Coeliac Disease (CD) is underdiagnosed due to the varied presentation of clinical signs and symptoms. This advice guide provides new and updated summary guidance from the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) on diagnosing children and adolescents with CD.

### Consider testing for CD with the following symptoms, signs and conditions:

#### Gastrointestinal
- chronic or intermittent diarrhea/constipation/abdominal pain
- distended abdomen
- recurrent nausea and/or vomiting

#### Extraintestinal symptoms
- weight loss/failure-to-thrive
- delayed puberty, amenorrhea
- irritability, chronic fatigue
- neuropathy
- arthritis/arthralgia
- chronic iron-deficiency anaemia
- decreased bone mineralization (osteopenia/osteoporosis), repetitive fractures
- recurrent aphthous stomatitis
- dermatitis herpetiformis–type rash
- dental enamel defects
- abnormal liver biochemistry

#### Specific conditions
- first-degree relatives with CD
- autoimmune conditions: T1DM, thyroid disease, liver disease
- Down syndrome
- Turner syndrome
- William’s-Beuren syndrome
- IgA deficiency

### What’s new in the 2020 guidelines?

- For initial testing, the combination of total IgA and IgA class antibodies against transglutaminase 2 (TGA-IgA) is recommended as this is the most accurate and cost-effective. EMA-IgA or DGP-IgG need not be tested initially.
- The no-biopsy approach for CD diagnosis is confirmed to be safe in children with high TGA-IgA values ≥10 times the upper limit of normal with accurate, appropriate tests and positive endomysial antibodies (EMA-IgA) in a second serum sample.
- Children with positive TGA-IgA but lower titers (<10 times upper limit of normal) should undergo biopsies to decrease the risk of false positive diagnosis.
- HLA testing and presence of symptoms are not obligatory criteria for a serology based diagnosis without biopsies.

### Abbreviations
- IgA: Immunoglobulin type A
- TGA-IgA: IgA against tissue transglutaminase 2
- EMA-IgA: IgA against endomysium
- IgG: Immunoglobulin type G
- DGP-IgG: IgG against Deamidated Gliadin Peptide
- HLA: Human leukocyte antigen
- ULN: Upper limit of normal
CD diagnosis can be accurately and safely established with or without duodenal biopsies if the following recommendations are observed:

**Initial testing**
Testing for total IgA and TGA-IgA should be used for children with suspected CD, after checking that the child is consuming normal quantities of gluten. In children with normal serum IgA values for age, TGA-IgA should be used, regardless of age. In children with low total IgA concentrations (low for age or <0.2 g/L above the age of 3 years), an IgG-based test (DGP, EMA or TGA) should be performed as a second step. If initial testing suggests coeliac disease, the child should be referred to a pediatric gastroenterologist/coeliac disease specialist.

**Biopsy**
A biopsy should be performed on children with positive TGA-IgA but lower titers (<10 times upper limit of normal). Patients should have ≥1 biopsies from the distal duodenum and ≥1 from the bulb, during a gluten-containing diet.

Evaluation of biopsies should be performed on optimally orientated biopsies. In cases of differing results between TGA-IgA-results and histopathology, re-cutting of biopsies and/or second opinion from an experienced pathologist should be requested.

**No biopsy**
A no-biopsy approach is appropriate for children with TGA-IgA values ≥10 times the upper limit of normal with appropriate tests and positive endomysial antibodies (EMA-IgA) in a second serum sample.

**Disclaimer**
ESPGHAN is not responsible for the practices of physicians and provides guidelines and position papers as indicators of best practice only. Diagnosis and treatment are at the discretion of physicians. This advice guide is produced and published by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and authored by members of the society’s Coeliac Disease Working Group.

Full references for the advice within this guide can be found within the following paper, which this guide is based upon: Husby, Steffen, et al. “European society paediatric gastroenterology, hepatology and nutrition guidelines for diagnosing coeliac disease 2020.” Journal of Pediatric Gastroenterology and Nutrition 70.1 (2020): 142-156.
Revise quality & orientation of the biopsy
Consult experienced pathologist

CD serology positive for any reason

Initial stage

Measure serum TGA-IgA and total IgA
TGA-IgA and total IgA
TGA-IgA positive
Refer to paediatric GI (specialist in CD)

Specialist care

See B

Discrepant serology

TGA-IgA
TGA-IgA positive
Consider TGA-IgA concentration (<ULN)
TGA-IgA >10xULN
Test for EMA (separate blood sample)
EMA-IgA negative
EMA-IgA positive

CD confirmed

Risk for false negative serology?
Consider HLA determination

Perform IgG test (TGA, EMA, DGP)
IgG tests positive
HLA-DQ2/DQB
HLA-DQ2/DQ8 positive
CD unlikely, consider other diagnosis
Follow and retest on a normal gluten intake, consider biopsy

Specialist care

Biopsy – See C

Risk of false seronegativity
Consult paediatric GI (specialist in CD)

Risk for false negative serology?
Consider risk of false negative serology:
• Low or short duration of gluten intake
• Immunosuppressive medication
• Extraintestinal manifestations

Total IgA low
Total IgA normal

Risk for false seronegativity
No risk
No CD

HLA negative
HLA-DQ2/DQ8 positive

IgG tests negative

Risk of false seronegativity
No risk
No CD

IgG tests positive

Biopsy – See C

Footnotes
1. Other than TGA-IgA, including point-of-care tests and DGP. 2. Check the value also in relation to the cut-off and repeat the test if questionable or borderline. No need to retest if done with validated assay with calibration curve. Test with conventional TGA-IgA test if positive POCT and TGA has not been measured quantitatively. 3. Convey the message that the diagnosis of coeliac disease with or without biopsy confirms the need for a lifelong gluten-free diet and that re-evaluation after introduction of the diet would need prolonged re-exposure to gluten with a series of further investigations. 4. If TGA-IgA is only borderline positive confirm sufficient gluten intake and consider re-testing of TGA-IgA and EMA. 5. Loss for age or <0.2 g/L above the age of 3 years. 6. For example, dermatitis herpetiformis, in which serology is frequently negative. 7. The cut-off for normal numbers of IEL is >25 cells/100 enterocytes.