Diagnosis of Celiac Disease according to Guideline S2k of 2014

Celiac disease is an **autoimmune disease** that is caused by gluten. It manifests in patients with genetic predispositions and leads to a life-long enteropathy. Thus, it is not an allergy. Celiac disease's auto allergen is tissue transglutaminase in the small intestine combined with gluten that is ingested via food intake. Since only HLA molecules DQ2, DQ7 or DQ8 are capable of binding and presenting gluten to the immune system, only carriers of these HLA characteristics will fall ill. With a prevalence of 1:200 to 1:500, the disease is far from rare.

The existence of one of the HLA characteristics DQ2, DQ7 or DQ8 is an absolute precondition regarding the development of celiac disease

All patients suffering from celiac disease are carriers of one of the HLA characteristics DQ2, DQ8 or DQ7. Demonstrably, these are the only molecules capable of presenting gliadin peptides. Hence, developing celiac disease without being a carrier of one of these HLA characteristics is virtually impossible. Testing for HLA-DQ2/DQ7/DQ8 is therefore of utmost importance in order to rule out celiac disease.

There are certain diseases that occur ten times more often in patients that suffer from celiac disease in comparison to the general population

Some, especially autoimmune diseases are closely associated with celiac disease (see below). When occurring simultaneously, celiac disease is often asymptomatic:

- Dermatitis herpetiformis Duhring
- primary biliary cirrhosis
- psoriasis
- collagenoses (Sjögren's syndrome; systemic lupus erythematosus)
- autoimmune hepatitis
- Diabetes mellitus type 1
- autoimmune thyroiditis
- Addison's disease
- Down's or Turner's syndrome
- Crohn's disease / colitis ulcerosa
- osteoporosis
- migraine
- irritable bowel syndrome
- depression and anxiety disorders
- increased transaminase levels
- selective IgA deficiency

Diagnosis

Pathophysiologically, celiac disease is a genetically determined, T-cell-induced, chronical inflammatory autoimmune process that targets the small intestine's tissue. Hence, the diagnostic spectrum comprises serological, genetic, and histological tests.

Serological laboratory tests are of high significance. Very sensitive antibody detection tests do not only allow for the diagnosis of celiac disease, but are furthermore important for clinical monitoring. The following antibody tests are available:

- antibody against tissue transglutaminase IgG/IgA
- antibody against endomysium IgG/IgA
- antibody against deamidated gliadin IgG/IgA

IgA antibodies against endomysium and transglutaminase are highly specific markers regarding the detection of celiac disease. The two assays' combination is both highly sensitive (~100 %) and specific (~100 %) for celiac disease's diagnostics.

Note:

➔ **Up to 6 % of all patients suffering from celiac disease have an IgA deficiency.**
In these cases, IgA antibody tests are false negative and thus do not deliver useful results for the diagnosis. Hence, the complete IgA should always be tested simultaneously.
In case of a known IgA deficiency, the respective IgG antibodies should be tested das well. Then, in addition to endomysium and transglutaminase IgG antibodies, IgG antibody tests for deamidated gliadin should be performed as well.

➔ **A diet low in gluten leads to decreased antibody titres.**
Therefore, in these cases, serology (as well as endoscopy) will only deliver limited results. Hence, a detailed dietary anamnesis before taking blood samples is recommended.

Testing for celiac disease's predisposition alleles HLA-DQ2, DQ7 and 8 is used primarily for the diagnostic exclusion of celiac disease

The existence of one of the HLA characteristics DQ2, DQ7 or DQ8 is an absolute precondition regarding the development of celiac disease. 100 % of celiac disease patients are carriers of one of these HLA characteristics. Developing celiac disease in the absence of these characteristics is virtually impossible. HLA tests are not influenced by dietary alternations. The test, as it is administered at the IMD, comprises all those HLA-DQ2/DQ7/DQ8 haplotypes (including those that are very rare) that are relevant for celiac disease according to scientific literature. Hence, negative test results definitely rule out the presence of celiac disease.

Since celiac disease is the one closest associated with HLA, the European Society of Paediatric Gastroenterology Nutrition (ESPGHAN) developed new guidelines and in 2014, the German Society for Digestive and Metabolic Diseases came up with a new S2k guideline. Those guidelines added HLA testing as a new diagnostic parameter. With regard to the

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recommended diagnostic algorithms, the two guidelines differentiate between:

- **Symptomatic patients with coeliac disease** and
- **Asymptomatic celiac disease risk patients**.

A new element is the diagnosis of celiac disease in symptomatic patients with celiac disease without prior biopsy, if a significantly positive serological test result regarding HLA characteristics DQ2/DQ7/DQ8 is accompanied by a classic (gastrointestinal) clinic.

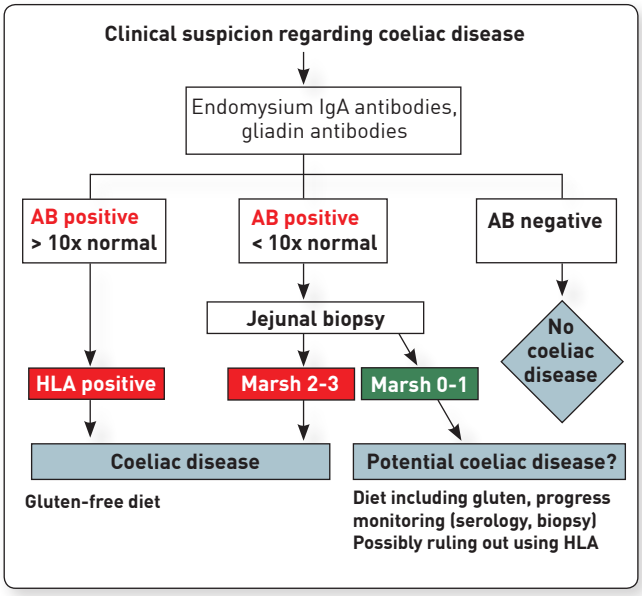

Fig. 1 Diagnostic procedure in case of clinical suspicion regarding celiac disease according to the ESPGHAN criteria of 2012 and the S2k guideline of 2014.

For patients with an increased risk for celiac disease, due to the aforementioned simultaneously occurring diseases, and first-degree relatives of celiac disease patients it is recommended to start the process of screening with an HLA test. That is because, in case of a negative HLA result, regular antibody screening is dispensable. In case of positive results regarding HLA-DQ2/7/8, IgA antibodies for transglutaminase should be tested every 2-3 years.

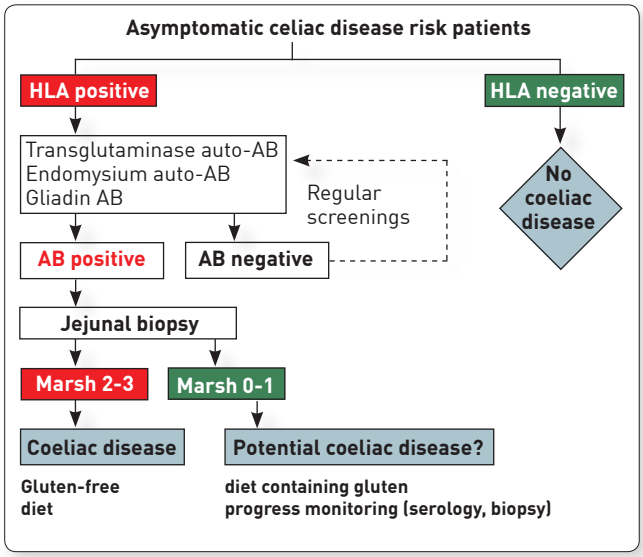

Fig. 2 Diagnostic procedure regarding Asymptomatic celiac disease risk patients according to the ESPGHAN criteria of 2012 and the S2k guideline of 2014.

Material

Serology: 5 ml of serum
HLA-genotyping: 2 ml EDTA blood
Request: HLA for suspicion of celiac disease
Transport to the laboratory is not time-sensitive and can be sent by mail.

Invoicing

HLA-genotyping: 209.83 €

Transglutaminase IgA/IgG: 52.46 €

Endomysium IgA/IgG*: 33.80 € (*Positive autoantibody results must be titrated, therfore the costs are 59.46 €.)

Gliadin IgA/IgG: 59.46 €

Serum IgA: 8.74 €

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Literature

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