Epidemiology of Celiac Disease: What Are the Prevalence, Incidence, and Progression of Celiac Disease?

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Celiac disease (CD) is a chronic systemic autoimmune disorder induced by gluten proteins present in wheat, barley, and rye. Contrary to common belief, gluten enteropathy is a systemic disease rather than merely an ailment of the alimentary tract. Genetically susceptible persons develop autoimmune injury to the gut, skin, liver, joints, uterus, brain, heart, and other organs (Figure 1). The classical definition of CD included gastrointestinal manifestations (chronic diarrhea, failure to grow, weight loss, vomiting, abdominal pain, bloating, distention, and constipation), confirmed by a small bowel biopsy (SBB) with findings of villous atrophy, crypt hyperplasia, and normalization of the villous architecture in response to a gluten-free diet.[1,2] Previously, CD was thought to be a disease primarily of infancy; however, with the widespread delay in introduction of wheat into the infant diet, the clinical manifestations have become more subtle, and diagnosis is now typically made in older children and adults.[3–5] SBB is poorly accepted by a majority of patients with mild or no symptoms, and the pathologic examination of biopsy material is suboptimal in most settings. The use of SBB as a "gold standard" for diagnosis has significant limitations. It is occasionally false-negative because of patchy mucosal changes. Villous atrophy is often most severe in the proximal jejunum, typically not reached by endoscopic biopsy. This has led some to propose a new definition of CD, based on the presence of serum IgA autoantibodies to tissue transglutaminase (IgA TG) and HLA-DQB1*0201 or *0302 alelles.[6] These markers are increasingly used in screening for CD, but their true sensitivity and specificity are debatable. Although efforts to standardize IgA TG assays have been undertaken,[7,8] previous reports have likely overestimated the sensitivity and underestimated the specificity because of verification bias[9] caused by the lack of SBB studies in patients negative on TG screening.

Spectrum of CD

The current model of the natural history of CD (Figure 2) recognizes that, at certain points in time, the disease is not associated with obvious clinical signs and symptoms.

Latent CD precedes diagnosis of CD or follows successful treatment of active disease with a gluten-free diet (GFD). The SBB does not show villous atrophy and crypt hyperplasia, but there are increased γ/δ intraepithelial T cells, higher proportion of dividing epithelial crypt cells,[10] and subtle morphometric abnormalities of the enterocytes,[11] pointing to a low-grade ongoing inflammation in the gut wall. IgA TG or endomysial autoantibodies can be detected in many of these patients. Prospective studies have shown that individuals with latent CD develop symptoms and positive SBB while on gluten-containing diet.[12–14]

Active CD is characterized by intestinal and/or extraintestinal symptoms, villous atrophy and crypt hyperplasia, and strongly positive IgA TG and endomysial autoantibodies. However, the latter can be undetectable in occasional patients with coexisting IgA deficiency. Atypical presentation has become increasingly frequent, with nonspecific abdominal discomfort or extraintestinal symptoms[5] such as dermatitis herpetiformis, iron-deficiency anemia, hepatitis, cholangitis, hypertransaminasemia, coagulopathy, short statue, pubertal delay, osteopenia, arthralgia, aphthous stomatitis, dental enamel defects, alopecia, edema, infertility, depressive symptoms, and cerebellar ataxia. Dermatitis herpetiformis—an extremely itchy, bullous skin rash of the extensor surface of the limbs, trunk, and scalp—is a good example of a predominantly extraintestinal form of CD. Patients with dermatitis herpetiformis have IgA TG (80%–95%), HLA-DQB1*0201 (90%), and villous atrophy (75%, the remaining 25% have increased intraepithelial lymphocytes) and respond to GFD, yet they are often treated as if they had a different disease (eg, using Dapsone and not GFD).[15]

Abbreviations used in this paper: IgA TG, IgA autoantibodies to tissue transglutaminase; CD, celiac disease; GFD, gluten-free diet; SBB, small bowel biopsy.

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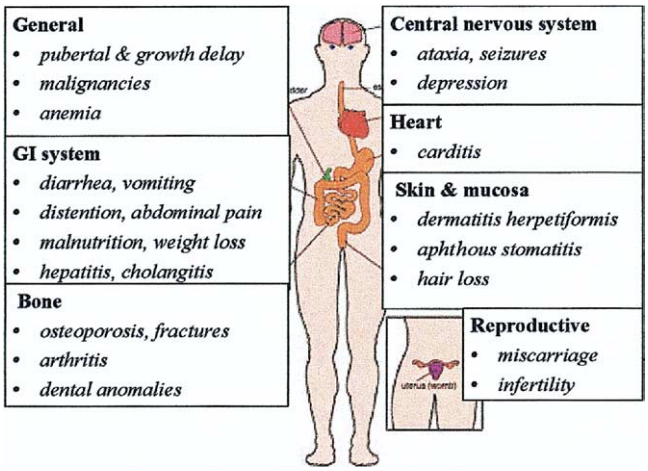

Figure 1. New paradigm: celiac disease is a multiorgan autoimmune disease caused by gluten intolerance.

Silent CD is characterized by the presence of IgA TG and endomysial autoantibodies, histologic lesions on SBB typical for CD, and CD-associated HLA-DQ genotypes in an asymptomatic individual. In retrospect, however, many patients or their relatives recollect typical symptoms.[16–18] Children with silent disease had decreased height z-scores that correlated with the degree of intestinal injury.[16,19] Silent CD has been suggested to cause nutritional deficiency of iron; zinc; folate; vitamins D, K, and E; osteoporosis[20]; lymphoma[21]; and neurological disease,[22] but the evidence is not very strong. There are no clear guidelines concerning the GDF in people with silent CD, especially those detected through serologic screening. However, preliminary reports appear to confirm that a GFD in silent cases prevents or reverses systemic complications such as delayed growth, weight loss,[23,24] or osteopenia.[10]

Prevalence

The proportion of people in a population who have CD at a specified time (prevalence rate) depends of course on definition of the disease. Figure 3 illustrates prevalence of preclinical (latent), undiagnosed (largely silent), and diagnosed (mostly active) CD in several European and US populations. Although the prevalence of *diagnosed* CD varied widely among these populations, the estimates of combined undiagnosed and diagnosed (or silent and active) CD were remarkably similar, between 0.7%–2.0% in most of the populations, including the United States. The prevalence of childhood CD has been reported to be between 1:285 and 1:77 in Sweden,[25,26] 1:99 (positive SBB) and 1:67 (presence of IgA TG and HLA- DQB1*0201 or *0302) in Finland,[6] and 1:230[27] and 1:106[18] in Italian schoolchildren. Generally, similar rates have been reported for non-European white populations, such as New Zealand,[28] Australia,[29] Argentina,[30] and Israel.[31]

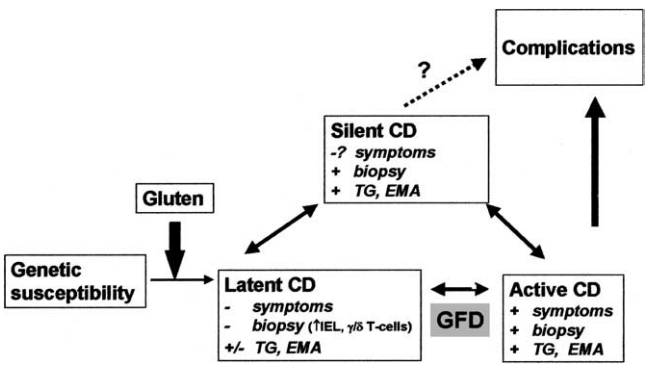

Figure 2. Natural history of celiac disease.

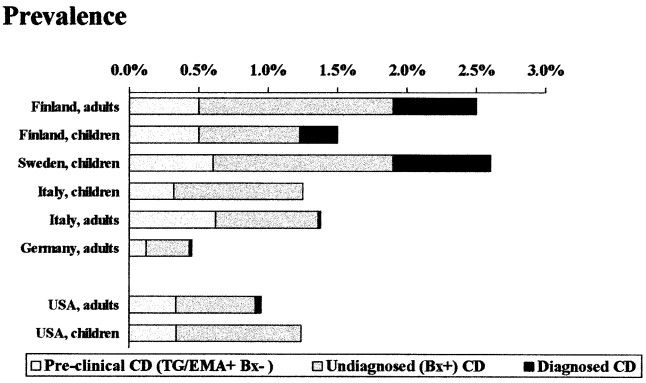

Figure 3. Prevalence of preclinical, undiagnosed and diagnosed CD based on work of Murray et al,[4] Mäki et al,[6] Carlsson et al,[26] Hoffenberg et al,[32] Fasano et al,[33] and Mustalahti et al.[55]

In the United States, cumulative incidence of persistent IgA TG positivity by the age of 5 years was 1:104 (95% CI: 1:49–221).[32] In US adults, the prevalence varied from 1:1750[4] (clinically diagnosed CD, including dermatitis herpetiformis) to 1:105[33] (presence of IgA endomysial antibodies). Ethnic-specific data for the US population are scarce; the cumulative incidence of persistent IgA TG in Hispanic children was reported to be more than 3 times lower than in non-Hispanic whites,[32] probably because of the low frequency of the HLA-DR3, DQB1*0201 haplotype in this population. CD is virtually unknown in East Asian populations who also lack this HLA haplotype; however, rates close to those in Europe have been reported from the Middle East and India. Although the disease is believed to be rare in Africa (and in African Americans), the highest prevalence has been reported for Saharavi in North Africa.[34]

The estimates based on seroepidemiologic studies suggest that, for each diagnosed case of CD, there may be 3–7 undiagnosed cases and that 1%–3% of the general

population in Europe and the United States becomes affected at some point in life. Most studies point to a secular increase in the prevalence of CD (Figure 4) that is largely due to increasing index of clinical suspicion and availability of highly sensitive and specific serologic screening tests.

Incidence

Population-based estimates of the incidence of SBB-confirmed CD in adults vary from 2–13/100,000 per year.[4,35] These rates have to be interpreted with caution because many patients diagnosed as adults likely have had 20–60 years of untreated CD, thus hardly represent truly incident (new) disease.

The recent increase in the incidence rates (Figure 5) is likely due to increasing use of serologic screening leading to diagnosis in milder cases. However, there is a paucity of incidence data that would represent the full spectrum of disease, including silent and latent cases. Infant and early childhood nutrition varies among populations. Differences in the prevalence of susceptibility HLA alleles may explain interpopulation variation in the incidence of CD. The effects of nutritional practices on the risk and severity of CD may also account for geographic and temporal variation in the incidence of CD and be of great public health importance.

Progression

Over time, individuals progress from latent to silent or active disease (Figure 2) and can reverse to the latent subclinical state on a strict GFD. It is not entirely clear how strict the GFD has to be in a given patient to avoid symptoms and long-term complications. Although there is growing evidence for a remitting-relapsing pattern of CD autoimmunity in some patients,[6,36] the disease process defined by current serologic and histopathologic techniques is remarkably persistent in the absence of a GFD. A 2- to 3-fold excess in all-cause mortality among CD patients, compared with the general population, has been reported in some studies[37,38] but not all.[39,40] The increased mortality has been attributed to gastrointestinal tract malignancies, especially lymphoma.[21,41–43]

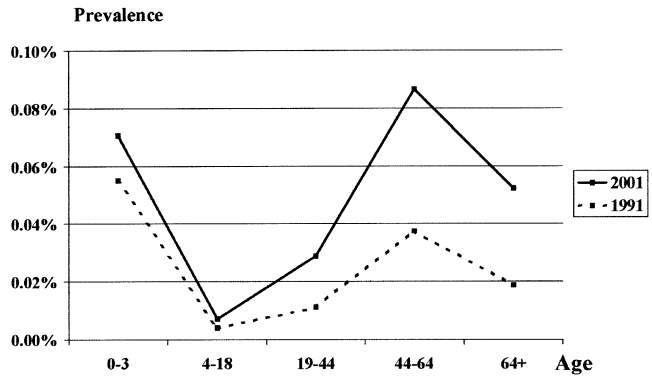

Figure 4. Prevalence of diagnosed celiac disease including dermatitis herpetiformis, Olmsted County, Minnesota, 1991 and 2001 (Data from Murray et al[4]).

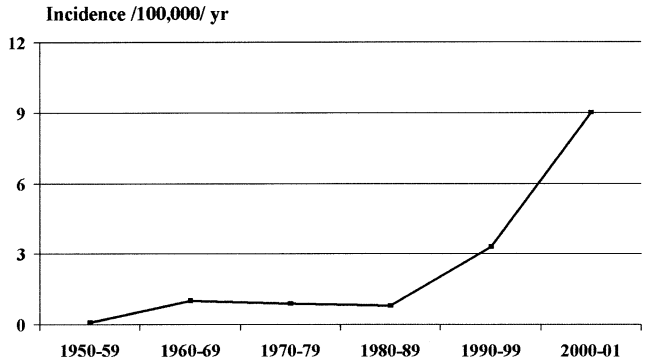

Figure 5. Age-adjusted incidence of diagnosed celiac disease, Olmsted County, Minnesota, 1950–2000 (Data from Murray et al[4]).

Patients with CD-associated T-cell lymphomas express the HLA-DR3/4 genotype (40%) more often than other CD patients (7%) or controls (2%).[44] Although the HLA class II genes are clearly important, they account for only approximately 30%–40% of the familial clustering of CD.[45] Additional loci, eg, CD28/CTLA4/ICOS 2q33,[46] 15q26,[47] *IDDM17*,[48] and 5qter[49] may be related to progression of CD and development of long-term complications.

Additional nongenetic candidate factors associated with progression to CD include early exposure to gliadins in utero or via breast milk,[3,50] dose, and age at introduction[51,52] and intestinal infections[53,54] with gut hyperpermeability. Infant and early childhood nutrition varies among populations. Although the effects of nutritional practices on the risk and severity of CD may be of great public health importance, these are largely unknown and need to be assessed in large prospective studies.

In summary, CD is a protean systemic disease affecting up to 1% of the general population. Appropriate screening, diagnosis, and treatment guidelines are being redefined, using improved diagnostic methods that include IgA TG testing and HLA-DQB1 typing, in addition to SBB.

References

1. Walker-Smith J, Guandalini S, Schmitz J, Shmerling D, Visakorpi J. Revised criteria for diagnosis of coeliac disease. Report of Working Group of European Society of Paediatric Gastroenterology and Nutrition. Arch Dis Child 1990;65:909–911.

2. Catassi C, Cellier C, Cerf-Bensussan N, Ciclitira PJ, Collin P, Corazza GR, Dickey W, Fasano A, Holmes GKT, Klincewicz P, Mearin ML, Mulder CJJ, Murray JA, Pena AS, Schuppan D, Sollid LM, Uil JJ, Wahab PJ, Walker-Smith JA, Watson P, Van Belzen M, von Blomberg BME, Bouquet J, Bijleveldt CMA, Crusius JBA, Douwes AC, George EK, Hamer RJ, Janssen FW, Meyer JWR, Sinaasappel M, Rostami K, Taminiau JAJM, Vader LW, Wijmenga C. When is a coeliac a coeliac? Report of a working group of the United European Gastroenterology Week in Amsterdam, 2001. Eur J Gastroenterol Hepatol 2001;13:1123–1128.
3. Maki M, Kallonen K, Lahdeaho ML, Visakorpi JK. Changing pattern of childhood coeliac disease in Finland. Acta Paediatr Scand 1988;77:408–412.
4. Murray JA, Van Dyke C, Plevak MF, Dierkhising RA, Zinsmeister AR, Melton LJ III. Trends in the identification and clinical features of celiac disease in a North American community, 1950–2001. Clin Gastroenterol Hepatol 2003;1:19–27.
5. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. Gastroenterology 2001;120:636–651.
6. Maki M, Mustalahti K, Kokkonen J, Kulmala P, Haapalahti M, Karttunen T, Ilonen J, Laurila K, Dahlbom I, Hansson T, Hopfl P, Knip M. Prevalence of celiac disease among children in Finland. N Engl J Med 2003;348:2517–2524.
7. Wong RC, Wilson RJ, Steele RH, Radford-Smith G, Adelstein S. A comparison of 13 guinea pig and human anti-tissue transglutaminase antibody ELISA kits. J Clin Pathol 2002;55:488–494.
8. Van MB, Hiele M, Hoffman I, Vermeire S, Rutgeerts P, Geboes K, Bossuyt X. Diagnostic accuracy of ten second-generation (human) tissue transglutaminase antibody assays in celiac disease. Clin Chem 2004;50:2125–2135.
9. Punglia RS, D'Amico AV, Catalona WJ, Roehl KA, Kuntz KM. Effect of verification bias on screening for prostate cancer by measurement of prostate-specific antigen. N Engl J Med 2003;349:335–342.
10. Mustalahti K, Collin P, Sievanen H, Salmi J, Maki M. Osteopenia in patients with clinically silent coeliac disease warrants screening. Lancet 1999;354:744–745.
11. Maki M, Holm K, Lipsanen V, Hallstrom O, Viander M, Collin P, Savilahti E, Koskimies S. Serological markers and HLA genes among healthy first-degree relatives of patients with coeliac disease. Lancet 1991;338:1350–1353.
12. Maki M, Holm K, Koskimies S, Hallstrom O, Visakorpi JK. Normal small bowel biopsy followed by coeliac disease. Arch Dis Child 1990;65:1137–1141.
13. Collin P, Helin H, Maki M, Hallstrom O, Karvonen AL. Follow-up of patients positive in reticulin and gliadin antibody tests with normal small-bowel biopsy findings. Scand J Gastroenterol 1993; 28:595–598.
14. Troncone R. Latent coeliac disease in Italy. The SIGEP Working Group on Latent Coeliac Disease. Italian Society for Paediatric Gastroenterology and Hepatology. Acta Paediatr 1995;84:1252–1257.
15. Reunala TL. Dermatitis herpetiformis. Clin Dermatol 2001;19: 728–736.
16. Hoffenberg EJ, Emery LM, Barriga KJ, Bao F, Taylor J, Eisenbarth GS, Haas JE, Sokol RJ, Taki I, Norris JM, Rewers M. Clinical features of children with screening-identified evidence of celiac disease. Pediatrics 2004;113:1254–1259.
17. Bingley PJ, Williams AJ, Norcross AJ, Unsworth DJ, Lock RJ, Ness AR, Jones RW. Undiagnosed coeliac disease at age seven: population based prospective birth cohort study. BMJ 2004;328: 322–323.
18. Tommasini A, Not T, Kiren V, Baldas V, Santon D, Trevisiol C, Berti I, Neri E, Gerarduzzi T, Bruno I, Lenhardt A, Zamuner E, Spano A, Crovella S, Martellossi S, Torre G, Sblattero D, Marzari R, Bradbury A, Tamburlini G, Ventura A. Mass screening for coeliac disease using antihuman transglutaminase antibody assay. Arch Dis Child 2004;89:512–515.
19. Hoffenberg EJ, Bao F, Eisenbarth GS, Uhlhorn C, Haas JE, Sokol RJ, Rewers M. Transglutaminase antibodies in children with a genetic risk for celiac disease. J Pediatr 2000;137:356–360.
20. Kemppainen T, Kroger H, Janatuinen E, Arnala I, Lamberg-Allardt C, Karkkainen M, Kosma VM, Julkunen R, Jurvelin J, Alhava E, Uusitupa M. Bone recovery after a gluten-free diet: a 5-year follow-up study. Bone 1999;25:355–360.
21. Catassi C, Fabiani E, Corrao G, Barbato M, De Renzo A, Carella AM, Gabrielli A, Leoni P, Carroccio A, Baldassarre M, Bertolani P, Caramaschi P, Sozzi M, Guariso G, Volta U, Corazza GR. Risk of non-Hodgkin lymphoma in celiac disease. JAMA 2002;287:1413–1419.
22. Hadjivassiliou M, Grunewald R, Sharrack B, Sanders D, Lobo A, Williamson C, Woodroofe N, Wood N, Davies-Jones A. Gluten ataxia in perspective: epidemiology, genetic susceptibility and clinical characteristics. Brain 2003;126:685–691.
23. Acerini CL, Ahmed ML, Ross KM, Sullivan PB, Bird G, Dunger DB. Coeliac disease in children and adolescents with IDDM: clinical characteristics and response to gluten-free diet. Diabet Med 1998;15:38–44.
24. Fabiani E, Catassi C, Villari A, Gismondi P, Pierdomenico R, Ratsch IM, Coppa GV, Giorgi PL. Dietary compliance in screening-detected coeliac disease adolescents. Acta Paediatr Suppl 1996;412:65–67.
25. Cavell B, Stenhammar L, Ascher H, Danielsson L, Dannaeus A, Lindberg T, Lindquist B. Increasing incidence of childhood coeliac disease in Sweden. Results of a national study. Acta Paediatr 1992;81:589–592.
26. Carlsson AK, Axelsson IE, Borulf SK, Bredberg AC, Ivarsson SA. Serological screening for celiac disease in healthy 2.5-year-old children in Sweden. Pediatrics 2001;107:42–45.
27. Catassi C, Ratsch IM, Fabiani E, Ricci S, Bordicchia F, Pierdomenico R, Giorgi PL. High prevalence of undiagnosed coeliac disease in 5280 Italian students screened by antigliadin antibodies. Acta Paediatr 1995;84:672–676.
28. Cook HB, Burt MJ, Collett JA, Whitehead MR, Frampton CM, Chapman BA. Adult coeliac disease: prevalence and clinical significance. J Gastroenterol Hepatol 2000;15:1032–1036.
29. Hovell CJ, Collett JA, Vautier G, Cheng AJP, Sutanto E, Mallon DF, Olynyk JK, Cullen DJE. High prevalence of coeliac disease in a population-based study from Western Australia: a case for screening? Med J Aust 2001;175:247–250.
30. Gomez JC, Selvaggio GS, Viola M, Pizarro B, la Motta G, de Barrio S, Castelletto R, Echeverria R, Sugai E, Vazquez H, Maurino E, Bai JC. Prevalence of celiac disease in Argentina: screening of an adult population in the La Plata area. Am J Gastroenterol 2001; 96:2700–2704.
31. Shamir R, Lerner A, Shinar E, Lahat N, Sobel E, Bar-or R, Kerner H, Eliakim R. The use of a single serological marker underestimates the prevalence of celiac disease in Israel: a study of blood donors. Am J Gastroenterol 2002;97:2589–2594.
32. Hoffenberg EJ, Mackenzie T, Barriga KJ, Eisenbarth GS, Bao F, Haas JE, Erlich H, Bugawan TL, Sokol RJ, Taki I, Norris JM, Rewers M. A prospective study of the incidence of childhood celiac disease. J Pediatr 2003;143:308–314.
33. Fasano A, Berti I, Gerarduzzi T, Not T, Colletti RB, Drago S, Elitsur Y, Green PH, Guandalini S, Hill ID, Pietzak M, Ventura A, Thorpe M, Kryszak D, Fornaroli F, Wasserman SS, Murray JA, Horvath K. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. Arch Intern Med 2003;163:286–292.
34. Catassi C, Ratsch IM, Gandolfi L, Pratesi R, Fabiani E, El Asmar R, Frijia M, Bearzi I, Vizzoni L. Why is coeliac disease endemic in the people of the Sahara? Lancet 1999;354:647–648.

35. Cook B, Oxner R, Chapman B, Whitehead M, Burt M. A thirty-year (1970–1999) study of coeliac disease in the Canterbury region of New Zealand. N Z Med J 2004;117:U772.
36. Liu E, Bao F, Barriga K, Miao D, Yu L, Erlich HA, Haas JE, Eisenbarth GS, Rewers MJ, Hoffenberg EJ. Fluctuating transglutaminase autoantibodies are related to histologic features of celiac disease. Clin Gastroenterol Hepatol 2003;1:356–362.
37. Ferguson A, Kingstone K. Coeliac disease and malignancies. Acta Paediatr Suppl 1996;412:78–81.
38. Corrao G, Corazza GR, Bagnardi V, Brusco G, Ciacci C, Cottone M, Guidetti CS, Usai P, Cesari P, Pelli MA, Loperfido S, Volta U, Calabro A, Certo M. Mortality in patients with coeliac disease and their relatives: a cohort study. Lancet 2001;358:356–361.
39. Collin P, Reunala T, Pukkala E, Laippala P, Keyrilainen O, Pasternack A. Coeliac disease—associated disorders and survival. Gut 1994;35:1215–1218.
40. Johnston SD, Watson RG, McMillan SA, Sloan J, Love AH. Coeliac disease detected by screening is not silent—simply unrecognized. QJM 1998;91:853–860.
41. O'Connor TM, Cronin CC, Loane JF, O'Meara NM, Firth RG, Shanahan F, O'Halloran DJ. Type 1 diabetes mellitus, coeliac disease, and lymphoma: a report of four cases. Diabet Med 1999;16:614–617.
42. Askling J, Linet M, Gridley G, Halstensen TS, Ekstrom K, Ekbom A. Cancer incidence in a population-based cohort of individuals hospitalized with celiac disease or dermatitis herpetiformis. Gastroenterology 2002;123:1428–1435.
43. Green PHR, Fleischauer AT, Bhagat G, Goyal R, Jabri B, Neugut AI. Risk of malignancy in patients with celiac disease. Am J Med 2003;115:191–195.
44. Howell WM, Leung ST, Jones DB, Nakshabendi I, Hall MA, Lanchbury JS, Ciclitira PJ, Wright DH. HLA-DRB, -DQA, and -DQB polymorphism in celiac disease and enteropathy-associated T-cell lymphoma. Common features and additional risk factors for malignancy. Hum Immunol 1995;43:29–37.
45. Petronzelli F, Bonamico M, Ferrante P, Grillo R, Mora B, Mariani P, Apollonio I, Gemme G, Mazzilli MC. Genetic contribution of the HLA region to the familial clustering of coeliac disease. Ann Hum Genet 1997;61:307–317.
46. Djilali-Saiah I, Schmitz J, Harfouch-Hammoud E, Mougenot JF, Bach JF, Caillat-Zucman S. CTLA-4 gene polymorphism is associated with predisposition to coeliac disease. Gut 1998;43:187–189.
47. Zhong F, McCombs CC, Olson JM, Elston RC, Stevens FM, McCarthy CF, Michalski JP. An autosomal screen for genes that predispose to celiac disease in the western counties of Ireland. Nat Genet 1996;14:329–333.
48. Redondo MJ, Eisenbarth GS. Genetic control of autoimmunity in type I diabetes and associated disorders. Diabetologia 2002;45:605–622.
49. Greco L, Corazza G, Babron MC, Clot F, Fulchignoni-Lataud MC, Percopo S, Zavattari P, Bouguerra F, Dib C, Tosi R, Troncone R, Ventura A, Mantavoni W, Magazzu G, Gatti R, Lazzari R, Giunta A, Perri F, Iacono G, Cardi E, De Virgiliis S, Cataldo F, De Angelis G, Musumeci S, Clerget-Darpoux F. Genome search in celiac disease. Am J Hum Genet 1998;62:669–675.
50. Auricchio S, Follo D, De Ritis G, Giunta A, Marzorati D, Prampolini L, Ansaldi N, Levi P, Dall'Olio D, Bossi A. Does breast feeding protect against the development of clinical symptoms of celiac disease in children? J Pediatr Gastroenterol Nutr 1983;2:428–433.
51. Ivarsson A, Persson LA, Nystrom L, Hernell O. The Swedish coeliac disease epidemic with a prevailing twofold higher risk in girls compared to boys may reflect gender specific risk factors. Eur J Epidemiol 2003;18:677–684.
52. Norris JM, Barriga K, Hoffenberg EJ, Taki I, Emery LM, Eisenbarth GS, Sokol RJ, Bugawan TL, Erlich HA, Rewers M. Timing of gluten introduction in the infant diet affects risk of coeliac disease autoimmunity. The 11th International Symposium: Coeliac Disease. Belfast, Northern Ireland Ed, 2004.
53. Howdle PD, Blair Zajdel ME, Smart CJ, Trejdosiewicz LK, Blair GE, Losowky MS. Lack of a serologic response to an E1B protein of adenovirus 12 in coeliac disease. Scand J Gastroenterol 1989;24:282–286.
54. Mahon J, Blair GE, Wood GM, Scott BB, Losowsky MS, Howdle PD. Is persistent adenovirus 12 infection involved in coeliac disease? A search for viral DNA using the polymerase chain reaction. Gut 1991;32:1114–1116.
55. Mustalahti K, Reunanen A, Heuer M, Metzger M-H, Fabiani E, Catassi C, Murray L, McMillan S, Caradonna M, Bravi E, Maki M. Prevalence of coeliac disease in four European countries. The 11th International Symposium: Coeliac Disease. Belfast, Northern Ireland, 2004:P60.

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