

Grażyna Rowicka, Halina Weker

GLUTEN-CONTAINING PRODUCTS IN THE DIET OF INFANTS IN NUTRITIONAL RECOMMENDATIONS – A RETROSPECTIVE VIEW AND CONCLUSIONS FOR THE FUTURE

PRODUKTY GLUTENOWE W DIECIE NIEMOWLĄT W ZALECENIACH ŻYWIENIOWYCH – SPOJRZENIE RETROSPEKTYWNE, WNIOSKI NA PRZYSZŁOŚĆ

Department of Nutrition, Institute of Mother and Child, Warsaw, Poland

Abstract

The discussion on the optimal timing of the introduction of gluten products and their quantity into the diet of infants in order to reduce the risk of the development of undesirable reactions to gluten, including celiac disease, has been going on for years.

The aim of this study was to present how the relevant Polish nutritional recommendations in this regard had changed over the last fifty years.

Key words: gluten, complementary feeding, celiac disease, infants

Streszczenie

Od lat trwa dyskusja dotycząca optymalnego czasu wprowadzania do diety niemowląt produktów glutenowych oraz ich ilości w kontekście zmniejszenia ryzyka rozwoju niepożądanych reakcji na gluten w tym glutenezależnej choroby trzewnej.

Celem pracy było przedstawienie jak na przestrzeni ostatniego półwiecza zmieniały się w tym zakresie polskie zalecenia żywieniowe.

Słowa kluczowe: gluten, żywność uzupełniająca, celiakia, niemowlęta

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Celiac disease (CD) is a genetically inherited enteropathy of the small intestine, triggered by an inappropriate immunological reaction to the gluten consumed. It may occur at any age, but most often manifests itself in early childhood and in people aged 30-50 years. According to epidemiological data, celiac disease occurs in approximately 1-3% of the population. The estimates based on screening studies show that the prevalence of asymptomatic celiac disease in white individuals ranges from 1:100 to 1:300, and the frequency of its symptomatic form amounts to 1:3000 people [1].

The pathogenesis of celiac disease is not fully known. The current theory is that apart from genetic predispositions, its risk factors comprise environmental, metabolic and immunological factors. Celiac disease is one of the most common genetic diseases of the white race, thus the incessant search for factors that could reduce the risk of its development. Some research focuses on environmental factors, including nutrition as the factor potentially affecting the risk of celiac disease.

Until 1963 there had been no uniform recommendations on the feeding of infants, including recommendations

on the optimal timing for the introduction of gluten products to the diet of infants and on the quantity of those products. In February 1963, the first infant feeding scheme recommendations "Formula Feeding" developed by the Institute of Mother and Child in Warsaw were presented at a symposium dedicated to the nutrition of children [2]. The aim of the publication was to introduce a uniform method of feeding of infants in Poland. Due to the lack of relevant recommendations, various groups used locally developed nutrition schemes which did not always correspond to the state of knowledge at that time. The guidelines were based on the results of experimental studies and on multidimensional observation research. They were also discussed by specialists in the nutrition of children. The guidelines developed on the formula feeding of infants recommended introducing gluten products to the diet of infants in the second month of their life. Children at that age should be fed 6 times a day with the so-called flour mixture II, in the amount of approximately 120-130 g per portion. Taking into account the recipe for flour mixture II, made of milk diluted with water in the proportion of 70:30, with the addition of 100 g of milk and 2 g of flour, an infant fed in this way and eating full portions received from 14.4 g to 15.6 g of a gluten product per day. In the third month of life, it was suggested to replace two feedings with mixture II, i.e. wheat flour / coarse-ground wheat flour, flour mixture III in the amount of approximately 120-150 g per portion. The mixture was made of whole milk and contained 3 g of flour per 100 g. Therefore, in the third month of life an infant received from 16.8 to 19.4 g of a gluten product per day.

The recommendations revised in 1975 suggested that gluten products should be introduced to the diet of infants later, i.e. in the third month of a child's life. The revision made the Polish recommendations more similar to those in place in other European countries at that time. According to the 1975 guidelines, a formula-fed infant in the third month of life could be given 6 milk meals with approximately 140 g per portion, including 4 meals with the addition of flour, i.e. the so-called flour mixture II. According to the recipe, the amount of flour in 100 g of this mixture made of milk powder or partly humanised milk – *Bebiko 1* amounted to 2 g (1 flat teaspoon). Mixture II with flour could be replaced with a ready-made milk and carbohydrate mixture, available on the market at the time, with the addition of wheat flour, called *Laktowit II* (vitaminised milk and carbohydrate mixture, wheat flour 2%). Therefore, an infant at the age of 3 months, fed in line with the recommendations, received approximately 11 g of a gluten product per day. In the fourth month of life, the recommendation was to introduce the so-called mixture III with flour in the amount of 5 x 130-140 g. As in the third month of life, the main ingredient of the mixture could be milk powder and the quantity of flour added to 100 g of the mixture amounted to 3 g. Mixture III with flour could be replaced with *Laktowit III* (vitaminised milk and carbohydrate mixture, wheat flour 3%). The subsequent source of gluten was vegetable soup in the amount of 150 g, with the addition of semolina (5 g of semolina per 100 ml of

soup). Thus, an infant at the age of 4 months received approximately 29 g of a gluten product per day.

In breastfed children, the recommendation was to introduce gluten products in the fifth month of life. The suggested amount was 160-180 g of semolina with milk (one flat teaspoon, i.e. approximately 5 g, per 100 g of milk); the meal included from 8 to 9 g of a gluten product [3].

The amendments introduced to the recommendations in 1981 did not affect the recommendation to introduce gluten products to the diet of formula-fed infants in the third month of life, but increased the gluten quantity to approximately 17 grams [4].

Another modification to the recommendations on introducing gluten products took place in 1984. It was suggested small amounts of gluten should be introduced to the diet of formula-fed infants in the fourth month of life – 5 x 140-160 g of *Bebiko 2GR*. At that time, buckwheat was considered to be a low-gluten product. In the fifth month of life, apart from *Bebiko 2GR* 5 x in the amount of 150-180 g, an infant could also receive one portion of semolina with milk in the amount of 150-180 g, i.e. approximately 11 g of a gluten product. Information included in the comments to the recommendations stated "exclusively formula-fed infants should, in the first six months of life, receive cornmeal and other gluten-free cereal products, e.g. rice, low-gluten buckwheat groats, instead of semolina, fine-milled buckwheat groats and others". However, the recommendations included an instruction to give cereal and oat gruel to infants approximately at the age of 9-12 months, in particular to exclusively formula-fed infants. The introduction of gluten products to the diet of breast-fed infants was recommended in the tenth month of life, e.g. a portion of semolina with milk/batter noodles with milk/bread rolls/rye sourdough bread [5].

Another revision of recommendations on the formula feeding of infants took place in 1988. According to the revised recommendations, "infants fed with a formula from their birth should receive cornmeal and other gluten-free cereal products in the first nine months of their life." As in the previous guidelines, buckwheat products were treated as low-gluten products and recommended in small quantities in the fifth month of life, e.g. milk mixture *2GR 2* x 150-180 g. More gluten products could be introduced to a child's diet in the ninth and tenth month of life – bread roll or rye sourdough bread, pearl barley [6, 7].

The recommendations from 1990 maintained the instruction that the diet of a child in the first nine months of his/her life should be gluten-free. Therefore, "flour used in that period should be gluten-free, e.g. made from rice, corn, or it may be wheat starch or buckwheat flour as a low-gluten product". Some gluten products could be introduced at the age of 9-12 months in order to, as the authors stated, "get the child used to tolerating this ingredient" [8].

The recommendations formulated in 1993 took into account the position of ESPGHAN (European Society of Paediatric Gastroenterology, Hepatology and Nutrition), and thus suggested that gluten products should not be

introduced to the diet of infants up to the age of 9 months: “until the ninth or tenth month of life of both formula-fed and breast-fed child no groats or flour with gluten should be given (fine-milled buckwheat groats, semolina, pearl barley, oat flakes)” [9]. An important reason for such a recommendation was the opinion that the elimination of gluten protects the child from developing an allergy due to its immature intestine barrier. In the fourth quarter, i.e. from 10 months of life, it was suggested to abandon the gluten-free diet and to gradually introduce all types of groats, i.e. semolina, pearl barley, oat groats, millet, buckwheat groats, fine-milled buckwheat groats, as well as wheat and rye flour (bread rolls, bread, rusks).

This position was upheld in the recommendations updated in 2001. Both the feeding scheme for breastfed infants and the one for formula-fed infants recommended introducing cereal products containing gluten in the tenth month of life in the form of porridge, gruels, groats, bread rolls, bread, rusks [10].

The research conducted in 2002 revealed that the introduction of small amounts of gluten to the diet of infants during the period of breastfeeding significantly reduced the risk of the onset of celiac disease in early childhood and probably also decreased the risk of this disease in older children [11]. Norris et al. proved that the risk of celiac disease is five times higher in infants who had received gluten before the 12th week of life and slightly higher in infants given gluten since the age of 6 months, as compared to children who started receiving gluten products between the fourth and sixth month of life [12]. The research by Akobeng et al. showed that the risk of the development of celiac disease decreased along with the duration of breastfeeding, particularly if gluten was introduced to the child’s diet when the child was still breastfed [13]. Those findings, as well as nutritional practices in other European countries and the United States, gave rise to the updating of the recommendation on the optimum timing for introducing gluten to the diet of healthy, maturely born Polish infants. In 2007, the Expert Team appointed by the National Consultant for Paediatrics amended the recommendations on the diet of children in the first year of age, presenting the feeding scheme for breastfed infants and the formula feeding scheme for children up to 12 months of age. The amendments concerned *inter alia* the rules of introducing gluten to the diet in order to reduce the risk of celiac disease. The new rules recommended the gradual introduction of gluten in small amounts (2-3 g of a product containing gluten per 100 g of a meal) to the diet of infants, preferably within the period when the infants are breastfed, at the age of 5-6 months. The recommendation for formula-fed infants was to introduce products with gluten not earlier than in the fifth month and not later than in the sixth month of life [14]. The recommendations aroused controversies and not all physicians agreed with the amendments introduced. This resulted in varying recommendations given to the parents of infants on the introduction of gluten products to the children’s diet. A pilot research assessing the implementation of the 2007 recommendations on the prevention of celiac disease three years after their presentation showed that

the majority of infants, both breast and formula-fed, were not covered by the prevention of celiac disease. As a result, products containing gluten were introduced to the diet of infants too early or too late, and in larger quantities than provided for by the recommendations [15]. The 2007 recommendations on earlier introduction of gluten products were not accepted by parents, either. One of the reasons for this attitude of parents could result from their transmitted nutritional patterns [16].

The results of two systemic reviews of literature published in 2012 and 2013 suggested that breastfeeding during the introduction of gluten to the diet had a protective effect against celiac disease [17, 18]. This contributed to upholding the position of the Committee on Nutrition of the ESPGHAN and the EFSA (European Food Safety Authority) on the timing of gluten introduction to the diet of infants. The position recommended avoiding introducing gluten to infants’ diet either too early (before fourth months of age) or too late (after seventh months of life); gluten should be introduced during the period of breastfeeding, which could protect children from the development of celiac disease. The position of the ESPGHAN and the EFSA constituted the basis for maintaining the 2007 recommendations on gluten in the subsequent revision of the Polish recommendations on feeding of infants, published in the Medical Standards 2014 – Nutrition of Healthy Term Infants. According to the revised recommendations, cereal products in small amounts should be introduced into the diet of both breastfed and formula-fed infants not earlier than in the fifth month of life and not later than in the sixth month of life (e.g. cereal groats containing gluten) [19].

The results of the multicentre randomised studies PreventCD and CELIPREV, published in 2014, constituted an important contribution to the ongoing discussion on the introduction of gluten to the diet of infants, i.e. on the optimal time of introduction and the amount of gluten, as well as the role of breastfeeding in celiac disease prevention [20, 21]. The PreventCD study proved that in children at a higher risk of celiac disease development, the introduction of a small quantity of gluten between the age of 4 and 6 months had not reduced – compared to the placebo – the risk of the development of celiac disease by the age of 3 years [20]. The findings of the CELIPREV study made it possible to formulate a conclusion that in children with a familial risk of celiac disease the timing of gluten introduction to the diet did not have an impact on the development of the disease within 5 years of the observation, but the earlier introduction of gluten was related to the onset of the disease at a younger age. Genetic factors had a significant impact on the development of celiac disease. Therefore, the results of both studies have shown that in groups at a high risk of celiac disease, specifying the time of gluten introduction to an infant’s diet and breastfeeding do not have an impact on the risk of celiac disease development, but may only delay its onset. Thus, the recommendations on the specific age and method of gluten introduction in order to reduce the risk of the disease have no grounds. This applied also to children who were not predisposed to the disease [21].

Table I Introduction of gluten-containing products into infants' diets - review of recommendations (1963-2016).
 Tabela I. Wprowadzanie produktów zawierających gluten do diety niemowląt – przegląd zaleceń z lat 1963-2016.

Year of revision of recommendations on gluten products in infants' diet Rok wprowadzenia zmian w zaleceniach dotyczących udziału produktów glutenowych w diecie niemowląt	Recommended age of introducing gluten products to the diet of infants Zalecany wiek wprowadzenia produktów glutenowych do diety niemowląt	Number and size of portions and the amount of gluten products per 100 g of a meal Liczba, wielkość porcji oraz ilość produktów glutenowych w 100 g posiłku
(I)	(II)	(III)
1963	Breastfeeding – 5th month of life Karmienie naturalne – 5. miesiąc życia Formula feeding – 2nd month of life Karmienie sztuczne – 2. miesiąc życia	1x 120-130 g mixture II with flour (100 g of milk -2 g of flour) or 1 x 120-130 g semolina/ fine-milled buckwheat groats /oat flakes in milk (100 g of milk - 4 g of groats) 1x 120-130 g mieszanka II z mąką (100 g mleka -2 g mąki) lub 1 x 120-130 g kasza manna/ drobna kasza krakowska/ płatki owsiane na mleku (100 g mleka-4 g kaszy) 6 x 120-130 g mixture II with flour (100 g of milk -2 g of flour) 6 x 120-130 g mieszanka II z mąką (100 g mleka -2 g mąki)

Table I. Cont.
Tabela I. Cd.

(I)	(II)	(III)
1975	Breastfeeding – 5th month of life <i>Karmienie naturalne</i> – 5. miesiąc życia Formula feeding – 3rd month of life <i>Karmienie sztuczne</i> – 3. miesiąc życia	1x 160-180 g semolina with milk (per 100 g of milk – 1 flat teaspoon of semolina, i.e. approx. 5 g) 1x 160-180 g kasza manna na mleku (na 100 g mleka – 1 płaska łyżeczka kaszy manny, tj. ok. 5 g)
1981	Breastfeeding – 5th month of life <i>Karmienie naturalne</i> – 5. miesiąc życia Formula feeding – 3rd month of life <i>Karmienie sztuczne</i> – 3. miesiąc życia	4 x 140 g mixture II with flour/Bebiko with added flour / Laktowit II 4 x 140 g mieszanka II z mąką/Bebiko z dodatkiem mąki/ Laktowit II 1x 150 g semolina with milk (per 100 g of milk – 1 flat teaspoon of semolina, i.e. approx. 5 g) 1x 150 g kasza manna na mleku (na 100 g mleka – 1 płaska łyżeczka kaszy manny, tj. ok. 5 g)
		4 x 130-140 g mixture II with flour (per 100 g of milk – 2 g of flour/ Laktowit II) 4 x 130-140 g mieszanka II z mąką (na 100 g mleka – 2 g mąki / Laktowit II)

Table I. Cont.
Tabela I. Cd.

(I)	(II)	(III)
1984	Breastfeeding – 10th month of life <i>Karmienie naturalne</i> – 10. miesiąc życia	1x semolina with milk, alternatively with pearl barley, oat groats, millet groats, fine-milled buckwheat groats 1x <i>kasza manna na mleku na zmianę z jęczmienną, owsianą, jaglaną, krakowską</i>
	Formula feeding – 4th month of life – 5th month of life <i>Karmienie sztuczne</i> – 4. miesiąc życia – 5. miesiąc życia	5x 150-180 g <i>Bebiko</i> 2GR 5x 150-180 g <i>Bebiko</i> 2GR 1x 150-180 g of semolina with milk 5x 150-180 g <i>Bebiko</i> 2GR 5x 150-180 g <i>Bebiko</i> 2GR 1x 150-180 g <i>kaszy manny na mleku</i>
1988	Breastfeeding – 10th month of life Karmienie naturalne – 10. miesiąc życia Formula feeding – 5th month of life – 9-10th month of life <i>Karmienie sztuczne</i> – 5. miesiąc życia – 9.-10. miesiąc życia	rusk with milk, bread roll/ 2x 150-180 g <i>Bebiko</i> 2GR rye sourdough bread / fine-milled buckwheat groats 2 x 150-180 g <i>Bebiko</i> 2GR <i>sucharek na mleku, butka/ chleb pytlowy/ kasza krakowska</i>

Table I. Cont.
Tabela I. Cd.

(I)	(II)	(III)
1990	Breastfeeding and formula feeding – 10th month of life <i>Karmienie naturalne i sztuczne</i> – 10. miesiąca życia	Gradual introduction of varied cereal products, i.e. semolina, pearl barley, oat groats, fine-milled buckwheat groats, and wheat and rye flour, slightly earlier Bebiko 2GR as a low-gluten product <i>Stopniowe wprowadzanie urozmaiconych produktów zbożowych, tj. kaszy miannej, jęczmiennej owsianej, krakowskiej oraz mąki pszennej i żytniej, nieco wcześniej</i> Bebiko 2GR jako produktu ubogoglutennego
1993	Breastfeeding and formula feeding – 10th month of life <i>Karmienie naturalne i sztuczne</i> – 10. miesiąca życia	Gradual introduction of all types of groats, i.e. semolina, pearl barley, oat groats, millet, buckwheat, fine-milled buckwheat groats, and wheat and rye flour (bread rolls, bread, rusks) <i>Stopniowe wprowadzanie wszystkich rodzajów kasz, tj. miannej, jęczmiennej owsianej, jaglanej, gryczanej, krakowskiej oraz mąki pszennej i żytniej (bułki, chleb, sucharki)</i>
2001	Breastfeeding and formula feeding – 10th month of life <i>Karmienie naturalne i sztuczne</i> – 10. miesiąca życia	Cereal products, including with gluten - porridge, gruel, groats, bread rolls, bread, rusks <i>Produkty zbożowe w tym glutenowe</i> - kaszki, kleiki, kasze, bułki, chleb, sucharki
2007	Breastfeeding – in the 5-6th month of life Formula feeding – not earlier than in the fifth month and not later than in the sixth month <i>Karmienie naturalne - w 5.-6. miesiącu życia</i> <i>Karmienie sztuczne - nie wcześniej niż w 5. miesiącu i nie później niż w 6. miesiącu życia</i>	Gradual introduction of gluten in small amounts - 2-3 g of a product with gluten per 100 g of a meal <i>Stopniowe wprowadzanie glutenu w małych ilościach</i> <i>- 2-3 g produktu zawierającego gluten/100 g posiłku</i>
(I)	(II)	(III)
2014	Breastfeeding and formula feeding – not earlier than in the 5th month and not later than in the 6th month of life <i>Karmienie naturalne i żywienie sztuczne - nie wcześniej niż w 5. m.ż., nie później niż w 6. m.ż.</i>	Cereal products in small amounts, e.g. gluten cereal groats <i>Produkty zbożowe w małych ilościach, np. kasza zbożowa glutenowa</i>
2016	Breastfeeding and formula feeding – at any time after the 4th month of life, which corresponds to 17 weeks of life by the twelfth month of life. <i>Karmienie naturalne i sztuczne</i> <i>- w dowolnym okresie po ukończeniu 4. miesiąca życia, co odpowiada 17 tygodniom do 12. miesiąca życia</i>	Small amounts of cereal products, including gluten <i>Niewielkie ilości produktów zbożowych, w tym gluten</i>

Table II. Quantities of gluten-containing products [g] recommended for non-breastfed children in the first year of life, according to medical standards/nutrition guidelines from the years 1963-2016 (approximate quantities calculated on the basis of portion sizes and recipes for meals /dishes).

Tabela II. Zestawienie ilości produktów zawierających gluten [g] zalecanych do spożycia dzieciom niekarmionym piersią w 1. roku życia według standardów medycznych/schematów żywienia z lat 1963-2016 (ilości orientacyjne obliczone na podstawie wielkości porcji i receptur posiłków/potraw).

Year Rok	Quantity of gluten products (g) to be introduced to infants' diet in subsequent months of life Ilość produktów glutenowych (g) do wprowadzenia do diety dziecka w kolejnych miesiącach życia											
	1 m	2 m	3 m	4 m	5 m	6 m	7 m	8 m	9 m	10 m	11 m	12 m
1963	*	15	19	26	31	38	45	45	64	28	37	37
1975	*	*	11	29	32	37	37	48	30	28	55	55
1981	*	*	17	35	35	37	39	50	35	34	31	31
1984	*	*	*	*	11	22	24	44	34	25	25	25
1988	*	*	*	*	*	*	*	*	30	30	31	31
1990	*	*	*	*	*	*	*	*	*	23	37	37
1993	*	*	*	*	*	*	*	*	*	30	30	30
2001	*	*	*	*	*	*	*	*	*	33	33	33
2007	*	*	*	*	5	5	14	26	36	29	29	29
2014	*	*	*	*	5	5	26	2	28	28	28	28
2016	*	*	*	*	5	5	26	2	28	28	28	28

*Gluten-free diet/Dieta bezglutenowa
m – month of life/miesiąc życia

According to the ESPGHAN Position Paper published in 2016, gluten may be introduced into the infant's diet any time between 4 and 12 completed months of age. In children at high risk of CD, the earlier introduction of gluten - 4 vs 6 months or 6 vs 12 months is associated with the earlier development of CD autoimmunity and CD, but the cumulative incidence of each in later childhood is similar. Consumption of large quantities of gluten should be avoided during the first weeks after gluten introduction and during infancy due to empirically confirmed association between the amount of gluten intake and the risk of CD. The optimal amounts of gluten to be introduced at weaning, however, have not been established [22, 23].

In 2016, an updated nutrition scheme, including recommendations regarding gluten, was published. According to the scheme, gluten may be introduced to the diet of Polish infants at any time after the age of 4 months, which is equivalent to 17 weeks of life, until the age of 12 months [24].

A retrospective analysis of Polish recommendations on gluten introduction to the diet of infants seems to confirm the results of the CELIPREV study with regard to the age of manifestation of celiac disease. The earlier introduction of gluten to children's diets in the 1970s resulted in an earlier occurrence of the disease. It also had an impact on the clinical manifestation. In the 1970s, classical celiac disease with the clinical manifestation of a celiac disease crisis with both quantitative and qualitative malnutrition, serious diarrhoea leading to severe dehydration, electrolyte disturbances, as well as hypoproteinaemia with hypoalbuminemia, was found relatively often in the population of infants and small children [25].

The change of recommendations in 1988 and the suggested later introduction of gluten to the diet of infants, i.e. in the tenth month of life, contributed not only to the delayed onset of the disease, but also to a change in its prevailing clinical presentation, i.a. less frequent incidence of classical celiac disease, and more frequent occurrence of its other forms, i.e. atypical, silent, latent and potential [26, 27]. Those forms of celiac disease currently constitute the greatest diagnostic challenge. It is estimated that per one case of classical celiac disease there are between three and seven cases of its atypical form. Reports on celiac disease in the form of a celiac disease crisis are now rare and concern infants and children who had gluten products introduced to their diet relatively early [28, 29, 30].

SUMMARY

It is currently known that the factors necessary for celiac disease to occur include genetic predispositions and the presence of gluten in the diet, but the disease does not manifest in all persons having the HLA DQ2 and/or HLADQ8 antigens who eat gluten products. Studies on the identification of environmental factors, including nutritional ones, which could constitute the "trigger mechanism" for celiac disease development have been conducted for years. The changes resulting from subsequent revisions of nutritional recommendations

constitute evidence of the search for those factors. Research has shown that the time of introducing gluten products to the diet of infants and their introduction during the period of breastfeeding does not have an impact on the risk of celiac disease development, but that earlier introduction of gluten products to the infants' diets is related to the onset of the disease at a younger age. Early introduction of gluten products to the diet of infants seems to affect the clinical presentation of the disease, as evidenced by the change of its clinical image along with the modifications of recommendations. Current knowledge on celiac disease reveals a need for further, well-planned studies. Some ongoing research concerns i.a. the reduction of immunogenicity of cereal grains containing gluten, using oral enzymes to break down immunogenic peptides that normally remain intact during digestion, methods of preventing the absorption of immunogenic peptides, preventing tissue transglutaminase from rendering gluten peptides more immunogenic, or development of a vaccine inducing gluten tolerance [31]. Currently the only available treatment for celiac disease is lifelong adherence to a gluten free-diet.

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Address for correspondence:

Grażyna Rowicka

Department of Nutrition, Institute of Mother and Child

Kasprzaka 17a, 01-211 Warsaw, Poland

Phone (+48 22) 32-77-366

e mail: growicka@gmail.com