biomnis
SPECIALISED MEDICAL PATHOLOGY
Focus
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New coeliac disease markers

Reminder

Coeliac disease is a chronic inflammatory autoimmune enteropathy. It is triggered by the food antigen gliadin, one of the proteins that make up gluten, and results in villous atrophy and malabsorption. The clinical picture of the disease is polymorphic, ranging from asymptomatic to severe malnutrition. The two frequency peaks observed are childhood (6 months to 2 years) and adulthood (between 20 and 40 years).

Diagnosis

Intestinal (duodenal) biopsies

Villous atrophy, crypt hypertrophy, increased number of intraepithelial lymphocytes.

- Reference test: although necessary in order to confirm diagnosis, it is invasive, costly and requires tissue samples from multiple sites in order to ensure adequate sensitivity.
- Its necessity is questioned in the event of positive serology results obtained with available sensitive and specific serological markers...

Serological diagnosis

November 2007 recommendations of the French National Authority for Health (HAS)/December 2008 schedule of accredited procedures (NABM)

- Anti-tissue transglutaminase IgA+++ antibodies associated with quantitation of IgA
- Anti-tissue transglutaminase IgG antibodies (if IgA deficiency detected)
- Anti-endomysium IgA/IgG++ antibodies
- Anti-gliadin and anti-reticulin antibodies are to no longer be used

	Anti-endomysium IgA	Anti-tissue transglutaminase IgA
Sensitivity	85 % - 100 %	90 % - 100 %
Specificity	95 % - 100 %	95 % - 100 %

	Anti-gliadin IgA	Anti-gliadin IgG
Sensitivity	60 % - 91 %	65 % - 100 %
Specificity	42 % - 89 %	50 % - 90 %

New coeliac disease (CD) markers: antigenic targets

New antigenic sites that are modified (deamidated, "co-bound") gliadin peptides have been developed. The new CD markers are antibodies directed against these peptides:

- **Anti-modified gliadin peptide antibodies:**

  As the tables on the following page show, this new generation of antibodies is significantly more sensitive and specific than anti-gliadin antibodies (Ag: native gliadin). Moreover, they are believed to have a stronger correlation with villous atrophy than conventional markers, therefore making them potentially valuable in monitoring the effectiveness of a gluten-free diet. Lastly, they may be very well correlated with biopsies, thus reducing the need for the latter.

  These antibodies include:

  - Anti-deamidated gliadin antibodies
  - Anti-gliadin II antibodies (II for second generation)
  - *Gliadin-analogue fusion peptide*

	Anti-gliadin IgA	Anti-gliadin IgG
Sensitivity	60 % - 91 %	65 % - 100 %
Specificity	42 % - 89 %	50 % - 90 %

	"New generation" anti-gliadin IgA	"New generation" anti-gliadin IgG
Sensitivity	73 % - 90 %	92 % - 98 %
Specificity	83 % - 95 %	84 % - 100 %

- **Anti-modified tissue transglutaminase antibodies:**

  Their name differs depending on the manufacturer.

  - Anti-gliadin-bound tissue transglutaminase antibodies
  - Anti-tissue transglutaminase neo-epitope antibodies

Their sensitivity and specificity are equivalent to those of the best anti-tissue transglutaminase (tTG) IgA assay kits and higher than those of conventional anti-gliadin antibodies.

The sensitivity and specificity of neo-epitope tTG IgG are higher than those of conventional tTG IgG.

	tTG IgA	tTG IgG
Sensitivity	90 % - 100 %	60 % - 83 %
Specificity	95 % - 100 %	95 %

	"neo-epitope" tTG IgA	"neo-epitope" tTG IgG
Sensitivity	87 % - 97 %	70 % - 87 %
Specificity	94 % - 96 %	94 % - 95 %

Summary

- Performance of anti-deamidated gliadin IgA and IgG Ab ›››› conventional anti-native gliadin IgA and IgG Ab
- Performance of anti-neo-epitope tTG IgA Ab › anti-tTG IgA Ab
- Performance of anti-neo-epitope tTG IgG Ab › anti-tTG IgG Ab

Important points to bear in mind

- Follow the current recommendations; "neo-epitope" tTG may be substituted for conventional tTG.
- Anti-deamidated gliadin antibodies have a higher sensitivity and specificity than anti-gliadin antibodies. However, as the latter are no longer listed in the French schedule of accredited procedures (NABM) it seems that they will remain relegated as second-line markers in France. They appear to play a role in diagnosis, but only in certain specific cases (children, IgA deficiency, etc.) and, primarily, in assessing villous atrophy.
- There are rapid strip tests (biocards) that both screen for anti-tTG IgA and measure total IgA. The performance characteristics claimed by the manufacturers of these tests appear to be equivalent to those of the ELISA.

Written by Dominique Brunengo, based on an article by Sophie Le Cam, Biomnis, Lyon.