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Celiac Disease Testing

Serologic tests have sensitivity and specificity of close to or above 95 percent.

By Jill Hoffman

In many populations, celiac disease (CD) has been found to occur as commonly as 1 in 100 people.[1] The lifelong, inherited autoimmune disease yields an immune-mediated toxic reaction causing damage to the small intestine and preventing proper food absorption in CD sufferers who eat foods containing gluten-the common name for proteins in specific grains, including all forms of wheat and related grains (e.g., rye, barley and triticale.)[2]

Serologic and increasingly genetic testing provides clues to whether a person is suffering from or may be at risk for CD.

Serologic Testing Types

Enzyme-linked immunosorbent assay (ELISA)-based serologic tests that exist for CD diagnosis have detection sensitivity and specificity of close to or more than 95 percent, making them a top diagnostic technology for this autoimmune disorder.[1]

Three primary antibody tests are available: anti-tissue transglutaminase (tTG), anti-endomysium antibody (EMA) and anti-deamidated gliadin peptide antibody (DGP) tests.

tTG

Because of high sensitivity/specificity/reliability, low cost and ease of interpretation, anti-tTG is the test of choice in most settings.[1]

The tTG test is an ELISA and IgA class antibody test. However, about 1 in 500 individuals are born without the ability to produce IgA antibodies or only make small amounts.

Dr. Leffler noted people can live without IgA and are generally asymptomatic, adding, "But it will make any IgA-based test negative, regardless of the actual disease state, so that would be 1 in 500, which doesn't sound too bad, but studies suggest that IgA deficiencies enriched in the celiac population may be as many as 1 in 50."

So for the tTG test to be valid, it is important to confirm that individuals have IgA antibodies, says Stefano Guandalini, MD, professor of Pediatrics, and chief, Section of Gastroenterology, founder and director, Celiac Disease Center, University of Chicago Comer Children's Hospital.

"Every time these clinical celiac disease tests are utilized, I always request the total serum IgA to make sure the patient is producing this class of antibodies," Dr. Guandalini said.

EMA

The EMA is also an IgA class antibody test but uses immunofluorescence that necessitates reading of each sample under a microscope. A study co-written by Dr. Leffler says the technology, which requires expensive, hard-to-come-by reagents (e.g., monkey esophagus) adds cost and leads to concerns about interobserver and inter-site variability, so it is difficult to standardize.[1]

"Those are some of the reasons it's for the most part fallen out of favor," Dr. Leffler said.

DGP

The DGP is an ELISA test measuring antibodies against gliadin peptide after it has been modified by enzyme tissue transglutaminase. Dr. Guandalini said the test has high sensitivity and specificity.

"The good thing about it is it turns positive if you eat gluten-faster than the other two antibody tests, so it is quite useful in following up diagnosed patients," Dr. Guandalini noted.

FDA-Approved Tests

Several manufacturers offer serologic tests for CD. They include Quest Diagnostics, INOVA Diagnostics Inc. (now owned by the Werfen Group), IMMCO Diagnostics Inc. and Prometheus.

Dr. Guandalini says standardization of serology tests has come a long way during the last 5 or 6 years, and most manufacturers "offer very reliable and consistent tests."

Dr. Leffer said the only CD test of significance not yet FDA approved is a fingerstick, tTG-based, patient-administered test. Dr. Leffer compared the technology, which is available in Europe and Canada, to a direct-to-consumer pregnancy test. "It's a very interesting new methodology that will likely be available in America in the next few years," he said.

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Genetic Tests

Human leukocyte antigen (HLA) testing for CD can be useful, Dr. Leffler said. HLA testing is different than genetic testing for other disorders because laboratories test for a haplotype rather than a gene causing a disease.

"These haplotypes are a major contributor to the genetic susceptibility of celiac disease," explained Dr. Guandalini. "But the remaining genetic contribution is being investigated, and studies have shown that other loci (not HLA-associated) are also important."

The DQ2 haplotype accounts for about 95 percent of all people with CD while DQ8 accounts for most of the remaining 5 percent, Dr. Guandalini added. (Researchers debate whether 1 percent of people with CD do not present either haplotype.) DQ2 and DQ8 haplotypes account for about 40 percent of CD's genetic makeup, "but other genes are certainly at play so we still have a long way to go to identify every single genetic component to celiac disease," Dr. Guandalini said.

HLA testing usually involves a blood or saliva sample. In-house tests are available from Prometheus, Quest Diagnostics and Kimball Genetics Inc. "My understanding is that all tests seem to be extremely reliable," Dr. Guandalini said.

Dr. Guandalini uses genetic testing to rule out CD as part of a battery of diagnostic strategies. The only down side to this methodology, he said, is that health insurance companies don't always cover the genetic tests, so patients may have to pay about $400 out of pocket.

"I always make sure patients know up front there may be an issue because the insurance might refuse to cover [the test], which I think is unwise," Dr. Guandalini said.

Jill Hoffman is on staff at ADVANCE.

Additional Reading

- Leffler D, Dennis M. *Real Life with Celiac Disease: Troubleshooting and Thriving Gluten Free*. Bethesda, MD: AGA Press, 2010.

References

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2. Celiac Disease Foundation. "About Celiac Disease." Available at: www.celiac.org/index.php?option=com_content&view=article&id=3&Itemid=9. Last accessed Oct. 10, 2011.

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