

Level 2

Genetics (Gene Testing)

KEY POINTS:

- HLA-DQ2 and DQ8 are genes that are necessary but not sufficient for the development of celiac disease (CD). HLA DQ2 (95%) or DQ8 (5%) is present in almost all patients with CD. ^{1,2}
- 30-40% of the general population carries these genes, but only 3% of individuals with these genes develop CD. People without these genes are not likely to develop CD. ^{3,4}
- HLA DQ2 /DQ8 testing is not routinely recommended in the initial diagnosis of CD. ⁴
- Negative tests for both of these genes makes CD highly unlikely (negative predictive value >99%). The genetic test is valuable for analysis of subjects with an equivocal diagnosis. For example:
 - (a) Equivocal small-bowel histological finding in seronegative patients
 - (b) Evaluation of patients on a gluten-free diet (GFD) in whom no testing for CD was done before GFD was started
 - (c) Patients with discrepant celiac-specific serology and histology
 - (d) Patients with suspicion of refractory CD where the original diagnosis of CD remains in question
 - (e) Patients with Down's syndrome. ^{4,7}
- Genetic analysis can also be used to rule out CD, and the subsequent need for further testing in individuals at high risk because of family history. Although only one third of family members will be spared repeated testing, particular combinations (eg, homozygosity for DQ2) increase the risk for CD (by up to 40%). ^{6,7}
- Other non-HLA genes and environmental factors may contribute to the development of CD. Current research is exploring what other factors contribute to the disease, and may help us come up with better treatments or prevention. ⁴
- Genes do not change during your lifetime, so they are not affected by a GFD. ⁴
- Of note, gastrointestinal symptoms are improved by the GFD in the absence of CD in about 60% of patients with diarrhea predominant irritable bowel syndrome, especially those with HLA DQ2. ⁵

- These genes are also associated with other autoimmune conditions such as type 1 diabetes and autoimmune thyroid disease.⁷

TAKE HOME MESSAGES:

1. Many people who carry the DQ2 or DQ8 genes will never develop CD.
2. If you do not have these genes, you probably do not have CD.
3. These tests are not used routinely for the initial diagnosis of CD. In select clinical situations, the celiac gene test can effectively rule out CD.
4. These genes are also present in other autoimmune conditions such as type 1 diabetes and autoimmune thyroid disease.
5. Any tissue sample can be used for genetic testing.
6. You do not need to be on a GFD to have the gene test.

References:

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