Detection of secretory IgA antibodies against gliadin and human tissue transglutaminase in stool to screen for coeliac disease in children: validation study
Matthias Kappler, Susanne Krauss-Etschmann, Veronika Diehl, Hannelore Zeilhofer, Sibylle Koletzko

Abstract
Objective To evaluate two commercial stool tests for detection of secretory IgA antibodies against gliadin and human tissue transglutaminase for diagnosis of coeliac disease in children with symptoms.
Setting Tertiary care children’s hospital.
Participants Coded stool samples from 20 children with newly diagnosed coeliac disease and 64 controls. Six children with coeliac disease had stool tests every two weeks for three months after starting a gluten-free diet.
Main outcome measures Secretory IgA antibodies against gliadin and human tissue transglutaminase in stool samples, determined in duplicate by using recommended cut-off limits.
Results Sensitivity of faecal antibodies against human tissue transglutaminase was 10% (95% confidence interval 1% to 32%), and specificity was 98% (91% to 100%). For antibodies against gliadin, sensitivity was 6% (0% to 29%) and specificity was 97% (89% to 100%). Optimisation of cut-off limits by receiver operating characteristic analysis and use of results of both tests increased sensitivity to 82%, but specificity decreased to 58%. All follow-up stool tests remained negative, except for two positive anti-gliadin results in one patient, six and 10 weeks after starting the gluten-free diet.
Conclusions Neither stool test was suitable for screening for coeliac disease in children with symptoms.

Introduction
Serological screening for antibodies against gliadin, endomysium, or tissue transglutaminase before the diagnostic biopsy is done is well established practice in patients with suspected coeliac disease. These antibodies can be detected in faecal supernatants,¹ and commercial stool tests have been developed and offered by many laboratories. However, no validation data on these tests have been published. We evaluated two stool tests (Immundiagnostik GmbH, Bensheim, Germany) in comparison with serological results and duodenal histology as “gold standard” in children who had had upper endoscopy for different abdominal conditions.

Methods
The study cohort consisted of 20 children with newly diagnosed coeliac disease (median age 5.4 (range 0.9-14.1) years), all with duodenal villous atrophy (Marsh III) plus positive endomysium antibodies in serum, and 64 control children (5.6 (0.9-17.5) years) with normal histology (Marsh 0) and negative endomysium antibodies (61/61 tested). We excluded patients with selective IgA deficiency, previously diagnosed coeliac disease, or bloody diarrhoea.

We analysed coded stool samples for secretory IgA antibodies against recombinant human tissue transglutaminase in all 20 children with coeliac disease and 62/64 children without coeliac disease. We analysed samples for antibodies against gliadin in 17/20 children with coeliac disease and 61/64 controls.

Results
Facial tissue transglutaminase antibodies were positive in two children with coeliac disease and two children without coeliac disease (sensitivity 10%, 95% confidence interval 1% to 32%; specificity 98%, 91% to 100%). Faecal anti-gliadin antibodies were positive in one child with coeliac disease and one control patient (sensitivity 6%, 0% to 29%; specificity 97%, 89% to 100%). Six patients with coeliac disease provided stool samples before and every two weeks for three months after starting a gluten-free diet, which all remained negative, except for two positive anti-gliadin test results in one patient, six and 10 weeks after starting the gluten-free diet.

The values between histology and stool test were 0.093 (−0.033 to 0.219) for tissue transglutaminase antibodies and 0.062 (−0.027 to 0.151) for anti-gliadin antibodies, indicating no agreement. The figure gives the individual titres in relation to age. When we optimised cut-off limits by receiver operating characteristic analysis and combined both tests, sensitivity increased to 82% but specificity decreased to 58%, with positive and negative predictive values of 37% and 92%. These figures may change when the tests are used prospectively on new cases. The prevalence of coeliac disease in our cohort was 29% (17/59), but in the general population, with an assumed prevalence of 0.5%, the positive predictive value would decrease to 1%, with marginal improvement of the negative predictive value compared with the pre-test situation (99.5% to 99.8%).

Discussion
Both stool tests were negative in most cases of coeliac disease and hence are not reliable as screening tests. We have validated these stool tests against the accepted diagnostic “gold standard” for coeliac disease. In many European countries, validation of a diagnostic test in the target population is not required before commercialisation, or diagnostic tests are marketed for years.

Reference

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Colour blindness on the football field

When George Wilson of Edinburgh gave an account of the mistakes made by colour-blind persons, including medical students who were unable to distinguish the colour of certain precipitates, of engine-drivers, and of sailors who mistook signal lights or flags, of tailors who matched red with green, and bookbinders who did the same for coloured leathers and papers, and when Jeffries in America added to an already long list the mistakes made by colour-blind Government officials who sold postage stamps, to neither of them does it seem to have occurred that this question touched the great realm of sport. The Referees Committee of the Lancashire Football Association have decided in consequence of numerous complaints that certain referees are shortsighted or colour blind, that prior to next season all referees on the junior list shall come up for examination, in order that their acuity of vision and their colour sense may be properly tested. (BMJ 1906;1:262)