*Aneta Czerwonogrodzka-Senczyna[1], Małgorzata Janusz[1], Anna Jeznach-Steinhagen[1], Beata Pyrżak[2]

Immunomodulators and immunostimulants in the diet of children and teenagers suffering from simple obesity

Składniki immunomodulujące i immunostymulujące w diecie dzieci i młodzieży z otyłością prostą

[1]Department of Human Nutrition, Medical University of Warsaw
Head of Department: Dorota Szostak-Węgierek, MD, PhD
[2]Department of Pediatrics and Endocrinology, Medical University of Warsaw
Head of Department: Beata Pyrżak, MD, PhD

Key words

obesity, children, teenagers, immunomodulators, immunostimulants, diet

Słowa kluczowe

otyłość, dzieci, młodzież, składniki immunomodulujące, składniki immunostymulujące, dieta

Summary

Introduction. A diet balanced for macrocomponents, minerals, and vitamins, is essential to achieving optimal immunity.

Aim. The purpose of this study was to evaluate immunomodulators and immunostimulants in the diet of children and teenagers suffering from simple obesity.

Material and methods. The study involved 100 children and teenagers aged 7-18 suffering from simple obesity. Each patient was interviewed on the products and meals consumed within the last 48 hours, their weight and height measurements were taken, and their Body Mass Index (BMI) was calculated. The estimation of consumed nutrients, including immunomodulators and immunostimulants, was based on the nutrition interview. The obtained results were then related to compared with the nutritional norms in place.

Results. The mean daily calorie intake in the studied group equalled 74%, and for proteins it was 151%. On average, the proportion of n-6:n-3 fatty acids equalled 10:1. For amino acids in the diet the highest intake values were observed for glutamic acid (1450.44 mg/day). The study demonstrated inadequate intake of iron (77% of Recommended Daily Allowance – RDA), folic acids (42% of RDA), vitamin C (84% of RDA) and lycopene (41% of RDA). The mean daily intake of other nutrients exceeded the RDA values.

Conclusions. The diet of the study participants was not properly balanced for macrocomponents and immunomodulators, which may be the reason of immunological disorders and immunodeficiency in this group of patients.

Streszczenie

Wstęp. Prawidłowo zbilansowana dieta pod względem zawartości makroskładników, składników mineralnych oraz witamin jest niezbędna do uzyskania optymalnej odporności.

Cel pracy. Celem pracy była ocena spożycia z dietą składników immunomodulujących oraz immunostymulujących przez dzieci i młodzież z otyłością prostą.

Materiał i metody. Badaniem objęto 100 dzieci i młodzież w wieku 7-18 lat z otyłością prostą. U każdego pacjenta przeprowadzono wywiad dotyczący spożycia produktów i potraw z ostatnich 48 godzin, wykonano pomiary masy i wysokości ciała, wyliczono wskaźnik BMI (ang. *body mass index*). Na podstawie wywiadu żywieniowego oszacowano spożycie składników pokarmowych, w tym o działaniu immunomodulującym oraz immunostymulującym. Otrzymane wyniki odniesiono do obowiązujących norm.

Wyniki. Średnia realizacja normy na energię w badanej grupie wynosiła 74%, w przypadku białka – 151%. Stosunek kwasów tłuszczowych n-6:n-3 wynosił średnio 10:1. Wśród aminokwasów największą zawartością w diecie cechował się kwas glutaminowy (1450,44 mg/dobę). Odnotowano nieadekwatne do potrzeb spożycie żelaza (77% normy), folianów (42%), witaminy C (84%) oraz likopenu (41%). Realizacja normy na pozostałe składniki przewyższała rekomendowane wartości.

Wnioski. Dieta badanych nie była prawidłowo zbilansowana pod względem zawartości makroskładników oraz składników immunomodulujących, co może się przyczyniać do występowania zaburzeń odporności w tej grupie pacjentów.

Address/adres:

*Aneta Czerwonogrodzka-Senczyna
Department of Human Nutrition
Medical University of Warsaw
ul. Ciołka 27, 01-445 Warszawa
tel. +48 (22) 836-09-13
fax +48 (22) 836-09-71
aneta.czerwonogrodzka@wum.edu.pl

INTRODUCTION

Apart from genetic predispositions for accumulation of body fat the factors that contribute to the development of simple obesity include positive energy balance resulting from excessive food consumption and sedentary lifestyle. Excessive weight and obesity are important risk factors for cardiovascular disease, diabetes, liver disease, and frequent upper respiratory tract infections. Previous studies have shown that infections are more common in obese people than in normal-weight persons. The risk of bacteraemia is also higher for overweight individuals in the case of burns, which may lead to life-threatening infections. The nutritional status has significant impact on the immunological system. Obesity manifests through changes in immunity, particularly in cellular response (1-4).

Human studies have demonstrated excessive body mass to be correlated with impaired activity of immunocompetent cells. Nutritional deficiencies of iron or zinc in obese persons responsible for changes in the immune system, may be reverted by supplementation of these components and restoration of their concentration balance. Researchers point to a direct correlation between the level of obesity and changes in cellular and humoral immunity. Moreover, the T and B lymphocyte response to pathogens proved to be significantly lower in obese persons (4).

Modulation of the immunological response in obese and overweight persons is particularly important, as it may affect the chronic inflammation associated with pro-inflammatory properties of body fat. Recent studies focus on inflammatory markers such as: C-reactive protein (CRP), cytokines (IL-1, IL-6), and tumour necrosis factor (TNF-α). Leptin deficiencies in obese persons lead to T cell proliferative disorders and to simultaneous impairment of cytokine secretion. In patients with normal leptin concentrations, which constitutes most obese persons, an increased tendency to secrete TNF-α and IL-6 in relation to the manifestations of insulin resistance and type 2 diabetes (1).

Following treatment targeted at reduction of body mass, the patients' health condition improved and asthma-associated symptoms subsided (1, 5).

Dietary components with immunomodulatory and immunostimulating characteristics/properties include: glutamine, arginine, cysteine, n-3 fatty acids, nucleotides, and nutrients, such as: zinc, iron, selenium, B vitamins, vitamin E, vitamin A, vitamin C, glutathione, lycopene, and the components of breast milk (6-8).

AIM

The purpose of the study was to evaluate immunomodulators and immunostimulants in the diet of children and teenagers suffering from simple obesity.

MATERIAL AND METHODS

The study involved a carefully selected group of children and teenagers, aged 7-18 (n = 100), diagnosed with simple obesity.

The study was based on data from direct interview on the participant's diet in the last 48 hours, as well as information on the level and type of their physical activity.

Information on nutrition/feeding during the first 12 months of life and chronic diseases, including allergies and asthma, were provided by the parents or legal guardians.

For each patient, body mass and height were measured, then used to calculate the Body Mass Index (BMI). BMI calculations were standardised using mean values and standard deviations for the population of Warsaw children. Normalised data (in SDS) were obtained (9).

Diets of study participants were analized according to the "Table of nutritional value of food products and dishes" (10). The energetic and nutritional value of the consumed foods was estimated, with particular emphasis on the percentage of intake of amino acids (arginine, methionine, and glutamic acid), minerals (zinc and iron), vitamins (C, E, A, and B), and n-3 and n-6 fatty acids. The calculation of cysteine and selenium intake was based on the American tables of composition and nutritional values of foods (11). The lycopene intake was calculated from the study by Hamułka and Wawrzyniak (12). The data obtained for each patient were compared to the Recommended Daily Allowance (RDA) values for both genders and different age groups (13), and the rate of conformity was calculated. A Microsoft Excel spreadsheet was used for analysis of questionnaire data and the statistical analysis was performed with Statistica 9.0 software. The level of statistical significance was established at $p < 0.05$.

RESULTS

In the study group (n = 100), the majority of participants were boys (52%). The highest SDS BMI values were observed for teenagers aged 16-18 years (4.32 ± 1.68). The lowest values were observed for children aged 10-12 years (3.00 ± 0.86) (tab. 1).

Table 1. Segmentation of the study group based on age, gender and SDS BMI values.

Age group	Number of boys	Number of girls	SDS BMI (mean ± SD)
7-9 years	11	11	3.73 ± 1.18
10-12 years	21	20	3.0 ± 0.86
13-15 years	12	7	3.64 ± 0.87
16-18 years	8	10	4.32 ± 1.68

SD – standard deviation

88% of the study children were breastfed until the 4-6 month of age. The same percentage of mothers then continued breastfeeding, and 48% of mothers still breastfed their child until 12 months of age, 10% continued breastfeeding for more than 2 years, and 5% for more than 3 years. Just under 40% of children, whose mothers declared that they were breastfed, were diagnosed with food or airborne allergies. A small group of participants (3%) was diagnosed with asthma.

The mean conformity rate with regard to energy intake was 74% for the whole group. The diets of children aged 7-9 years were most often within the range of recommended values. The lowest conformity rates were observed for teenagers aged 16-18 years (tab. 2).

Table 2. Median and range of energy values of consumed food (kcal) and the rate of conformity with the recommended values of diets in various age groups.

Age group	Number of people	Median	Range	Rate of conformity with regard to energy
7-9 years	22	1642 kcal	961-3030 kcal	93.8%
10-12 years	41	1635 kcal	701-2882 kcal	74.0%
13-15 years	19	1697 kcal	983-2960 kcal	66.3%
16-18 years	18	1783 kcal	904-2509 kcal	60.1%

The mean conformity rate with the recommended values with regard to proteins was 151%. The mean percentage of this component in the total energy value of the consumed food was estimated at 17 ± 4%, on average.

For carbohydrates, the rate of conformity was 172%. The mean percentage of this macrocomponent in the total energy value of the consumed food was 50 ± 7.38%.

On average, 88% of the recommended values for fat was consumed. The percentage of energy obtained from this component was 33 ± 7%. The mean intake of n-3 polyunsaturated fatty acids was 1 g/day and of n-6, 10 g/day. The mean proportion of n-6:n-3 fatty acids equalled 10:1.

The analysis of diets showed that the mean intake of arginine in the study group was 3772.25 mg/day. The mean values for glutamic acid consumed by the study children was 1450.44 mg/day. The mean percentage of methionine intake equalled 1749.93 mg/day. For cysteine, this value was 943 mg/day.

The mean zinc intake in the study group was estimated at 8.5 ± 2.8 mg/day and the rate of conformity was 112%. The rate of conformity with recommended values with regard to selenium equalled 260% (mean intake 108 ± 36.3 μg/day). Nutrient deficiencies were mostly observed with regard to iron. This component was provided with diet at the level of 77% of the Recommended Daily Allowance.

Most of the vitamins of the B group was consumed by children in excess. The rate of conformity for thiamine was 111%, for riboflavin, 121%, and for niacin, 103%. The intake of pyridoxine and cyanocobalamin was higher than the recommended values and it was 146% of RDA for both components. The only RDA value that was not conformed to was the recommended value of folic acid intake (42%).

The mean intake of fat-soluble vitamins equalled 147% for vitamin A and 82% for vitamin E. The rate of conformity with the recommended allowance values of vitamin C equalled 84% for the entire study group.

In the study group the mean lycopene intake was 2.45 mg/day, which accounted for a 41% rate of conformity with the recommended values.

A statistically significant correlation between body mass and consumption of n-6 polyunsaturated fatty acids was observed. Children and teenagers with higher body mass consumed significantly more n-6 fatty acids (fig. 1).

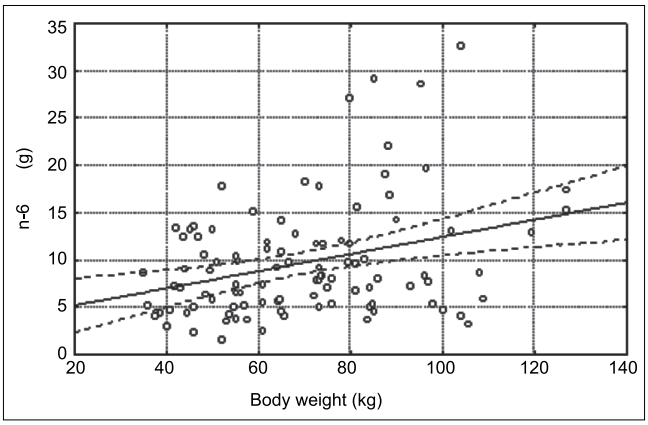

Fig. 1. The correlation between body mass and the percentage of n-6 fatty acids in the diet ($r = 0.322$; $p < 0.05$).

The rate of conformity with the recommended values for zinc was negatively correlated with body mass ($p < 0.05$) (fig. 2).

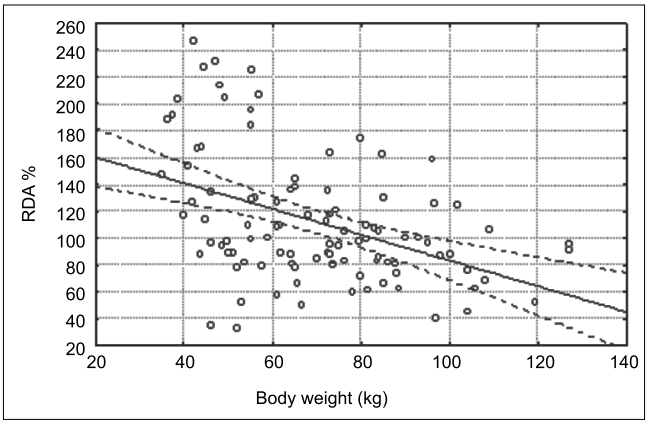

Fig. 2. The correlation between body mass and rate of conformity with recommended values for zinc ($r = -0.433$; $p < 0.05$).

Similar correlations were observed for conformity with recommended values of energy intake and components such as: fat, iron, and selenium (tab. 3).

Table 3. P and r values for body mass vs. selected nutrients.

Component	p	r
Body mass vs. energy	0.000	-0.3614
Body mass vs. fat	0.004	-0.2882
Body mass vs. iron	0.008	-0.2641
Body mass vs. selenium	0.001	-0.3393

With age, the participants consumed significantly more fat, selenium, zinc, and vitamin A, and their diets were characterised by lower energy value.

DISCUSSION

In the recent years, the number of people diagnosed as overweight or obese has been gradually increasing. Excess body fat leads to various health consequences. Additionally, fat secretes pro-inflammatory substances, which impair menthe functions of the immunological system.

It is commonly believed that high-energy diets lead to excess weight and obesity (14). However, the authors of this study draw attention to the fact that such diet is more often the result of a positive energy balance resulting from low levels of physical activity (15). This study demonstrated a 74% mean rate of conformity with the RDA recommended energy values. The available and commonly used methods of analysis do not fully reflect the amounts of consumed foods (16). The errors in the study may therefore be attributed both to the incorrect estimation of the actual amount of consumed food as well as the tendency so commonly observed in obese people of not disclosing full information about food consumption (in particular food commonly believed to lead to obesity).

The authors observed high levels of consumption (mean intake of 151% RDA), which is also confirmed by the protein analyses performed by other authors/researchers (17).

Excess intake of carbohydrates, particularly monosaccharides, may also contribute to the development of simple obesity (14). As demonstrated in this study, the intake of this component exceeded 170% of RDA.

Diet analysis demonstrated that the intake of fatty acids in this group was lower than recommended. The rate of conformity with recommended values for this nutrient was only 88%, while the ratio of n-6:n-3 fatty acids was also incorrect. The correct proportion of these acids ensures their effective functions. Excess intake of n-6 fatty acids, together with a high ratio of n-6:n-3, leads to pathogenesis of many diseases, including, among others vascular disease, tumours, inflammatory and autoimmune disorders/diseases (18). As the study demonstrates the mean ratio of polyunsaturated fatty acids in the diet of obese children and teenagers was 10:1, so the potentially pro-inflammatory n-6 acids are in majority. Dry and Vincent (19) analized the impact of n-3 acids on asthma progression. They demonstrated the intake of n-3 acids to be associated with relatively less frequent occurrence of inflammatory diseases. The first effects of therapy were already observable after 9 months. The impact of n-3 acids on asthma progression was particularly important as allergies and asthma are often concomitant with obesity. The study demonstrated that 3% of study children suffered from asthma, and just under 40% suffered from various allergies that enhance the risk of asthma later in life. Intake of alpha-linolenic acid in the study group was 1.02 g/person per day.

The immunomodulatory properties of arginine are primarily related to its function in the production of nitrogen oxide and glutathione synthesis (8). On the other hand, glutamine plays an important part in T lymphocyte proliferation and differentiation of B lymphocytes (20). The properties of taurine result from its antioxidant properties, which also contribute to stability of cellular membranes (21). The study group demonstrated the mean intake of 3772.25 mg/day of arginine, 14 050.44 mg/day of glutamic acid, 1749.93 mg/day of methionine, and 943 mg/day of cysteine. The high intake values for proteins may suggest that the consumption of these amino acids was also high however, the lack of set recommended values of intake makes it impossible to conduct a detailed data analysis.

Analysis of study results demonstrated insufficient iron intake in the diets of children and teenagers. The mean rate of conformity with the daily recommended values was 77%. Experiments conducted on animal models demonstrated that insufficient iron intake results in the impairment of NK cells functions as well as of B lymphocytes responsible for antibody production (22).

A noteworthy fact were the significantly exceeded selenium intake values. The mean value for the entire group of participants was 260%. Such extreme values may be explained by the fact the databases of American tables of composition and nutritive values of food products were used to estimate the percentage of this element in the diets of our study patients (11). Nevertheless, excessive intake of selenium may be toxic. In the 1980s, LeBoeuf et al. conducted studies on rat models (23) and demonstrated that excessive intake of selenium provoked adaptive changes in the liver as result of increased oxidation of glutathione. Cells of the immune system are particularly sensitive to the deficiency of this component. Its antioxidant properties protect immunological components against the destructive properties of free radicals.

Insufficient intake of B vitamins leads to cell-mediated immunity disorders (24). The study demonstrated that in most cases the mean B vitamin intake exceeded the recommended values. The rate of conformity with the recommended values for folate was only 42% of the RDA. Green vegetables such as spinach, lettuce, cabbage, broccoli, and asparagus are a good source of folic acids (10). Insufficient intake of this component among children and teenagers may be associated with poor consumption of vegetables rich in folic acid which may lead to severe nutrient deficiencies. The deficiency of this component is usually associated with neural tube defects that occur in the first few weeks of foetal life or with megaloblastic anaemia (25). Folic acid deficiency impairs/limits theability of hemopoietic cells to synthesize nucleic acids (26). Deficiency of folic acid seem to play an important part in Cell-mediated immunity. Prolonged insufficient folic acid intake may result in reduction of T lymphocyte count and, as a consequence, to a weaker immunological response (27).

Ascorbic acid deficiency may impair T lymphocyte proliferation and cytotoxicity of neutrophils and Tc lymphocytes. The study demonstrated insufficient intake of

vitamin C (85% of RDA). Supplementation of ascorbic acid to improve the functioning of the immune system has shown positive results. The study demonstrated a positive effect of dietary supplementation of this component which led to regression of changes resulting from insufficient intake of vitamin C (28).

The authors also determined a low level of vitamin E intake in the study group. The mean rate of conformity for this component was 82% of RDA. Vitamin E is an antioxidant and protects the cells of the immune system. Insufficient intake of this component leads to the impairment of protective functions of the body and ineffective defence against potential pathogens (29).

Lycopene intake values vary according to geographical region. The estimated mean intake of this component in the USA falls within the 3.7-16.2 mg/day range. In Canada, this value fluctuates around 25.2 mg/day, and in Germany, around 1.3 mg/day (30). The study demonstrated that the lycopene intake in obese children and teenagers was 2.45 mg/day (41% of RDA). Lycopene has photoprotective properties therefore its insufficient intake may enhance the destructive properties of UV light and contribute to the weakening of the immunological system. Insufficient lycopene intake may also result in a simultaneous decrease in the NK cell count, as well as their cytotoxic capability (31).

Most study participants were breastfed during infancy. Those who were not constituted 12% of the study group. The choice of formula feeding may result in disorders of the newborn's immunological system. Formula feeding also increases the risk of child obesity and type 1 and type 2 diabetes (32) while breastfeeding at the early stages of life decreases the risk of adult obesity (33). Immunomodulatory properties of breast milk support the development of immunological mechanisms in infants. Breast milk constitutes an optimal food for the newborns, as it has antibacterial properties and is rich in components that promote development of the immune system (34).

Excess weight and obesity are strongly associated with the way the immune system functions. There is a significant correlation between excess body fat and changes in the immunological response. Excess body fat is responsible for lower immunity against bacterial and viral pathogens (1). What is more, fat produces (among others) pro-inflammatory cytokines, which contribute to the occurrence of chronic inflammations (4). Effective immune system has a crucial role to play in the treatment of obesity. Improvement of the health condition may be significantly affected by the reduction of body mass and improved intake of all the necessary nutrients, including immunomodulators and immunostimulants.

CONCLUSIONS

1. The diet of children and teenagers suffering from simple obesity were not properly balanced with regard to nutrients and immunomodulators.
2. Improper functioning of the immune system as result of obesity and inappropriate diet may lead to allergies and asthma in obese children and teenagers.
3. Insufficient intake of crucial immunomodulatory and immunostimulating nutrients (such as iron, folic acid, vitamin E, vitamin C, and lycopene), as well as an incorrect ratio of polyunsaturated n-6:n-3 fatty acids, may lead to impairment of the immunological system later in life.

BIBLIOGRAPHY

1. Matarese G, La Cava A: Immune responses in obesity models. Drug Discov Today: Disease Models 2005; 3: 177-181.
2. Kumari S, Chandra RK: Overnutrition and immune responses. Nutr Res 1993; 1: 3-18.
3. Nieman DC, Henson DA, Nehlsen-Cannarella SL: Influence of Obesity on Immune Function. J Am Diet Assoc 1999; 3: 294-299.
4. Samartin S, Chandra RK: Obesity, overnutrition and the immune system. Nutr Res 2001; 21: 243-262.
5. Shore SA, Johnston RA: Obesity and asthma. Pharmacol Ther 2006; 110: 83-102.
6. Wichers H: Immunomodulation by food: promising concept for mitigating allergic disease? Anal Bioanal Chem 2009; 1: 37-45.
7. McCowen KC, Bistrian BR: Immunonutrition: problematic or problem solving? Am J Clin Nutr 2003; 77: 764-770.
8. Evoy D, Lieberman M, Fahey TJ 3rd, Daly JM: Immunonutrition: The role of arginine. Nutrition 1998; 14: 611-617.
9. Palczewska I, Niedźwiecka Z: Somatic development indices in children and youth of Warsaw (in Polish). Med Wieku Rozwoj 2001; 5 (2 suppl. 1): 18-118.
10. Kunachowicz H, Nadolna I, Przygoda B, Iwanow K: Tables of nutritional value of food products and dishes (in Polish). 3rd ed., PZWL, Warszawa 2005.
11. United States Department of Agriculture. The USDA National Nutrient Database for Standard Reference. 2011. http://fnic.nal.usda.gov/food-composition/usda-nutrient-data-laboratory. Accessed 12 January 2014.
12. Hamułka J, Wawrzyniak A: Lycopene and lutein – the pro-health role and content in products (in Polish). SGGW, Warszawa 2004.
13. Jarosz M, Bułchak-Jachymczyk B: Standards of human nutrition. Fundamentals of prevention of obesity and non-communicable diseases (in Polish). PZWL, Warszawa 2008.
14. Collison KS, Zaidi MZ, Subhani SN et al.: Sugar-sweetened carbonated beverage consumption correlates with BMI, waist circumference, and poor dietary choices in school children. BMC Public Health 2010; 10: 234.
15. Berkey CS, Rockett HR, Field AE et al.: Activity, dietary intake, and weight changes in a longitudinal study of preadolescent and adolescent boys and girls. Pediatrics 2000; 4: 56-64.
16. Burrows T, Golley RK, Khambalia A et al.: The quality of diet intake methodology and reporting in children and adolescent obesity intervention trials: a systematic review. Obes Rev 2012; 13: 1125-1138.
17. Velasco J, Mariscal-Arcas M, Rivas A et al.: Assessment of the diet of school children from Granada and influence of social factors. Nutr Hosp 2009; 24: 193-199.
18. Simopoulos AP: The importance of the ratio of omega-6/omega-3 essential fatty acids. Biomed Pharmacother 2002; 8: 365-379.
19. Dry J, Vincent D: Effect of a fish oil diet on asthma: results of a 1-year double-blind study. Int Arch Allergy Immunol 1991; 95: 156-157.
20. Newsholme P, Curi R, Pithon Curi TC et al.: Glutamine metabolism by lymphocytes, macrophages, and neutrophils: its importance in health and disease. J Nutr Biochem 1999; 10: 316-324.
21. Roth E: Immune and cell modulation by amino acid. J Clin Nutr 2007; 26: 535-544.
22. Kuvibidila S, Baliga BS: Role of iron in immunity and infection. [In:] Calder P, Field C, Gill H (eds): Nutrition and Immune Function. CABI Publishing in association The Nutrition Society. New York, NY, USA 2002: 209-228.

23. LeBoeuf RA, Hoekstra WG: Adaptive changes in hepatic glutathione metabolism in response to excess selenium in rats. J Nutr 1983; 113: 845-854.
24. Beisel WR: Nutrition and immune function: overview. J Nutr 1996; 126: 2611-2615.
25. Tamura T, Picciano MF: Folate and human reproduction. Am J Clin Nutr 2007; 83: 993-1016.
26. Jones PA, Baylin SB: The fundamental role of epigenetic events in cancer. Nature Rev Genet 2002; 3: 415-428.
27. Beisel WR: Single nutrients and immunity. Am J Clin Nutr 1982; 35: 417-468.
28. Noh K, Lim H, Moon SK et al.: Mega-dose Vitamin C modulates T cell function in Balb/c mice only when administrated T cell activation. Immunol Lett 2005; 1: 63-72.
29. Mitchell B, Ulrich C, McTiernan A: Supplementation with vitamins or mineral and immune function: can the elderly benefit? Nutr Res 2003; 23: 1117-1139.
30. Rao AV, Rao LG: Carotenoids and human health. Pharmacol Res 2007; 55: 207-216.
31. Chew BP: Role of Carotenoids in the Immune Response. J Dairy Sci 1993; 9: 2804-2811.
32. Stuebe A: The Risks of not breastfeeding for mothers and infants. Rev Obstet Gynecol 2009; 2: 222-231.
33. Owen CG, Martin RM, Whincup PH et al.: Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. Pediatrics 2005; 115: 1367-1377.
34. Brandtzaeg P: Role of local immunity and breast-feeding in mucosal homoeostasis and defence against infections. [In:] Calder P, Field C, Gill H (eds): Nutrition and Immune Function. CABI Publishing in association The Nutrition Society: New York, NY, USA, 2002: 273-320.

received/otrzymano: 02.07.2014
accepted/zaakceptowano: 19.09.2014