

Celiac Disease: Its Many Faces and Relevance to Developmental Disabilities

Abstract

Celiac disease (CD) is a very common medical disorder in the general population. It results from sensitivity to a protein called gluten that is found in many grains. There presently is no cure for CD, but treatment with a gluten-free diet can effectively control or reverse symptoms in a high percentage of patients. CD is under recognized and under diagnosed in the general population and in those with developmental disabilities. Consequences of CD can include symptoms referred to as "digestive" as well as others that are behavioural, neurological or neuropsychological. Furthermore, there is evidence for an association between CD and early cognitive decline or dementia in the general population. In this short report, we briefly review what is known about CD and its consequences in the general population and in people with developmental disabilities. Unusual terms are explained briefly in the Glossary. This report was first presented in poster form at the 2007 Annual Symposium of the Research Special Interest Group.

Authors

Maire Percy^{1,2}
and
Evan Propst³

¹Surrey Place Centre

²Departments of
Physiology and Obstetrics
& Gynaecology, University
of Toronto

³Department of
Otolaryngology, Head and
Neck Surgery, University of
Toronto.

Correspondence

maire.percy@utoronto.ca
or
evan.propst@utoronto.ca

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Celiac disease (CD) is a medical disorder in which the surface of the small intestine is damaged as the result of intolerance to the protein "gluten" found in many grains, including wheat, barley, rye and triticale. CD is considered an autoimmune disease because people with CD have higher than normal levels of certain autoantibodies in their blood. Autoantibodies are immunoglobulin molecules that react with substances in one's own tissues or body fluids. There presently is no cure for CD, but it can be effectively treated and controlled by elimination of gluten from the diet. This is a lifelong requirement. If treatment is started early enough, CD and its symptoms/consequences can be halted, reversed, or prevented. Many gluten-free products are currently available in North America and the number of these continues to increase (Canadian Celiac Association,

2008; National Digestive Diseases Information Clearing House, 2007; No authors listed, 2004).

With a prevalence of approximately 1 in 133 (0.75%), CD is one of the most common medical disorders in North America. Despite important advances in its diagnosis and etiology, CD is under-recognized and under-diagnosed. It has been estimated that approximately 97% of people with CD are unaware that they have it (Canadian Celiac Association, 2008; National Digestive Diseases Information Clearing House, 2007; No authors listed, 2004). This, in part, is due to a lack of education about CD among physicians and in the general population. It also may be a consequence of the facts that CD can develop at any time during one's life in association with one or more seemingly unrelated symptoms, or that it can be apparently asymptomatic (see below).

As is evident from the listing of references in this report, the literature about CD in developmental disabilities is scant. The purpose of the present paper is to provide a brief overview of CD so that the developmental disability field can benefit from recent knowledge and advances in the CD field.

Cause of CD

CD has a strong genetic predisposition. It is associated with genes located in the major histocompatibility complex (called the human leukocyte antigen locus or HLA locus in humans). Genes in the HLA locus on chromosome 6 code for proteins on leukocytes (white blood cells) that are involved in immune regulation including graft rejection. Approximately 97% of people with CD have been found to carry two particular sets of HLA genes called DQ2 and DQ8, but other genes are thought to confer an additional genetic risk (Stepniak & Koning, 2006; Torres,

López Casado, & Ríos, 2007). Two different DNA alleles within the HLA locus called DQA1*0501 and DQB1*0201 encode for DQ2 protein. The DQ8 protein is encoded by the DQA1*0301 and the DQB1*0302 alleles. The DQ2 genes and protein are present in 95% of all celiac patients compared to about 20% of controls. Of patients with CD who are negative for DQ2, the majority are positive for DQ8. (An allele is an alternative form of a gene that is located at a specific position on a specific chromosome.) Determining if one carries DQ2 or DQ8 can be done by analysis of DNA or serum (Autoimmun Diagnostika GMBH, n.d.).

Diagnosis of CD

CD is often diagnosed by blood tests known to detect immune abnormalities associated with the disorder. These are called serology tests because they are done on the serum fraction of blood samples. The serology tests include measuring levels of immunoglobulin A (IgA), anti-tissue transglutaminase (tTGA), and IgA anti-endomysium antibodies (AEA). Although the diagnostic accuracy of such tests is quite high, they do not identify everyone with CD. Because CD results from intestinal damage, biopsy of the small intestine and detection of characteristic histopathological changes of CD is considered to be the "gold standard" for a definite diagnosis. The term histopathology refers to the study of the microscopic anatomical changes in diseased tissue. Characteristic histopathological changes of celiac disease include partial or complete flattening of the finger-like projections in the small intestine called intestinal villi as well as other abnormalities. The diagnosis of CD is considered to be definite when the serology and biopsy results are both positive. The term silent celiac disease refers to that in individuals who are asymptomatic yet have both positive serology and biopsy. The term latent celiac

disease refers to that in individuals with positive serology and negative biopsy, but who may later present with positive symptoms or intestinal changes. (For more information see National Digestive Diseases Information Clearing House, 2007; No authors listed, 2004; Wallace & Dalton, 2006.)

Symptoms of CD

Symptoms of CD can result from the consequences of production of auto-antibodies as well as from malnourishment that is the result of damaged small intestine. There can be malabsorption of virtually any food substance including proteins, fats, carbohydrates, vitamins and minerals. Certain symptoms of CD are sometimes referred to as “digestive.” These include failure to thrive; delayed or stunted growth (in children); weight loss or gain; gas, loose stools or diarrhea; foul-smelling or grayish stools that may be fatty or oily; abdominal pain; and, pale sores in the mouth. Some complications of CD include general weakness, osteoporosis, iron deficiency anemia, bruising, night blindness, irritability, anxiety and depression. CD may also result in neurological and neuropsychological complications. These include peripheral neuropathy, migraine headache, hypotonia, learning disorders, “developmental delay,” ataxia, attention deficit hyperactivity disorder, and seizures that are treatment resistant. (Please note that there is a glossary below.) Of these latter complications, transient hypotonia in infants and migraine headaches are reported to have been alleviated by a gluten-free diet. Some common disorders that co-exist with CD include dermatitis herpetiformis, lactose intolerance, type 1 diabetes, autoimmune thyroid disease, rheumatoid arthritis, systemic lupus, liver disease, Sjogren’s syndrome, and certain cancers (lymphoma and adenocarcinoma). (For more information see Bushara, 2005;

Canadian Celiac Association, 2008; Lurie, Landau, Pfeffer, & Oren, 2008; Grossman, 2008; Martínez-Bermejo & Polanco, 2002; National Digestive Diseases Information Clearing House, 2007; Wallace, 2007; Wallace & Dalton, 2006; Zelnick, Pacht, Obeid, & Lerner, 2004.)

Relation Between CD and Developmental Disability

The literature on the relationship between CD and developmental disabilities is sparse. It is known that fetal health and development can be affected by maternal CD if this is associated with malnutrition (Hadziselimovic, Geneto, & Buser, 2007; Ludvigsson, Montgomery, & Ekblom, 2005). Aside from an association with caesarean section, there appears to be no adverse risk for fetal outcome associated with paternal CD (Ludvigsson, Montgomery, & Ekblom, 2006). People with CD may be at increased risk for developmental delay, learning difficulties and attention deficit hyperactivity disorder (Zelnick et al., 2004). An association of CD with Floating-Harbor syndrome has been suggested (Chudley & Moroz, 1991). CD is much more common in people with Down syndrome than in those without this disorder in the general population (7-16% vs. 0.75% (i.e., it is 10-20-fold increased) (Lovering & Percy, 2007; Wallace, 2007; Wallace & Dalton, 2006). There is a high frequency of gastrointestinal problems in people with autistic spectrum disorders (ASD), with as many as 15-20% affected. Although not all gastrointestinal symptoms in ASD result from CD, there now is evidence for an increased prevalence of definite CD in pediatric cases of autism (3.3%) compared to the general pediatric population (Barcia, Posar, Santucci, & Parmeggiani, 2008). Furthermore, there are anecdotal reports that some people with autism have benefited from a diet that is gluten-free and dairy free (Mick, 2007). The NIH is currently conducting a clinical trial of diet

and behaviour in young children with autism (ClinicalTrials.gov, 2008).

Relation Between CD and Early Cognitive Decline or Dementia

One study in 2006 has reported an association between CD and early cognitive decline or dementia in the general population. In this study, a gluten-free diet halted or reversed early cognitive decline in 3 of 13 (23%) persons from the general population who had dementia and/or early cognitive decline associated with CD (Hu, Murray, Greenaway, Parisi, & Josephs, 2006). People with Down syndrome are at high risk of developing not only CD, but also early onset dementia of the Alzheimer's type (DAT) (Prasher, Percy, Jozsvai, Lovering & Berg, 2007). It therefore is hypothesized that treatment with a gluten-free diet should halt or reverse DAT in some individuals with Down syndrome who also have CD, as in the general population.

Limitations of This Review

Because of space limitation, the authors have not provided a comprehensive reference list for this brief review. We apologize to authors whose important papers may not have been cited. For in-depth information about CD, refer to the publications listed in References.

Glossary

Adenocarcinoma—a cancer that originates in glandular tissue; the most common form is adenocarcinoma of the colon.

Anti-endomysium antibody—antibody that binds to the thin connective tissue covering each muscle cell.

Anti-tissue transglutaminase antibody—antibody that binds to the enzyme

transglutaminase. The normal function of transglutaminase is thought to be the repair of injured or inflamed tissue by cross-linking of the extracellular matrix proteins in the tissue. This cross-linking stabilizes the damaged tissue and protects the surrounding tissue from further damage.

Ataxia—the loss of coordination of parts of the body. It affects the parts of the nervous system that control movement and balance.

Autoimmune thyroid disease—autoimmune diseases that attack the thyroid. The most common are Graves' disease (hyperthyroidism with excessive thyroid hormone) and Hashimoto's thyroiditis (hypothyroidism with deficient thyroid hormone).

Dermatitis herpetiformis—an intensely itchy skin eruption in which the elbows, knees, scalp, buttocks and back are commonly affected.

Floating-Harbor syndrome—A genetic condition characterized by the "triad of short stature apparent at birth with significantly delayed bone age; expressive language delay, usually in the presence of normal motor development; and a triangular face with a prominent nose and deep-set eyes." The syndrome name "reflects the fact that patients with the syndrome were first described in 1973 at the Boston Floating Hospital and in 1975 at Harbor General Hospital in California." (MedicineNet.com. (2008). Retrieved June 2, 2008, from <http://www.medterms.com/script/main/art.asp?articlekey=21932>)

Hypotonia—a condition of abnormally low muscle tone (the amount of tension or resistance to movement in a muscle).

Immunoglobulin A (IgA)—an antibody playing a critical role in immunity at mucosal surfaces.

Lactose intolerance—the inability to metabolize lactose, a sugar found in milk and other dairy products. This occurs because the enzyme lactase, which is needed to break down the sugar, is absent or reduced in amount.

Lymphoma—a type of solid cancer that originates in lymphocytes (a type of white blood cell).

Migraine headache—disabling headaches thought to result from problems with the nerves and blood vessels in the head.

Peripheral neuropathy—damage to the peripheral nervous system (that residing outside of the brain and the spinal cord).

Rheumatoid arthritis—a chronic, systemic autoimmune disorder that causes the immune system to attack the joints and sometimes organs such as the lungs and skin.

Sjogren's syndrome—an autoimmune disorder characterized by dry eyes and dry mouth..

Small intestine—the part of the gut between the stomach and the large intestine where most of the digestion and nutrient absorption takes place.

Systemic lupus (erythymatosus)—a serious disease affecting the joints, kidney and skin.

Type 1 diabetes—an autoimmune disease that results in the permanent destruction of insulin producing beta cells of the pancreas. Formerly called childhood diabetes, juvenile diabetes, and insulin dependent diabetes

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