks in the field of improving and protecting the health of the society [2, 4].

However, the post-war situation for the State School of Hygiene was misfortune. The School of Hygiene building in ruined after the war Warsaw, was temporarily occupied by the Ministry of Health. The School of Hygiene had only two rooms where lectures and exercises were held. A bursa (in Amelin) was made available to the students. Soon, the Ministry of Health left the occupied premises of the School of Hygiene, but some of the rooms were handed over to the Board of Polish Health Resorts, and the ground floor was partially occupied by the Medical Scientific and Publishing House.

The State School of Hygiene organized trainings not only in Warsaw, but also in four centres in the branches of the National Institute of Hygiene in Gdańsk, Łódź, Poznań and Wrocław [12].

The State School of Hygiene was also the patron of the journals "Zdrowie Publiczne" (Public Health), "Medycyna Doświadczalna i Społeczna" (Experimental and Social Medicine), "Na Straży Zdrowia" (Healthcare) published in 1946 in the National Institute of Hygiene.

In 1952, the tasks of the State School of Hygiene were taken over by the Sanitary and Hygiene Study at the Medical Academy in Warsaw, but the post-graduate trainings were left the National Institute of Hygiene [4].

The main goal of the educational activity was to train public health service employees who could supplement the lack of doctors, administrators of health service (municipal and district doctors, occupational doctors, sanitary controllers and other health service personnel). In Warsaw courses for doctors were held, in Kraków, where the lack of laboratory staff was severely felt, a course for technical assistants was organised, and in Łódź, a training course for disinfectors. Courses were also held in Płock, Pruszków, Garwolin, Witkowiec, Bydgoszcz, Wieluń, Suwałki, Lublin, Wrocław, Gdańsk and Konin. The lack of textbooks necessary for the education process was supplemented by the National Institute of Hygiene own publications [13].

The tradition of the own publications, used to improve the skills of employees of the sanitary and epidemiological stations, has been preserved in the National Institute of Hygiene (PZH) to this day. They were published as needed in the form of the Methodical Publications of the National Institute of Hygiene (PZH) and are intended for the use of the Sanitary and Epidemiological Stations. This resulted from the fact that one of the statutory duties of the National Institute of Hygiene was to supervise laboratory activities of the sanitary and epidemiological stations.

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## COMMENT ON PERIODIC VEGETARIANISM AND THE FIRST MENTIONS OF A PLANT DIET IN POLAND (ROCZ PANSTW ZAKL HIG 2019;70:217-223)

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In 1880 *Alfred von Seefeld* (25.08.1825–12.08.1893) published in Hannover a book devoted to vegetarianism [1], which four years later was translated into Polish, with the subtitle “wegeteryjanizm” and a commentary on plant-only diet (“pożywienie wyłącznie roślinne”) by *Konstanty Moes-Oskragiello* (6.01.1850–27.01.1910) [2]. In the late 19<sup>th</sup> century, *Moes-Oskragiello*’s own literary output on a plant-based diet [3, 4] initiated an emotional discussion among Polish medical practitioners [5, 6] and, once translated into Russian, went on to have a big impact on Russian vegetarians, including *Lev Tolstoy* [7]. In 1883, *Moes-Oskragiello* founded a natural medicine clinic (“Lecznicy Zakład Termopatyeczny”) offering vegan dishes in Otwock near Warsaw [6]. In this respect, *Skorek et al.*’s [8] claim that the first mention of a plant diet in Polish society and its scientific literature appeared as late as 1912 must be corrected.

Moreover, in discussing the history of vegetarianism in Poland, it is worth mentioning that a large part of the former Polish–Lithuanian Commonwealth’s population adhered closely to the dietary recommendations of Eastern Orthodox Christianity, which advocated so called periodic vegetarianism [9] and from which we can discern the origins of contemporary so-called fast dishes in Polish cuisine [10, 11]. It is also worth noting that *Moes-Oskragiello*, born in a family with Dutch roots, grew up in an area inhabited by numerous Eastern Orthodox Christians [6]. Reduced intake or complete abstinence from food of animal origin is practised by Orthodox Christians for a total of 180–200 days annually [12]. The duration of fasting periods can range from seven weeks, in the case of the Great Lent (meat, dairy products and eggs are not allowed, but fish can be consumed on Lady Day and Palm Sunday, and caviar on Lazarus Saturday) and 40 days, in the case of the Christmas fast, to a single day (e.g. Wednesdays, Fridays, the eve of the Epiphany [18 January in the Gregorian calendar], the Beheading of St John the Baptist [11 September] and the Exaltation of the Holy Cross [27 September]).

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The Editorial Office invites to read the above Letter to Editor and encourages our Readers for comments.

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2. *Lopes M.C., Giudici K.V, Marchioni D.M., Fisberg R.M., Martini L.A.*: Relationships between n-3 polyunsaturated fatty acid intake, serum 25 hydroxyvitamin D, food consumption, and nutritional status among adolescents. *Nutr Res* 2015;35(8):681-688.
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*Books and chapter in a book:*

5. *Riley D.M., Fishbeck P.S.*: History of methylene chloride in consumer products. In: *Salem H., Olajos E.J.* (eds.). *Toxicology in Risk Assessment*. London, Taylor & Francis, 2000.

*Legislative acts:*

6. Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. *Off J EU L* 364, 20.12.2006.

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7. The Rapid Alert System for Food and Feed (RASFF) Portal. Available <https://webgate.ec.europa.eu/rasff-window/portal> (accessed 18.10.2010)

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