Dermatitis herpetiformis and celiac disease – symptoms, diagnostics and treatment. A literature review

Magdalena Stachurska[1], Szymon Krzewski[2], Maciej Stachurski[3], Piotr Stachurski[2], Andrzej Bożyk[4]

[1] Department of Conservative Dentistry with Endodontics, Medical University of Lublin, Poland

[2] Department of Pediatric Dentistry, Medical University of Lublin, Poland

[3] Department of Dental Prosthetics, Medical University of Lublin, Poland

[4] Private Practice, Warsaw, Poland

European Journal of Medical Technologies
2019; 2(23): 48-56

www. medical-technologies.eu
Published online 21.03.2019

Corresponding address:
Magdalena Stachurska
Tel.: +48 882 093 008
wielgusmmm@gmail.com

ABSTRACT

This article presents a review of the literature on the symptoms, diagnosis and treatment of celiac disease (celiac disease, enteropathy from hypersensitivity to gluten, celiac sprue, latin: dolor coeliacus-CD) and dermatitis herpetiformis (latin: morbus Duhring, dermatitis herpetiformis-DH) Celiac sprue is a disease caused by the inappropriate immune response of the human body to gluten. Gluten is a composite of prolamins and glutelins. It is a plant protein contained in some cereals, such as wheat, barley, rye or oats. CD very of ten occurs with family members. It is usually inherited in the first line of kindred, and is often diagnosed in monozygotic twins [1]. The main manifestation is gastrointestinal disorder, although symptoms from other systems appear quite often.

Duhring's disease is an intestinal-skin manifestation of celiac disease, also appearing on the autoimmune basis among people with genetic predispositions. The symptoms of DH are mainly manifested on the skin, rarely coexisting with the dyspepsia. The disease may occur independently or be associated with celiac disease.

Key words:

Duhring's disease, dermatitis herpetiformis, celiac disease, celiac sprue, gluten-free diet, gluten

Undoubtedly, a common triggering factor for both diseases is a strong immune response to gluten contained in food. However, the dissimilarity of the symptoms occurring determines their classification into separate disease entities. A diet without gluten is the main rule of the prevention and treatment of both Duhring's disease and celiac disease.

Introduction

Gluten is a protein fraction of wheat soluble in alcohol. For many centuries it has been one of the dominant elements in the ingredients of human meals. In modern times, many people use a diet without gluten in fear of hypersensitivity and problems associated with the digestive system. It is worth emphasizing, however, that gluten is an ingredient contained in many grains that a person consumes from the very beginning of humanity. Over the years genetically modified plants have led to the present situation, in which wheat is a much bigger, stronger plant and produces many large grains containing many Amylopectin A. The structure of the gluten itself has also been transformed.

In 2011, a cardiologist from the USA William Davis has published a book about not eating wheat - "Wheat Belly". This publication has contributed to the development of the anti-gluten movement, also among people who are not burdened with any disease.[2] Celiac disease (CD) is a genetic intestinal problem caused by an abnormal reaction to gluten protein and tissue transglutaminase. The pathogenesis of CD is mediated by the tTG enzyme, whose product - the deamid aldehyde peptide is presented to T cells and human leukocyte antigens. [8]

Today, the disease is spreading fairly quickly. It occurs around the world – among Caucasian race, mainly living in northern and western Europe. According to research, Western Samara (5.6%), Mexico (1.5-3.5%), Finland and Sweden (2-3%) present the highest rates of distribution. In India, 1.04-1.44% of people with celiac disease were registered, while in Turkey 0.8-2.5%. In Europe and the USA, the index is 1.0%, and the lowest rate was observed in Germany (0.2%) and in Brazil (0.2-0.6%). [48] (Figure 1) [48].

This is the most common Caucasian disease, which is currently quite high and counts to 1% of population. [3,5,6]. It is assumed that about 80% of patients are undiagnosed [7]

Until recently, celiac disease was thought to be particularly specific to early childhood, but due to the increase in gluten consumption by the society, occurance of this disease is already observed at any age. Dermatitis herpetiformis (DH, Duhring's disease) is an autoimmune disorder classified as bullous. It may occur at any age, however, the highest increase in disease is observed in the third decade of life [8], more often among the female sex and people genetically burdened in the first degree of kinship. [9] The risk of DH in first-degree relatives of people with celiac disease is about 15 times higher than in the general population. [9]

The occurance of Duhring's disease is definitely less than of celiac disease. It can appear both depending on celiac disease or independently. The main symptoms of CD are skin eruptions in the form of grouped vesicles or papules that spread as a result of heavy scratching. [10] Extreme surfaces of limbs are the most frequently affected, lesions also appear on the rear, in the sacro-lumbar area, on the scalp, scapula or shoulders. [10,11,12]

Table 1.
Occurrence of celiac disease in several countries. [48]

Region	% of affected patients
USA	1,0%
Mexico	1,5-3,5%
Brasil	0,2-0,6%
Western Samara (Africa)	**5,6%**
Europe	1,0%
Germany	0,2%
Finland and Sweeden	2-3%
Turkey	0,8-2,5%
India	1,04-1,44%

Etiopathogenesis

Factors determining the occurance of Duhring's disease can be both genetic and environmental. Studies show close relation to HLA-DQ2 and HLA-histocompatibility antigens in patients suffering from celiac disease. [6,13] Characteristic for DH is the deposition of granular IgA deposits in the dermal papilla, also often admixed with the epidermal transglutaminase autoantigen eTG, other immunoglobulins or complement. This process stimulates the neutrophil influx and the formation of papules or other skin lesions. [13]

Huma A. Mirza and Amani Gharbi has also reported a link between non-MHC genes and GSEs throughout the entire genome, including myosin IXB, IL-12, IL-23 and CCR3, although their function in DH pathogenesis is still unclear. [6]

Prolamines that can initiate celiac disease are gliadin (from wheat), sekalin (from rye) and hordein (from barley). Those are factors chich activate the sequence of reactions mobilizing TCD4 lymphocytes. The sequence is initiated by Th1 lymphocytes. Those, however, produce interferon g, which stimulates macrophages, cytotoxic CD8 + lymphocytes and T lymphocytes. It is followed by production of inflammatory cytokines IL-1, TNF-alpha, INF-b, resulting in damage of the intestinal mucosa. At the same time, Th2 lymphocytes produce cytokines Il-4, IL-5, IL-10 stimulating B-lymphocytes to produce autoantibodies and antibodies against gliadin. Similar reactions may also occur in other organs. [4]

The risk of occurrence of DH and CD increases when the first-degree relative suffers from celiac disease, but celiac disease's additionally when one of the monozygotic twins is affected. Dermatitis herpetiformis may also be caused by external factors, such as exposure to excessive iodine or smoking. Those may trigger the disease or exacerbate its course. [6]

Prevention

Currently, several methods are known to prevent getting sick with CD and DH.

Primary prophylaxis:

concerns breastfeeding and progressive intake of gluten by children. H. Szajewska's research has shown that, the risk of celiac disease occurance in infants who were not breastfed was up to 2 times higher than babies fed breast milk. [14] According to the recommendations of the ESPGHAN Nutrition Committee, gluten should be added to diet gradually between 5 and 6 months of age. This helps to prevent from celiac disease, type 1 diabetes and from develop an allergy to gluten.

Secondary prophylaxis:

this is an active diagnosing of CD and DH among patients.

Tertiary prophylaxis: this is a scrupulous and conscientious adherence to a gluten-free diet by patients suffering from celiac disease or dermatitis herpetiformis. [14,15]

Diagnostics

The CD is a fairly widely recognized disorder of the immune system, yet there are still many undiagnosed cases of disease among patients around the world. [16]

What distinguishes the CD from many other digestive system disorders is the coexistence of a significant number of comorbidities such as dermatitis herpetiformis, autoimmune thyroid inflammatory diseases, type 1 diabetes and other neurological and genetic disorders. [5]. The CD is most often diagnosed during infancy (9-24 months). Diagnoses in the 3rd and 4th decades of human life may also occur. The CD affects women three times more frequently than men. [3] CD diagnostics is based on the criteria from 1990 published by the European Society for Child Gastroenterology and Nutrition. [3]

During last 30 years, small intestine biopsy was the most common method of CD detection. Currently, serological tests are used to monitor the patient's response to a gluten-free diet. [1] Duodenal biopsy and serological test should be performed simultaneously when the patient shows symptoms of the disease and when he has not yet implemented a gluten-free

diet. Biopsy may reveal the atrophy of the intestinal villi. [17]

It is recommended to consume gluten-containing food minimum for a few days or weeks before the serological examination, as the serum antibody half-life ranges from 30 to 60 days. [11]

The test of choice for the presence of IgA deposits is direct immunofluorescence, consisting in getting the tissue sample from pathology unchanged area, at maximum 1 cm distance from the lesion. [10,11,12] This makes imaging the three main patterns and their combinations characteristic for DH possible:

- grainy deposits in the papilla tips;
- grainy deposits in the peaks along the skin-epidermal border;
- fiberal deposits in the papilla tips. [20,21]

The observance with a gluten-free diet can be controlled by serum testing for antibodies against smooth muscle endomysium. That metod is called indirect immunofluorescence test. It is effective for control, but the diagnosis of Duhring or celiac disease cannot be established just on the basis on antibodies occurance. Serum IgA antibodies against tTG (tissue transglutaminase) may also be determined by ELISA test with a single substrate of choice (tTG, eTG, npG, neo-tTG), which is recommended as the primary screening test for celiac disease. [22,23] Diagnosis of herpetic dermatitis is mainly assessed on the basis of skin eruptions and the results of histopathological examinations, direct and serological immunofluorescence. [24,45]

Helpful for diagnostics is histopathological examination of the skin, which may reveal characteristic microabscesess with significant predominance of neutrophils and an admixture of eosinophils at the top of papillas. This method is not recommended though, because it does not allow to differentiate CD/DH from linear IgA bullous dermatosis. [26] Determination of antibodies from stool and saliva has no diagnostic value. In addition, marking of the serum gliadin antibodies using ELISA or indirect immunofluorescence is used in diagnostics. [27]

Clinical symptoms

Dermatitis herpetiformis

DH distinctive symptoms are symmetrical, multiform exanthemas: papules, urticaria, follicles on the erythematous ground with herpetic-like arrangement, or erosions, polymorphic rash, which is always accompanied by severe pruritus.

The appearance of these changes is preceded by the sensation of burning and pricking. They disappear without leaving scars, but discolorations may occur instead. [7,11,13,29,37]

Dermatitis herpetiformis, as a chronic disease, manifests as periods of exacerbation and remission, in some patients they are abrupt. [30] Celiac disease in DH is usually asymptomatic, although in some cases, especially in children, it is accompanied by flatulence, abdominal pain and vomiting. Women may sometimes experience rash before menstruation, which disappears after menstrual bleeding. Similarly during pregnancy, skin pathologies may appear for the first time, and disappear after delivery. [30] Symptoms such as decrease of iron, folic acid, calcium, magnesium, B12 and D vitamins level, fatty stools and low levels of zinc in serum and epidermis may occur additionally. [31]

Dermatitis dermatitis is highly associated with gluten-dependent enteropathy (GSE), although its symptoms are much milder compared with GSE occurring in celiac disease or it might be completely asymptomatic. [32,.33]

Celiac disease

The CD manifestations are maliny gastrointestinal: weight loss as a result of frequent diarrhea, bloating or abdominal pain. [34] Those are the consequences of chronic inflammation of the small intestinal mucosa associated with malabsorption syndrome. That may also lead to iron deficiency anemia, megaloblastic anemia, vitamins or folic acid defficiency, weakness and drowsiness, recurrent oral aphtes and hypertransaminases. [35,36,37]

The musculoskeletal system pathologies may manifest in the form of tetany, osteoporosis and nanism, urogenital system by delayed puberty and menarche.

Lack of micronutrients may also cause enamel hypoplasia, endocrinopathies and herpetic dermatitis. [37] According to D.Schuppan and K-P.Zimmer, patients also complain about chronic chest pain and headache, depression and problems with concentration. [17]

Treatment

Although the major treatment principle of celiac and Duhring's disease is a gluten-free diet, there are many attempts to treat CD in a pharmacological way. According to Detlef Schuppan and Klaus-Peter Zimmer, attempts have been made to develop vaccines, drugs decreasing interstine permeability and numerous inhibitors. [18]

All these methods are currently being tested,still the main treatment as well as prevention of CD and DH is sticking to a strict gluten free diet (GFD). Eliminatng gluten from diet is a reliable, effective and safe method of treatment. Patients afflicted with CD and DH should follow the dietary recommendations (GFD) continuously, eliminating the triggering factor. [17,38,40]

GFD includes abandonment of food containing wheat, triticale, barley, rye, plain oats (due to pollution), semolina, couscous, muesli, cereal and milk cereal instant cereals, breadcrumbs, barley malt, baking powder, hydrolyzed protein vegetable and many more. The term "gluten-free product" can be used in food industry labels and in product advertisements on products with gluten content up to 20 mg/kg. [17,39,40]

Treatment with GFD is relatively difficult for patients because many products contain some amounts of gluten. The GFD diet should not be self-administered by the patient, but should be preceded by a specialist dietary consultation. Nowadays, CD patients' capabilities o because gluten free products are becoming more common and general public awareness has increased significantly. [17,41]

After implementing GFD, the first symptoms of recovery are visible quite quickly. During the first two weeks almost 70% of patients' quality of life is improving. Normalization of serological disorders start sin three to six months, however, treatment of inflammation of the intestinal mucosa is lass much longer. [17,42]

Treatment with GFD is less effective in the multiform celiac disease, but it is still used to reduce the severity of mucosal changes.

Benefits of being on GFD also concerns patients with type 1 diabetes – GFD might make controlling glycemia level more easy. Studies have also shown the advantages of GFD in pregnant women with CD. Pregnant women suffering from celiac disease are protected from premature delivery or infant's low birth weight by keeping gluten-free diet. [43,44]

Indispensable part of treatment is supplementation of vitamins A, D, E, K, folic acid, magnesium, selenium, iron or calcium, which is often neglected by patients. In addition to the gluten free diet, doctors also recommend excluding lactose and other strong allergens. [45]

GFD may not exert any therapeutic effect on some patients. In that case, treatment of choice is based on the combination of Dapson and GFD.

Dapson is a medication listed in World Health Organization (WHO). It is also used for the treatment of leprosy. One of the most characteristic features is quick response to its therapeutic effect on people suffering from DH. It affects the subjective symptoms (decreasing them the fastest) and skin changes. It does not affect any pathologic changes in the intestine. Dapson, however, has no effect on the whole human organism, mainly due to the problematic dosage and relatively frequent side effects, such as, for example, dangerous methemoglobinemia associated with the dapsone's metabolite – hydroxylamine.

A very important part of drug treatment is controlling the level of methaemoglobin in the blood. [46] While planning an individual therapy, the coordinating specialist endevors to reach the minimum effevtive dose of the medicine. The amount of Dapson needed for individual patient therapy depends on the season, food intake, and the iodine concentration in the air. For children above 2 years old 0.5-1 mg/kg mc is effective, but no therapeutic dose has been established for younger children. Women during pregnancy and breastfeeding should be particularly careful- there is no evidence Dapson is harmless

for fetus, but there are researches proving the drug penetrates into breast milk. However, other restrictions for using Dapson had been specified: anemia, hypersensitivity to the substance and a deficiency of glucose-6-phosphate dehydrogenase have been determined. [46]

Unfortunately despite its advantages, Dapson is not a flawless medicine. Patients during Dapson therapy frequently experience gastrointestinal disorders, nervousness, fatigue, pain or dizziness. Patients also complain about dyspnea and fatigability associated with methaemoglobinaemia and peripheral cyanosis. [46] Despite the occurrence of those symptoms, this drug is invaluable in treatment of DH.

Studies have shown that patients are usually dissatisfied with strict, gluten-free diet.

Nowadays, rapid revolution in CD treatment methods is being observed, due to awareness and understanding of triggering mechanisms, and at the same time an increasing percentage of patients affected by this disease.

The influence of certain drugs on dh development

Patients who's experiencing chest pains or headache should be particularly careful on Rusing non-steroidal anti-inflammatory drugs. Indomethacin, acetylsalicylic acid, diclofenac, flurbiprofen and ibuprofen may adversely affect skin changes and enhance their development. Studies by Tousignant J., Lafontaine N., Rochette L., Rozenfarb E. also showed the intensification of rash after taking doxorubicin, vincristine, propafenone, famidia, lithium, contraceptive hormones, amitriptyline and levothyroxine. [47]

Differentiation

Celiac disease: parasitic infections, chronic intestinal diseases, for example Crohn's disease, enteropathy, irritable bowel syndrome, allergies to various foods, lactose intolerance, casein, malabsorption of fructose, immunity disorders [17], non-aberrant hypersensitivity to gluten.

Duhrig's disease: autoimmune pemphigus diseases (herpetiformis, IgG / IgA), dermatoses from the group of acquired epidermal detachment, disseminated eczema, human scabies, allergy to endogenous progesterone, senile, psychogenic and neurogenic pruritus and occurring in metabolic diseases, atopic dermatitis. [10,11,30]

Complications

Over the years, the GFD diet has shown that it effectively protects patients from the consequences and complications of classical CD (including Duhring's dermatitis herpesisis and osteoporosis). Inobservance of the disease may generate refractory celiac disease (RCD), chich is resistant to treatment. That is usually diagnosed in patients over 50 years of age, in which after 12 months of gluten-free regime no improvement is seen.

According to Alaedini A, Green PH, other visible complications in the whole organism are possible:

- Gastrointestinal tract: throat, esophageal or colon cancer; EATL-enteropathy associated T-cell lymphoma, ulcerative jejunal and ileitis
- Nervous system: epilepsy, migraine, depression, ataxia
- Hematopoietic system: non-Hodgkin's lymphoma, hyposplenism
- Musculoskeletal system: osteoporosis and osteomalacia, pathological fractures
- Genito-urinary system: fertility disorders, recurrent miscarriages, premature delivery, premature menopause. [37]

Summary

Nowadays, celiac disease and dermatitis herpetiformis are much more widespread diseases than before. Over the centuries, human-induced activity, that was aimed to upgrade the efficiency of crop production have led to a significant increase in the amount of gluten consumption. Negative effects of that are clearly visible nowadays. People suffering from CD and DH are no longer an anonymous group, they became a significant part of the population. Due to the genetic basis of both diseases, it is difficult in protect against it.

CD, as a disorder with dyspeptic symptoms, may affect many aspects of life. Patients afflicted with the disease, that want to avoid experiencing discomfort associated with gastrointestinal disorders, are forced to modify the current diet completely. That requires a lot of persistance and self-determination, which is why patients often stop following dietary recommendations until negative reactions occur.

DH also impedes normal functioning due to persistent pruritus exacerbated by contact with the triggering factor. Skin lesions may develop depression and concentration disturbances in patients, thereby they isolate themselves from society.

The evolution of technologies and food concerns in modern times makes struggling with CD and DH more easy. The technology of food processing developed significantly, which allowed to obtain many gluten-free, commonly used nutrients. The taste and organoleptic properties of gluten-free foods are being constantly improved, so changing the dietary rules to gluten-free and strictly sticking to the regime is much more simple and achievable for patients.

Pharmacological treatment with dapsone also allows to reduce the symptoms but, like any medication, may exert many unwanted effects on the organism. New, promising methods of treatment are being researched, but still are on too early stage of development to enter the market and replace the gluten-free diet instead.

Many science publications about gluten have definietly influenced society's behavior. Numerous people are choosing gluten-free food following today's fashion and trends despite not being afflicted neither with celiac nor Duhring disease. Currently there are too few scientific reports about the influence on GFD on healthy people to find out how it may affect the general population in the future.

References

1. Kaukinen, K., Collin, P., Laurila, K., Kaartinen, T., Partanen, J., & Mäki, M. (2007). Resurrection of gliadin antibodies in coeliac disease. Deamidated gliadin peptide antibody test provides additional diagnostic benefit.Scandinavian journal of gastroenterology, 42, 1428-1433.
2. Bushak L. A Brief History Of Gluten And 'Wheat Intolerance' [Internet]. Medical Daily. 2015 [cytowane 13 luty 2019]. Dostępne na: https://www.medicaldaily.com/brief-history-gluten-protein-baked-goods-how-wheat-intolerance-has-risen-over-years-353244.
3. Gupta S, Kaushal A, Kumar A, Kumar D Recent advances in biosensors for diagnosis of celiac disease: A review. Biotechnol Bioeng. 2019 Feb;116(2):444-451.
4. Magdalena Kaniewska, Grażyna Rydzewska Choroba trzewna u dorosłych – patogeneza, manifestacje kliniczne, współistnienie z nieswoistymi chorobami zapalnymi jelit i innymi chorobami o podłożu immunologicznym Przegląd Gastroenterologiczny 2009; 4 (4): 173–177.
5. Briani, C., Samaroo, D., & Alaedini, A. (2008). Celiac disease: From gluten to autoimmunity. Autoimmunity Reviews, 7, 644–650.
6. Huma A. Mirza; Amani Gharbi Dermatitis, Herpetiformis StatPearls Publishing, January 2018(Mirza HA, Gharbi A. Dermatitis Herpetiformis. [Updated 2018 Mar 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493163/ Accessed May 1, 2018.)
7. Panagiotou S., Kontogianni M.D. (2007): The economic burden of gluten-free products and gluten--free diet: a cost estimation analysis in Greece, Journal of Human Nutrition and Dietetics, 2017 May 8. doi: 10.1111/jhn.12477.
8. Karczewska K. Choroba trzewna, współczesny obraz kliniczny i diagnostyka. Pediatr Współcz Gastroenterol Hepatol Żywienie Dziecka 2006;8:220-1.
9. Humbert PH, Pelletier F, Dreno B, et al. Gluten intolerance and skin diseases. Eur J Dermatol 2006;16:4-11.
10. Rose C., Zillikens D.: Dermatitis herpetiformis Duhring. [w]: Autoimmune disease of the skin. Pathogenesis, diagnosis, management. M. Hertl (red.), Springer, Wien, 2001, 85-98.
11. Nicolas M.E., Krause P.K., Gibson L.E., Murray J.A.: Dermatitis herpetiformis. Int J Dermatol 2003, 42, 588-600.
12. Oxentenko A.S., Murray J.A.: Celiac disease and dermatitis herpetiformis: the spectrum of gluten--sensitive enteropathy. Int J Dermatol 2003, 42, 585-587.

13. Mariola Pawlaczyk, Sonia Milewska, Anita Rokowska-Waluch, Katarzyna Korzeniowska Leczenie dietetyczne w celiakii i opryszczkowatym zapaleniu skóry. Farmacja Współczesna 2012; 5: 9-20.
14. Szajewska H. Czy można zapobiec celiakii? Alergia 2007;3:17-20.
15. Szajewska H. Zasady żywienia zdrowych niemowląt. Zalecenia Polskiego towarzystwa Gastroeneterologii, Hepatologii i Żywienia Dzieci 2014;11:321-338.
16. Van Heel, D. A., & West, J. . Recent advances in coeliac disease genetics. Gut 2006; 55, 1037–1046.
17. Schuppan D, Zimmer KP: The diagnosis and treatment of celiac disease. Dtsch Arztebl Int 2013; 110(49): 835-46. DOI: 10.3238/arztebl.2013.0835
18. Leffler DA, Schuppan D: Update on serologic testing in celiac disease. The American Journal of Gastroenterology 2010; 105; 2520-4.
19. Mutasim D.F., Diaz L.A.: The relevance of immunohistochemical techniques in the differentiation of subepidermal bullous diseases. Am J Dermatopathol 1991, 13, 77-83.
20. Dmochowski M.: O typach złogów IgA w skórze chorych na opryszczkowe zapalenie skóry. Adv Dermatol Allergol 2003, 20, 46-48.
21. Hendrix J.D, Magnum K.L., Zone J.J., Gammon W.R.: Cutaneous IgA deposits in bullous disease function as ligands to mediate adherence of activated neutrophils. J Invest Dermatol 1990, 94, 667-672.
22. Beutner E.H., Chorzelski T.P., Kumar V., Leonard J., Krasny S.: Sensitivity and specificity of IgA-class antiendomysial antibodies for dermatitis herpetiformis and findings relevant to their pathogenic significance. J Am Acad Dermatol 1986, 15, 464-473.
23. Chorzelski T.P., Rosinska D., Beutner E.H., Sulej J., Kumar V.: Aggresssive gluten challenge of dermatitis herpetiformis cases converts them from seronegative to seropositive for IgA-class endomysial antibodies. J Am Acad Dermatol 1988, 18, 672-678.
24. Dmochowski M. Opryszczkowate zapalenie skóry. Post Dermatol Alergol 2003;22:274-91;20,257-291.
25. Caproni M, Antiga E, Melani L, et al. Guidelines for the diagnosis and treatment of dermatitis herpetiformis. J Eur Acad Dermatol Venereol 2009;23:633-38.
26. Blenkinsopp W.K, Haffenden G.P., Fry L., Leonard J.N.: Histology of linear IgA disease, dermatitis herpetiformis, and bullous pemphigoid. Am J Dermatopathol 1983, 5, 547-554.
27. Kasperkiewicz M., Dähnrich C., Probst C., Komorowski L., Stöcker W., Schlumberger W. and others: Novel assay for detecting celiac disease--associated autoantibodies in dermatitis herpetiformis using deamidated gliadin-analogous fusion peptides. J Am Acad Dermatol 2012, 66, 583-588.
28. Mariola Pawlaczyk, Sonia Milewska, Anita Rokowska-Waluch, Katarzyna Korzeniowska Leczenie dietetyczne w celiakii i opryszczkowatym zapaleniu skóry. Farmacja Współczesna 2012; 5: 9-20
29. Zone J.J., Meyer L.J., Petersen M.J.: Deposition of granular IgA relative to clinical lesions in dermatitis herpetiformis. Arch Dermatol 1996, 132, 912-918.
30. Rasi A., Khatami A.: Autoimmune progesterone dermatitis. Int J Dermatol 2004, 43, 588-560.
31. Gomułka K, Demkow U. Celiakia – etiopatogeneza, klinika i diagnostyka laboratoryjna. Nowa Pediatr 2010;2:44-9.
32. Stone OJ. Dermatitis herpetiformis and gluten sensitive enteropathy (including celiac disease)--increased subepithelial extracellular matrix viscosity due to gliadin. Med Hypotheses. grudzień 1990;33(4):283–8.
33. Zebrowska, Agnieszka & Waszczykowska, Elzbieta & Kowalewski, Cezary & Woźniak, Katarzyna & Olszewska, Małgorzata & Placek, Waldemar & Czajkowski, Rafał & Szepietowski, Jacek & Białynicki-Birula, Rafał & Dmochowski, Marian. (2016). Diagnostic and therapeutic guidelines of dermatitis herpetiformis (Duhring's disease) – consensus of Polish Dermatological Society. Dermatology Review. 2. 95-101. 10.5114/dr.2016.59130.
34. Whyte LA, Jenkins HR: The epidemiology of coeliac disease in South Wales: a 28-year perspective. Archives of disease in childhood 2013; 98: 405–7.
35. Kruszewski J. Celiakia. Od patogenezy do leczenia. Alergia 2001;1:8-12.
36. Czerwionka-Szaflarska M, Szaflarska-Popławska A, Mueller L. Celiakia – choroba trzewna dzieci i dorosłych. Alergia 2006;2:20-4.
37. Alaedini A, Green PH. Narrative review: celiac disease: understanding a complex autoimmune disorder. Ann Intern Med 2005;142:289-98.

38. Schuppan D, Junker Y, Barisani D: Celiac disease: from pathogenesis to novel therapies. Gastroenterology 2009; 137: 1912–33.
39. Zimmer KP: Nutrition and celiac disease. Current problems in pediatric and adolescent health care 2011; 41: 244–7.
40. Rashid M, Butzner D, Burrows V, et al.: Consumption of pure oats by individuals with celiac disease: a position statement by the Ca- nadian Celiac Association. Canadian journal of gastroenterology = Journal canadien de gastroenterologie 2007; 21: 649–51.
41. Elfstrom P, Granath F, Ekstrom Smedby K, et al.: Risk of lympho- proliferative malignancy in relation to small intestinal histopathology among patients with celiac disease. Journal of the National Cancer In- stitute 2011; 103: 436–44.
42. Mukherjee R, Kelly CP, Schuppan D: Nondietary therapies for celiac dis- ease. Gastrointestinal endoscopy clinics of North America 2012; 22: 811–31.
43. Hansen D, Brock-Jacobsen B, Lund E, et al.: Clinical benefit of a gluten- free diet in type 1 diabetic children with screening-detected celiac disease: a population-based screening study with 2 years' follow-up. Diabetes care 2006; 29: 2452–6.
44. Khashan AS, Henriksen TB, Mortensen PB, et al.: The impact of maternal celiac disease on birthweight and preterm birth: A Danish population-based cohort study. Hum Reprod 2010; 25: 528–34.
45. Hozyasz K. Gluten i dieta bezglutenowa. Pediatr Pol 1999;74:799-811.
46. Coleman M.D.: Dapsone: modes of action, toxicity and possible strategies for increasing patient tolerance. Br J Dermatol 1993, 129, 507-513.
47. Tousignant J., Lafontaine N., Rochette L., Rozenfarb E.: Dermatitis herpetiformis induced by nonsteroidal anti-inflammatory drugs. Int J Dermatol 1994, 33, 199-200.
48. Csapóné Riskó, Tünde & Péntek, Ádám & Wiwczaroski, Troy. (2017). BREAD Consumption Habits In The Gluten Free Diet. Applied Studies in Agribusiness and Commerce. 11. 113-120. 10.19041/Apstract/2017/3-4/16.