

Allergy prevalence in adult celiac disease

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Background: Celiac disease is considered to arise from an inappropriate T-cell-mediated immune response against ingested gluten in genetically predisposed people, whereas the T_H2-type lymphocytes are mostly involved in IgE-mediated reactions. The matter of possible coexistence of T_H1- and T_H2-type diseases is still debated.

Objective: This study was aimed to evaluate the allergy prevalence in a large series of adults with untreated celiac disease and their families at the moment of diagnosis. We also evaluated whether 1 year of gluten-free diet had any effect on allergy prevalence in our cohort.

Methods: At the moment of celiac disease diagnosis a standardized questionnaire was administered for detailed information on presence and type of any allergy symptoms in 1044 adult patients with celiac disease, 2752 relatives, and 318 spouses. Those reporting any allergy underwent tests with dosage of serum levels of total IgE and search for serum specific IgE with a standard makeup of 20 antigens and PRICK tests in selected individuals. At follow-up visit patients with celiac disease were administered the same allergy questionnaire.

Results: One hundred seventy-three patients with celiac disease (16.6%), 523 relative (19%), and 43 spouses (13.5%) had at least 1 allergy (*P* = not significant). Atopic dermatitis was more frequent in patients with celiac disease (3.8%) and their relatives (2.3%) than in spouses (1.3%). The presence of allergy in general and atopic dermatitis was not affected by presence of overt malabsorption or duration of undiagnosed disease. Follow-up data showed no change in allergy prevalence in the cohort examined.

Conclusion: Allergy prevalence in a large series of patients with celiac disease is not different from that of their relatives and spouses. However, atopic dermatitis was about 3 times more frequent in patients with celiac disease and 2 times more frequent in their relatives than in spouses. One year of gluten-free diet did not change allergy prevalence in the celiac group under investigation. (*J Allergy Clin Immunol* 2004;113:1199-203.)

Key words: Celiac disease, allergy, atopy, atopic dermatitis, adult, eczema, intestine, gastrointestinal disease, intestinal biopsy

Gluten ingestion in patients with celiac disease causes a variety of gastrointestinal and nongastrointestinal symptoms and biochemical abnormalities¹⁻³ that ameliorate

Abbreviations used

EmA: Antiendomysial antibody
a-tTG: Antitissue-transglutaminase

rate after gluten withdrawal. Diagnosis is often made in adulthood. In patients with a long personal history of disease that runs misdiagnosed for years.⁴ Celiac disease is considered to arise from an inappropriate T-cell-mediated immune response against ingested gluten in genetically predisposed people,⁵ whereas the T_H2-type lymphocytes are mostly involved in allergic, IgE-mediated reactions.⁶ Thus, one would hypothesize that T_H1- and T_H2-type immunity are present in a distinct patient population, but this is still a matter of controversy.⁶⁻⁸ In fact, some reports have suggested that allergy manifestations are more frequent in patients with celiac disease,⁹ and asthma incidence is increased in celiac disease diagnosed in childhood.¹⁰ Atopic disorders were more frequently found in children¹¹ and adult patients with celiac disease and their relatives than in normal control subjects,^{12,13} and urticaria was associated with celiac diseases.¹⁴⁻¹⁶ Celiac disease prevalence was found to be increased in a population of atopic patients.¹⁷ On the contrary, one single case-control study in children with celiac disease denies the link between celiac disease and allergy.¹⁸ Most of the cited studies were performed and published some decades ago, and the series of patients were quite different for clinical manifestations from the patients with celiac disease whom we investigate nowadays. In fact, more recent studies encompass overt, subclinical, and silent forms of celiac disease,¹⁹ whereas years ago patients were mostly affected by overt malabsorption.^{9,11-13,16} To our knowledge, the prevalence of allergy in a large series of adult patients with celiac disease has not been investigated so far.

The aim of this study was to evaluate the prevalence of allergy in a large series of adults with untreated celiac disease and in their families at the moment of diagnosis. We also evaluated whether 1 year of gluten-free diet had any effect on allergy prevalence in our cohort.

METHODS

Baseline data

Data from adult patients with celiac disease, diagnosed at our center from February 1992 to December 2002, their relatives, and

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TABLE I. Gender, age, anthropometric data, and allergy prevalence in patients with celiac disease, their relatives and spouses

N (%)	Patients with celiac disease (n = 1044)	Relatives (n = 2752)	Spouses (n = 318)
M/F	263/781	1102/1650	223/95
Body mass index (kg/m ²)	20.7 ± 3.0	26.1 ± 2.1	25.9 ± 3.6
Age at first onset of celiac disease–related symptoms (mean ± SD in y)	22.7 ± 14.2	—	—
Age at diagnosis of celiac disease (mean ± SD in y)	35.3 ± 13.4	—	—
Age at first onset of allergy symptoms (mean ± SD in y)	21.4 ± 13.3	22.4 ± 14.3	20.7 ± 16.4
At least 1 allergy	173 (16.6%)	523 (19%)	43 (13.5%)
Two allergies	19 (1.8%)	101 (3.7%)	12 (3.8%)
Three or more allergies	4 (0.4%)	52 (1.9%)	5 (1.6%)
No allergy	871 (83.4%)	2229 (81%)	275 (86.5%)

spouses living in the same household were analyzed. Patients with celiac disease (older than 17 years) had positive antiendomysial antibody (EmA) and/or antitissue-transglutaminase (a-tTG) results and had an intestinal biopsy indicative of gluten-induced damage. First-degree relatives of patients with celiac disease were all tested for presence of EmA or a-tTG.

The medical history was collected with attention to clinical features suggestive of malabsorption and allergy. A standardized questionnaire was administered for detailed information on (1) presence of any allergy symptom, (2) age of onset of first allergy symptoms, if any, (3) type of symptoms, (4) allergens reported as responsible for allergy symptom reaction, and (5) any food intolerance.

All persons reporting allergy symptoms underwent tests for allergy by using a makeup of 20 major antigens among most frequent food and respiratory allergens in our nation (testing serum specific IgE), plus any other allergen they reported to be sensitive to, and determination of serum levels of total IgE and, in selected cases with doubtful results for IgE, PRICK tests (Stallergenes srl, Saronno, Italy). Participants reporting any cutaneous allergy underwent a dermatology visit and, in case of active lesions, skin biopsy to avoid bias in collecting data for dermatitis. All subjects with skin biopsy results suggesting herpetiform dermatitis underwent complete tests for celiac disease and were not included in the atopic dermatitis group. All subjects with contact dermatitis (ie, dermatitis due to continuous contact with irritating substances) were not included in the atopic dermatitis group. If the patient exhibited eczematous lesions of skin fulfilling criteria for atopy, but they had no respiratory allergy-related symptoms, normal total serum IgE levels, no specific IgE, and negative skin prick test results to aeroallergens or foods, they were coded as having intrinsic atopic dermatitis,²⁰ although no other testing was performed (such as cell and cytokine pattern in peripheral blood and in the skin and/or study of epidermal dendritic cells). They were not counted in the group of persons with allergy.

On the basis of allergy tests the antigens were grouped as follows: respiratory: *Graminaceae*, *Parietaria officinalis*, *Dermatophagoides*, *Alternaria*; skin: nickel, chrome, latex, cosmetics, soaps, dye; food: milk, eggs, fish, shellfish, nuts and peanut, tomato, citrus fruits, soya; and miscellaneous: all the reactions provoked by less common antigens, for example, pigeon's feathers, cloves, cinnamon, olive tree pollen.

Subjects not reporting allergy symptoms and without clinical or laboratory evidence of allergic reaction were defined as nonallergic. It must be noted that food intolerance is a commonly reported disease in Italy, in particular from patients with irritable bowel disease and/or milk intolerance. Those reporting food intolerance and without

clinical or laboratory (total IgE, EmA, PRICK tests, lactose breath test) evidence of food intolerance or allergic reaction were defined as nonallergic. Persons with positive lactose or whole milk–based breath test results were coded as milk intolerant and not allergic.

For patients with celiac disease only, we analyzed, as our diagnostic protocol requires, routine blood laboratory test results with the inclusion of blood hemoglobin, plasma concentration of iron, ferritin, total calcium, total protein, albumin, cholesterol, plasma enzymatic activity of transaminases and total serum IgE. Height and weight for all subjects were measured to estimate body mass index (BMI: weight/height²).

Follow-up data

In Italy the cost of gluten-free food for people with celiac disease is charged to the National Health System, and patients with celiac disease must undergo yearly follow-up visits for certification of disease. At the 1-year follow-up visit patients with celiac disease were administered the same questionnaire that was administered at baseline visit. Patients also underwent the same laboratory tests performed at baseline examination.

Data collection and statistical analysis were performed with SPSS 10 package for Windows (SPSS, Inc, Chicago, Ill).

The study was approved by the Ethics Committee of the Federico II University, Naples, Italy.

RESULTS

Baseline data

The target cohort was made up of 1115 patients with celiac disease, 2817 first-degree relatives, and 339 spouses living in the same household. We collected complete data for 1044 patients with celiac disease, 2752 first-degree relatives, and 318 spouses.

Table I shows sex, age, anthropometric data, and allergy prevalence in patients with celiac disease, their relatives, and their spouses. Female to male ratio was 3:1 in patients with celiac disease. The difference in prevalence of allergy was not significant. Findings were similar in separate analyses for men and women (data not shown). Table II shows prevalence of the main allergic symptoms. Atopic dermatitis was more frequent in patients with celiac disease (3.8%) and their relatives (2.3%) than in spouses (1.3%). Prevalence of other allergy symptoms was found to be not significantly different between patients with

TABLE II. Prevalence of single allergy manifestation in adult patients with celiac disease, their relatives, and their spouses

	Patients with celiac disease (n = 1044) (%)	Relatives (n = 2752) (%)	Spouses (n = 318) (%)
With any allergy	173 (16.6)	523 (19)	43 (13.5)
Rhinitis	72 (6.9)	180 (6.5)	21 (6.6)
Asthma	38 (3.6)	102 (3.7)	13 (4.1)
Atopic dermatitis	40 (3.8)	62 (2.3)	4 (1.3)
Food allergy	17 (1.6)	42 (1.5)	3 (0.9)
Conjunctivitis	6 (0.6)	11 (0.4)	1 (0.3)
Occasional urticaria	2 (0.2)	5 (0.2)	0 (0)

celiac disease, relatives, and spouses. Table III shows selected main classes of allergens found to be responsible for allergies. The 3 groups under study were quite different in number of participants. The number of persons coded as having intrinsic atopy was 6 in celiac group, 16 in relatives group, and 5 in spouses group. To investigate the odds ratios for atopy, we compared data of the 318 families with 1 component affected with celiac disease. Data are shown in Table IV. Patients with celiac disease were found to have a 3-fold risk and relatives a 2-fold risk to have atopic dermatitis when compared with control subjects (spouses). Our spouse group was made up mainly of men, whereas the celiac group was made up of women. The latter comparison could be affected by this sex difference. When the analysis was limited to the 95 women of the control group and 95 age-matched (randomized and selected by a computer program) women with celiac disease, the difference in prevalence of atopic dermatitis was similar to that described for the entire group (2 of 95, 2.1% in spouse group vs 4 of 95, 4.2% in the celiac group).

When the patients with celiac disease were divided into 2 groups according to the presence or not of overt malabsorption, no significant statistical difference was found for allergy prevalence in the 2 groups (data not shown). Estimated duration of undiscovered celiac disease, calculated as the time from first celiac disease-related symptoms and celiac disease diagnosis, was not related to presence of allergy (8.2 ± 3.5 years in patients with celiac disease with allergy vs 9.6 ± 4.1 years in patients with celiac disease without allergy).

Thirty-five celiac patients (3.3%), 84 relatives (3.5%), and 13 spouses (4.4%) reported allergy or intolerance to drugs (ie, aspirin, antibiotics, other nonsteroidal anti-inflammatory drugs). No tests were performed to confirm the reported allergy/intolerance.

Follow-up data

Forty-two patients did not participate in a follow-up visit because they had moved (n = 21), decided not to respect a gluten-free diet (n = 5), did not come to the scheduled visit (n = 14), or were not found (n = 7). Thirty-five of 42 patients answered the allergic questionnaire by phone. Table V summarizes data for the follow-

TABLE III. Prevalence of major classes of antigens causing allergies in our cohort

Allergy	Patients with celiac disease (n = 173)	Relatives (n = 523)	Spouses (n = 43)
Achari, molds	49	127	12
Pollens, leaves	53	109	16
Nuts/peanut	4	19	1
Fruits	3	33	2
Vegetables	12	29	3
Fish	6	18	2
Seafood	0	10	1
Egg	2	11	0
Milk	1	7	0
Meat/poultry	2	14	0
Soap/cosmetics/essence	11	39	3
Metals	6	19	1
Latex	1	5	0
Miscellaneous	32	84	9

A single patient may have reported more than 1 allergy or allergen.

up visit for the patients with celiac disease with allergies who also came to the follow-up visit. As expected, patients had significantly increased body mass index and hemoglobin levels, lower EmA positivity, and lower a-tTG levels after 1 year of gluten-free diet. No significant differences were found between first and follow-up visits for prevalence of allergic symptoms (P = not significant; McNemar test). The inclusion of data collected by telephone interview did not change the overall percentage of allergy (data not shown). Four patients with celiac disease reported allergic symptoms for the first time (2 rhinitis, 1 food allergy, and 1 conjunctivitis).

DISCUSSION

The data of this article indicate that overall allergy prevalence in a large series of patients with celiac disease is not different from that of their relatives and spouses. It should be noted that we used spouses as control group because they are not genetically related to the celiac group, and this let us compare persons of similar socioeconomic level living in similar environment. The analysis of prevalence of a single allergy manifestation, however, showed that atopic dermatitis is about 3 times more frequent in patients with celiac disease and 2 times more frequent in their relatives than in spouses; we did not find any difference among groups for any particular class of antigens. One-year gluten-free diet did not change allergy prevalence in the celiac group under investigation. Presence of allergy was not related to overt malabsorption at celiac disease diagnosis. Estimated duration of undiagnosed celiac disease did not affect presence of allergy in our cohort. In contrast to the previous report of increased respiratory^{9,10,14} and food allergy in children with celiac disease,^{9,13} adults with celiac disease from our cohort showed no increase in respiratory and food allergies. The celiac group was largely made up of

TABLE IV. Allergy prevalence in the families with 1 member with celiac disease and odds ratios of having an allergy in comparison with spouses

	Patients with celiac disease (n = 318) (%)	Relatives (n = 917) (%)	Spouses (n = 301) (%)
With atopic dermatitis	13 (4.1)	21 (2.3)	4 (1.3)
Odds ratio	3.17	1.74	—
95% Confidence interval	1.02-9.82	0.59-5.11	—

women; the spouse group was made up mainly of men. The sex difference could have biased our comparison; for that reason an analysis was made with data from 95 women with celiac disease age-matched with the 95 women of the spouse group. Prevalence of atopic dermatitis was similar to that of the entire cohort under study, and we can conclude that there is not a sex bias in our data.

Our data are in keeping with the concept that T_H1- and T_H2-type diseases may coexist in celiac disease and confirm previous reports of data on a smaller series of patients observed some decades ago.^{9,10,13} More recently, Greco et al¹⁸ have suggested that there is no link between atopy and celiac disease and have hypothesized that a possible bias can arise because most studies are based on reported symptoms of allergy, and families with celiac disease might pay more attention to all symptoms including allergy symptoms. Our data on allergy are generally in keeping with those of Greco et al, although the increased prevalence of atopic dermatitis in adults with celiac disease and their relatives is at odds with the report of Greco et al and deserves some attention. All patients of our series reporting allergy underwent laboratory testing, dermatology visit, PRICK tests, and, in presence of skin lesions, skin biopsy. This procedure excluded the presence of herpetiform dermatitis coexisting with celiac disease in patients with celiac disease or relatives/spouses in whom dermatitis was found. Another difference is the age at which the patient is examined, which is also the age of celiac disease diagnosis. The longer exposure of our cohort to gluten and to the antigens causing atopic dermatitis may account for the difference in data. It has to be made clear that every patient/control subject reporting skin lesion (even not active) underwent a dermatology visit in a university dermatology unit; they all underwent total IgE testing and, if the skin examination was positive, biopsy. The final diagnosis of atopic dermatitis was, at the end, the result of anamnesis and clinical data, IgE testing, and biopsy.²¹

The present study did not aim to investigate the pathogenesis of increased atopic dermatitis incidence in patients with celiac disease and their relatives. Only speculative hypothesis can be carried out to explain the data.

A deficiency in local immune response as a result of abnormal IgA responses was at first hypothesized,¹⁰ although never proved. Permeability of the damaged intestinal mucosa is increased in celiac disease²²⁻²⁴ and

TABLE V. Prevalence of allergic disorders before (baseline) and after (follow-up) 1-year gluten-free diet in the subgroup of patients with celiac disease (n = 168) reporting 1 or more allergy symptoms at baseline

	Baseline (n = 173)	Follow-up (n = 131)
Body mass index (kg/m ²)	20.7 ± 2.7	22.6 ± 2.9*
Hemoglobin (g/dL)	12.5 ± 1.8	13.1 ± 1.6†
a-tTG (U/mL)	28.4 ± 31.1	2.8 ± 2.6‡
EmA (positive/negative)	171/173	10/131§
Rhinitis	69	59
Asthma	38	32
Dermatitis	26	25
Food allergy	13	11
Conjunctivitis	5	4
Occasional urticaria	2	0

**P* = .001 by Student *t* test for paired data (CI, -2.71 to -1.5).

†*P* = .006 by Student *t* test for paired data (CI, -1.0 to 0.32).

‡*P* = .002 by Student *t* test for paired data (CI, 10.31 to 40.78).

§*P* = .001 by McNemar test for nonparametric data.

may play a role in determining the passage of antigens through the intestine. The damage of the intestinal barrier exposes the lymphoid tissue to a larger amount of macromolecules and particles and triggers allergy reactions in sites far away from the intestine.²⁵ In fact, atopy has been linked to the pathogenesis of the mucosal damage.¹⁷ A number of clinical observations, such as microscopic colitis due to food allergy in patients with treated celiac disease²⁶ or cases of familial chronic urticaria associated with celiac disease,¹³⁻¹⁵ are based on the notion that intestinal damage is the pathogenetic basis for the increased prevalence of allergy manifestations. In celiac disease the passage of antigens throughout the intestinal mucosa has been shown. Serum from adult patients with atopic dermatitis showed polymorphic IgG and IgA binding to cereal peptides as a result of natural exposure, identical to that of control subjects. Patients with celiac disease, however, exhibited more intense IgA-stained bands as a result of increased exposure to cereal antigens.²⁷ Silent celiac disease was diagnosed in atopic patients, suggesting that atopy was a consequence of nondiagnosed gluten intolerance without the clinical signs of malabsorption.¹⁷

Intestinal permeability was also shown to be altered in relatives of patients with celiac disease,²³ and this may account for their 2-fold increased risk to have atopy compared with control subjects. It cannot be excluded, however, that allergy and celiac disease share a similar genetic background.²⁸⁻³¹

Our data are in keeping with recent observation of coincidence of atopy and adult patient reports of physician-diagnosed common autoimmune disorders³² and support the hypothesis that T_H1 and T_H2 paradigm (ie, the inverse relationship between T_H1- and T_H2-mediated disorders) might be inconsistent.

Follow-up in the present study was limited to 1 year. One year of gluten-free diet did not abate allergic

manifestations. It cannot be excluded that a longer period of gluten-free diet may have an effect on allergy in patients with celiac disease.

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REFERENCES

1. Kolgnoff MF. Coeliac sprue. In: Sleisenger MH, Fordtran JS, editors. *Gastrointestinal diseases*. Philadelphia: WB Saunders Co; 1996. p. 113.
2. Marsh MN, editor. *Coeliac disease*. Oxford: Blackwell Scientific Publications; 1992.
3. Collin P, Reunala T, Pukkala E, Laippala P, Keyrilainen O, Pasternack A. Coeliac disease: associated disorders and survival. *Gut* 1994;35:1215-8.
4. Ciacchi C, Cirillo M, Sollazzo R, Savino G, Sabbatini F, Mazzacca G. Gender and clinical presentation of adult coeliac disease. *Scand J Gastroenterol* 1995;30:1077-81.
5. Schuppan D. Current concepts of celiac disease pathogenesis. *Gastroenterology* 2000;119:234-42.
6. Del Prete G. Human Th1 and Th2 lymphocytes: their role in the pathogenesis of atopy. *Allergy* 1992;47:450-5.
7. Romagnani S, Parronchi P, D'Elios MM, Romagnani P, Annunziato F, Piccinni MP, et al. An update on human Th1 and Th2 cells. *Int Arch Allergy Immunol* 1997;113:153-6.
8. Benn CS, Bendixen M, Krause TG, Olesen AB. Questionable co-existence of T(H)1- and T(H)2-related diseases. *J Allergy Clin Immunol* 2002;110:328-9.
9. Williams AJ. Coeliac disease and allergic manifestations. *Lancet* 1987;1:808.
10. Kero J, Gissler M, Hemminki E, Isolauri E. Could TH1 and TH2 diseases coexist? evaluation of asthma incidence in children with coeliac disease, type 1 diabetes, or rheumatoid arthritis: a register study. *J Allergy Clin Immunol* 2001;108:781-3.
11. Kelly CP, O'Shea B, Kelly J, Feighery C, Weir DG. Atopy in childhood coeliac disease. *Lancet* 1987;2:109.
12. Hodgson HJ, Davies RJ, Gent AE. Atopic disorders in adult coeliac disease. *Lancet* 1976;1:115-7.
13. Cooper BT, Holmes GKT, Cooke WT. Coeliac disease and immunological disorders. *Br Med J* 1978;1:537-9.
14. Scala E, Giani M, Pirrotta L, Guerra EC, De Pita O, Puddu P. Urticaria and adult coeliac disease. *Allergy* 1999;54:1008-9.
15. Levine A, Dalal I, Bujanover Y. Coeliac disease associated with familial chronic urticaria and thyroid autoimmunity in a child. *Pediatrics* 1999;104:e25.
16. Hautekeer ML, DeClerck LS, Stevens WJ. Chronic urticaria associated with coeliac disease. *Lancet* 1987;1:157.
17. Zauli D, Grassi A, Granito A, Foderaro S, De Franceschi L, Ballardini G, et al. Prevalence of silent coeliac disease in atopics. *Dig Liver Dis* 2000;32:775-9.
18. Greco L, de Seta L, D'Adamo G, Baldassarre C, Mayer M, Siani P, et al. Atopy and coeliac disease: bias or true relation? *Acta Paed Scand* 1990;79:670-4.
19. Bode S, Gudmand-Hoyer E. Symptoms and haematologic features in consecutive adult coeliac patients. *Scand J Gastroenterol* 1996;31:54-60.
20. Wuthrich B, Schmid-Grendelmeier P. The atopic eczema/dermatitis syndrome: epidemiology, natural course, and immunology of the IgE-associated ("extrinsic") and the nonallergic ("intrinsic") AEDS. *J Invest Allergol Clin Immunol* 2003;13:1-5.
21. Bos JD, Van Leent EJ, Sillevius Smitt JH. The millennium criteria for the diagnosis of atopic dermatitis. *Exp Dermatol* 1998;7:132-8.
22. Bjarnason I, MacPherson A, Hollander D. Intestinal permeability: an overview. *Gastroenterology* 1995;108:1566-81.
23. DeMeo MT, Mutlu EA, Keshavarzian A, Tobin MC. Intestinal permeation and gastrointestinal disease. *J Clin Gastroenterol* 2002;34:385-96.
24. van Elburg RM, Uil JJ, Mulder CJ, Heymans HS. Intestinal permeability in patients with coeliac disease and relatives of patients with coeliac disease. *Gut* 1993;34:354-7.
25. Bischoff SC, Mayer JH, Manns MP. Allergy and the gut. *Int Arch Allergy Immunol* 2000;121:270-83.
26. Barbato M, Viola F, Russo LL, Lucarelli S, Frediani T, Cardi E. Microscopic and collagenous colitis in treated coeliac disease due to food allergy? *Gastroenterology* 1999;116:778.
27. Varjonen E, Kalimo K, Savolainen J, Vainio E. IgA and IgG binding components of wheat, rye, barley and oats recognized by immunoblotting analysis with sera from adult atopic dermatitis patients. *Int Arch Allergy Immunol* 1996;111:55-63.
28. Verkasalo M, Tiilikainen A, Kuitunen P, Savilahti E, Backman A. HLA antigens and atopy in children with coeliac disease. *Gut* 1983;24:306-10.
29. Romagnani S. Atopic allergy and other hypersensitivities interactions between genetic susceptibility, innocuous and/or microbial antigens and the immune system. *Curr Opin Immunol* 1997;9:773-5.
30. Perichon B, Krishnamoorthy R. Asthma and HLA system. *Allerg Immunol* 1991;23:301-7.
31. Mowat AM. Coeliac disease: a meeting point for genetics, immunology, and protein chemistry. *Lancet* 2003;361:1290-2.
32. Sheikh A, Smeeth L, Hubbard R. There is no evidence of an inverse relationship between TH2-mediated atopy and TH1-mediated autoimmune disorders: lack of support for the hygiene hypothesis. *J Allergy Clin Immunol* 2003;111:131-5.