Publication of the Month

June 06/08: High diagnostic value of anti-tTG

In the general population, most of the patients affected by Celiac disease (CD) have a silent or atypical clinical presentation, and a non-invasive test is therefore necessary to select subjects for a biopsy of the small intestine. At present, the tissue transglutaminase (TG)-based ELISA is the method of choice for serological screening of CD. However, comparative studies showed that anti-tTG kits from different manufacturers vary in their analytical and diagnostic performance and laboratories should ensure that they are using a thoroughly validated method. Manufacturer's diagnostic cut-offs should always be confirmed, preferably using the range of samples routinely received by the laboratory.

With the advent of accurate, quantitative serological tests, the requirement for small bowel biopsy to establish the diagnosis of CD in every case has been questioned. If biopsy could be avoided, some patients would be spared an uncomfortable procedure, and treatment with a gluten-free diet to alleviate symptoms could be prescribed earlier
In the following study, the authors assessed both the anti-tTG levels at which the positive predictive value for CD was 100%, and the delay in diagnosis and treatment in their patients due to the present requirement for small bowel biopsy.

Hill PG, Homes GKT
Coeliac disease: a biopsy is not always necessary for diagnosis
Aliment Pharmacol Ther (2008) 27:572 - 577

Small bowel biopsy results were available on 146 patients with anti-tTG above 10 U/ml using Varelisa Celikey. Of these patients, 139 had CD. Seven patients had anti-tTG results between 10 and 30 U/ml (range: 11.1-21.8 U/ml) and normal biopsies. In five of these endomysial antibody was positive. All patients with anti-tTG levels above 30 U/ml (i.e. 10 x upper limit of normal) had characteristic small bowel mucosal lesions. In a subsequent audit, 58% of 112 new diagnoses of celiac disease had levels above this value.
The mean interval between serology and biopsy was 108 days (range 6-319 days) for the 65 patients whose anti-tTG was above 30 U/ml, half of patients had to wait more than 90 days for their biopsy and, thus, for both their final diagnosis and start of gluten-free diet.
The authors conclude that an anti-tTG level can be defined which gives a positive predictive value of 100% for CD and that diagnostic guidelines could be modified so that small bowel biopsy is no longer regarded as mandatory in patients with such high anti-tTG levels. This will avoid an invasive procedure and lead to a more rapid diagnosis and earlier treatment for over half of the new patients with celiac disease.

Probably, the hypothesis that biopsy could be avoided will be discussed controversely. One question will be if high anti-tTG levels are really specific enough. A new study from the US had the objective to determine whether high anti-tTG are exclusively associated with CD:

Donaldson MR, Book LS, Leiferman KM, Zone JJ, Neuhausen SL
Strongly positive tissue transglutaminase antibodies are associated with Marsh 3 histopathology in adult and pediatric celiac disease
J Clin Gastroenterol (2008) 42: 256 - 260

The authors found that high level anti-tTG IgA occur almost exclusively (96%) in a setting of Marsh 3 duodenal histopathology. All individuals without Marsh 3 changes were likely to develop CD or had CD with patchy lesions missed on biopsy.