

Unexpected Health Risks Found in Celiac Patients

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Children diagnosed with celiac disease usually experience complete remission once they are started on a gluten-free diet, and thus early diagnosis can be beneficial. But early diagnosis may have adverse effects as well. A large British study has found that a diagnosis of celiac disease in childhood, as opposed to adulthood, is associated with threefold higher mortality—largely due to suicide, accidents, and violence.

The findings are “really surprising and unexpected,” according to Dr. Stefano Guandalini, chief of pediatric gastroenterology and director of the Celiac Disease Program at the University of Chicago. As one of the reviewers of the British study, he said he is confident that the increased mortality is more than a chance finding, but the reasons for it are open to interpretation.

“One certainly cannot ignore this report; it’s a well-done study. We may discuss the finer details of interpreting them but I think the data seem to be believable,” he said in an interview.

The investigators analyzed data on a cohort of 625 celiac patients and found that those who were diagnosed in childhood (47%) had mortality rates three times higher than would be expected in the general, age-matched population, “with the main cause of the increase being deaths from accidents, suicide, and violence,” reported Dr. Masoud Solaymani-Dodoran and colleagues from the University of Nottingham (England). This increase was not seen in the cohort of patients diagnosed in adulthood (*Am. J. Gastroenterol.* 2007;102:864-70).

“One explanation for this could be the psychological status of the children and possible changes in their risk-taking behaviors,” said Dr. Solaymani-Dodoran in an interview.

The median age at diagnosis was 1.5 years in study subjects diagnosed in childhood (compared with 46 years in those diagnosed as adults), with the threefold increased mortality risk remaining through adolescence and beyond, to more than 25 years after diagnosis.

The Impact of Nonadherence

“Unfortunately [the researchers] had no available data to tell us what percentage of the subjects was on a gluten-free diet,” Dr. Guandalini said in an interview. Nonadherence with the diet has been reported, in other studies, in up to 60% of celiac patients during the rebellious teenage years.

This could explain the increased mortality, he suggested, because in some celiac patients, dietary lapses can have a dramatic effect on the brain. Gluten restriction is recommended, both to relieve the myriad and varied symptoms of celiac disease—ranging from dental to dermatologic to neurologic—and to reduce the potential long-term effects of prolonged exposure, including osteoporosis and malignancies.

“My speculation is that most of these deaths occurred in people who were not following the diet, and this caused the be-

havioral and psychiatric milieu that would lead to that kind of outcome,” Dr. Guandalini said.

Finnish authors have suggested that exposure to gluten in adolescents with celiac disease can impair the availability of tryptophan “and the possible consequent serotonergic dysfunction may play a role in vulnerability to depressive disorders” (*BMC Psychiatry* 2005;5:14-9). They noted that five of nine newly diagnosed, untreated adolescent celiac patients had depressive disorders and abnormal tryptophan levels, all of which improved after gluten was removed from their diets.

“I am personally convinced that eating gluten if you have celiac disease really induces serious changes in brain chemistry that would make you inclined to aggressive, depressive behavior and therefore expose you to this risk,” said Dr. Guandalini, who

has seen such psychiatric effects in a celiac patient as young as 5 years old. “This child was not on a gluten-free diet, her parents did not consider it important, and she had to be admitted for hallucinations. It was a serious psychiatric problem, but putting her back on the diet resulted in a complete resolution within weeks,” he said.



The Impact of Adherence

“We know adherence [to the diet] and depression and anxiety are related,” said Jessica Edwards George, Ph.D., psychologist and researcher at The Celiac Center at Beth Israel Deaconess Medical Center in Boston. But the relationship between adherence and psychological symptoms is not well understood, she said in an interview. Just as poor adherence is linked with psychiatric pathology, so too is good adherence—an aspect highlighted by the British authors, who acknowledged an assumed, but not documented, adherence in their cohort.

“The actual process of labeling a child with celiac disease and requiring them to adhere to a gluten-free diet may be, in some way, detrimental,” they wrote. “As treatments go, taking a gluten-free diet must rank as one of the most intrusive for a child—more so than something like, for example, epilepsy or asthma,” coauthor Dr. Richard Logan said in an interview. “We wondered what were the psychological effects on a child of being brought up with a condition whose treatment has such a profound effect on daily life—something I suspect most adult gastroenterologists overlook.”

The psychological research on adults regarding this question leaves little open to debate. The symbolism of “breaking bread” together—sharing in a common meal—crosses all cultural and religious boundaries, and studies have shown that adults with celiac disease struggle daily with their exclusion from, or isolation in, such rituals.

“There’s a lot of anger and frustration about the rigidity of the diet, as well as the fact that it is chronic,” said Sharon Jedel, Psy.D., a clinical psychologist at Rush Uni-

versity’s adult celiac disease program in Chicago. “A child doesn’t necessarily have the developmental capacities to cope the way an adult might.”

As a former school psychologist, Dr. Edwards George agreed. “Children report feeling different and embarrassed, left out, and angry,” she wrote in a recent article for the *National Association of School Psychologists (NASP Communiqué* 2006 June;34:8). “It can be heart-breaking for a child to be unable to eat gluten-containing treats at special occasions, such as birthdays or holidays.”

However, both Dr. Edwards George and Dr. Jedel treat psychological issues in adult patients only, and there are very few studies examining the social burden of following a gluten-free diet in the vulnerable adolescent years.

An Italian study which included 39 adolescent patients pointed to the ages between 12 and 17 years as being the most problematic. “That is the period of life in which the individual tends to oppose the adult world in search of an individual personality,” wrote Dr. M. Cinquetti and colleagues from Verona (Italy) University (*Pediatr. Med. Chir.* 1999;21:279-83). “In this group, the search for an individual personality is disturbed.”

Even after adolescence, such experiences can have lasting effects. In one study of adult patients, a subset of patients who were diagnosed as children remembered situations from their childhood “with intense emotions, even if the events had occurred many years ago” (*J. Hum. Nutr. Dietet.* 2005;18:171-80).

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In Search of Normalcy

Even in the absence of anger or depression about their condition, adolescents with chronic diseases are more likely to be “risk takers,” and this is another possible explanation for the increased deaths by accident and violence, noted the British authors. “Adolescents in general don’t have to prove they are ‘normal’, but adolescents with chronic conditions do,” explained Dr. Joan-Carles Suris, head of the research group on adolescent health at the Institute of Social and Preventive Medicine of the University of Lausanne (Switzerland).

In his analysis of almost 7,000 adolescents, 665 (9.5%) had a variety of chronic conditions including diabetes, asthma, allergy, scoliosis, epilepsy, arthritis, kidney disease, and ocular conditions. Dr. Suris found higher rates of risky sexual activity, history of pregnancy, history of sexually transmitted disease, smoking, drinking, and illegal drug use among those with the chronic conditions, compared with their healthy peers (*Eur. J. Public Health* 2005;15:484-8).

While Dr. Suris’ study did not include patients with celiac disease, he said any condition involving food restriction presents limitations to an adolescent’s social life. “It is hard to go out for pizza with your friends

and not be able to eat it,” he said. “It has been said that the best contribution for diabetic patients after insulin was the introduction of sugar-free beverages, because this allowed them to socialize with their peers without being seen as different. Maybe we should try to do that with other food problems, so that cafeterias or restaurants have options for them,” he said.

While such options are becoming more widely offered, Dr. Edwards George said that children with celiac disease also need the tools to cope in a gluten-filled world—lessons they might be taught with the help of more psychological research. “We hear a lot of stories about adolescents and young adults going away to college and then not being in that protective bubble anymore and having a really difficult time.”

Her research in the field of adult celiac disease is uncovering personality traits and coping mechanisms associated with better adjustment to and adherence to the diet—information she believes can be used to provide targeted guidance to children. “There are lots of strategies that can come from the psychological world that really can help,” she said. “They need skills to advocate for themselves, and we can build in supports to help them be more organized and more conscientious. It’s not changing their personality but it’s helping them change the environment around them to make them more likely to adhere.”

In the meantime, she also believes that vigilance is of utmost importance for physicians. “We need to be more aware of mood factors and more proactive about screening and treatment for depression, anxiety, and suicidal ideation.” Included in this careful follow-up should be targeted screening for eating disorders, she said—a practice soon to be adopted at her center—since her research suggests that these disorders may often be missed in this perhaps more vulnerable population.

“Patients ... learn to deal with hunger and do not notice hunger signs as often as someone else would,” because they are often faced with situations where there are no gluten-free options. Such disturbed eating patterns and hypervigilance, coupled with a common increase in weight after a malnourished patient is diagnosed and treated, can be a cause for concern, especially in adolescent girls who are already more vulnerable to eating disorders. In one of her studies “we did find some people who actually ate gluten in order to lose weight,” just as diabetic patients have been known to withhold insulin for the same reason, she said (*Eur. J. Gastroenterol. Hepatol.* 2007;19:251-5).

As awareness about celiac disease continues to grow, experts agree that the current average 11-year gap between symptom onset and diagnosis will shrink, resulting in more diagnoses in childhood and adolescence.

There was also a consensus among all the experts interviewed that, given the recent findings of an increased mortality rate associated with this earlier diagnosis, any attempts to reduce this higher mortality must begin with a better understanding of the unique burdens that childhood diagnosis and treatment may bring. ■