Paediatrics

Screening for coeliac disease in children and young people with type 1 diabetes.

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The prevalence of coeliac disease in people with type 1 diabetes is higher than that of the general population (1–10% vs 0.5–1% respectively [Fasano and Catassi, 2001]). In addition, there is increasing evidence that coeliac disease is an independent risk factor for retinopathy and nephropathy in individuals with type 1 diabetes (Rohrer et al, 2015). Untreated coeliac disease is associated with other complications including poor growth, osteoporosis, increased risk of small bowel lymphoma and reproductive complications. Many children with type 1 diabetes report no symptoms when initially diagnosed with coeliac disease; in a recent case report, two young people with type 1 diabetes and severe hypoglycaemia were diagnosed with coeliac disease without displaying any of the symptoms (Khoury et al, 2014 [summarised on opposite page]). There is understandably controversy as to the management of children with asymptomatic coeliac disease.

Although there is consensus in the literature that people with type 1 diabetes should be screened for coeliac disease, there is less agreement as to the timing and frequency of screening and what screening test should be undertaken. The NICE guideline (2012) advocates screening at diagnosis of type 1 diabetes only, whilst the International Society for Pediatric and Adolescent Diabetes (ISPAD) advises screening at diagnosis, then annually for the first 5 years and bi-annually thereafter (Kordonouri et al, 2009). Both NICE and ISPAD advocate screening with coeliac disease-specific antibodies while the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) advocate assessing the human leukocyte antigen HLA-DQ2.5/DQ8 genotype of all individuals diagnosed with type 1 diabetes and restricting further screening with coeliac-specific antibodies only to those with the high-risk genotype (Husby et al, 2012).

In the paper summarised alongside, Elias et al review the cost effectiveness and clinical relevance of the ESPGHAN guideline. All 110 children in a Dutch hospital diagnosed with type 1 diabetes between January 1996 and January 2013 had their HLA genotype analysed. They found that only 14% of Dutch children with type 1 diabetes are HLA-DQ2.5/DQ8 negative and could, therefore, be excluded from further coeliac disease screening. The ESPGHAN guideline was, therefore, twice as expensive as screening with coeliac-specific antibodies alone. Seven children were diagnosed with coeliac disease, and the mean duration of time between type 1 diabetes and coeliac disease was 1.8 years (±1.6 years). Three out of the seven children were asymptomatic at coeliac disease diagnosis.

All cases would have been diagnosed following the ISPAD guideline, but we do not have enough information in the paper to know if any of the asymptomatic participants would have been missed if the NICE guideline was followed. This paper confirms that HLA-genotyping all children with type 1 diabetes at diagnosis is not cost-effective and helps resolve at least one of the controversies in the coeliac screening saga. ■

Fasano A, Catassi C (2001) Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology* **120**: 636–51

Husby S, Koletzko S, Korponay-Szabo IR et al (2012) European Society for Pediatric Gastroenterology, Hepatology and Nutrition guidelines for the diagnosis of celiac disease. *J Pediatr Gastroenterol Nutr* **54**: 136–60

Khoury N, Semenkovich K, Arbel AM (2014) Coeliac disease presenting as severe hypoglycaemia in youth with type 1 diabetes. *Diabet Med* **31**: e33–6

Kordonouri O, Maguire AM, Knip M et al (2009) ISPAD clinical practice consensus guidelines 2009. Other complications and associated conditions. *Pediatr Diabetes* **10**: 204–10

NICE (2012) *Coeliac disease: Recognition and assessment of coeliac disease* (CG86). Available at: https://www.nice.org.uk/guidance/cg86 (assessed 09.04.15)

Rohrer TR, Wolf J, Liptay S et al (2015) Microvascular complications in childhood-onset type 1 diabetes and celiac disease: A multicenter longitudinal analysis of 56,514 patients from the German-Austrian DPV Database. *Diabetes Care* 17 Feb [Epub ahead of print]

Diabet Med

Screening tool for coeliac disease: HLA genotyping

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 A retrospective analysis was performed to investigate the clinical relevance and cost-effectiveness of human leukocyte antigen (HLA)-genotyping as a screening tool for the development of coeliac disease in children with T1D.

2 In total, 110 Dutch children were screened, and there were seven confirmed incidences of coeliac disease.

3 Eighty-six per cent of the participating children had one of the variants of HLA-DQ2.5 and DQ8. The HLA genotypes observed in children with T1D and coeliac disease were heterozygote DQ2.5, homozygote DQ2.5 and heterozygote DQ2.5/DQ8.

4 The European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPHGAN) recommends using HLA-genotyping in all children with T1D to discount those without the risk factor genotype from further coeliac disease screening.

5 Therefore, 86% of this cohort would still need further screening with coeliac disease-specific antibodies.

6 HLA genotyping costs €326 per child, and screening for antibodies costs €182 per child, which would be an additional cost to those who had a positive HLA-genotype after screening.

7 This study found that HLA-genotype testing is neither cost-effective nor distinctive in screening for coeliac disease, and should be reconsidered as a first-line screening tool for coeliac disease in children with T1D.

Elias J, Hoorweg-Nijman JJ, Balemans WA (2014) Clinical relevance and cost-effectiveness of HLA genotyping in children with type 1 diabetes mellitus in screening for coeliac disease in the Netherlands. *Diabet Med* 4 Dec [Epub ahead of print]

J Pediatr

Metabolic control from T1D onset to adulthood

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 In a cohort of 1156 people in Austria and Germany, long-term metabolic control was tracked from childhood T1D onset to adulthood.

2 The original database included 15 162 people, but there were only complete records for 1156 people, mainly as a result of loss to follow-up especially at transition from paediatric to adult care.

3 Metabolic control for prepuberty (≤13 years), puberty (14–19 years) and adulthood (≥20 years) were compared.

4 Forty-nine per cent of participants were male and the median age at T1D onset was 7.2 (interquartile range [IQR], 4.7–9.4) years. In the prepubertal stage, median HbA_{1c} was 7.5% (58 mmol/mol; IQR, 6.8–8.3% [74.3–90.7 mmol/mol]), during puberty HbA_{1c} was 8.0% (64 mmol/mol; IQR, 7.3–8.9% [79.8–97.3 mmol/mol]), and after puberty HbA_{1c} was 7.8% (62 mmol/mol; IQR, 7.1–9.0% [77.6–98.4 mmol/mol]).

5 Better initial metabolic control in childhood was associated with an enhanced long-term outcome of metabolic control after more than a 20-year observational period.

6 Metabolic control is not just a result of short-term influences or different personality traits or a combination of both; it may be affected by metabolic control in younger years. These data suggest there is a need for an early focus on metabolic control after diagnosis, aiming for the lowest possible HbA_{1c} levels from diabetes onset in childhood.

Hofer SE, Raile K, Fröhlich-Reiterer E et al (2014) Tracking of metabolic control from childhood to young adulthood in type 1 diabetes. *J Pediatr* **165**: 956–61

Diabet Med

Case reports: Asymptomatic coeliac disease

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓

1 Two female adolescents with T1D who experienced recurrent hypoglycaemic seizures with no gastrointestinal symptoms or poor growth were diagnosed with coeliac disease. Treatment was to follow a gluten-free diet.

2 Six months' after the coeliac disease diagnosis, both had improved hypoglycaemia awareness and hypoglycaemic symptoms had resolved. One female still had fear of hypoglycaemia so had an HbA_{1c} of 92 mmol/mol (10.6%).

3 Although the method and procedure for screening remains controversial, these cases highlight the importance of screening for coeliac disease in children with T1D.

Khoury N, Semenkovich K, Arbeláez AM (2014) Coeliac disease presenting as severe hypoglycaemia in youth with type 1 diabetes. *Diabet Med* **31**: e33–6

Diabetes Care

Breast-feeding

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 The risk of developing islet autoimmunity or T1D in association with duration of breast-feeding and age at the introduction of solid foods was determined among genetically predisposed children.

2 Among 50 000 Norwegian newborns born between 2001 and 2007, 908 infants had high-risk human leukocyte antigen (HLA) genotype screening. This sub-group was followed up at age 3, 6, 9 and 12 months, and then annually with further blood sampling and questionnaires. There were complete data for 726 infants.

3 Breast-feeding for 12 months or longer predicted a decreased risk of developing T1D compared with breast-feeding for less than 12 months. This was after adjusting for having a first-degree relative with T1D, and other confounding factors.

4 Although not a significant association, the results suggest that breast-feeding for 12 months or longer predicts a lower risk of progression from islet autoimmunity to T1D among children who are genetically susceptible.

Lund-Blix NA, Stene LC, Rasmussen T et al (2015) Infant feeding in relation to islet autoimmunity and type 1 diabetes in genetically susceptible children: The MIDIA study. *Diabetes Care* **38**: 257–63

Diabetes Technol Ther

Insulin pump use: Associated adverse events

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 Adverse events (AEs) related to insulin pump use were recorded over a 16-week period and analysed.

2 AEs were reported on a 24-hour hotline, and, out of 405 children and adolescents, 45 patients experienced 50 confirmed AEs.

3 Within 96 hours of the AE being reported, phone interviews were conducted with the parent or patient.

4 The most common reported events were pump malfunction (54.0%) and infusion set/site failure (36.0%). User- or education-related issues were reported and pump replacement occurred in 19 of the 50 events. There were 16 reported hospital admissions or emergency department visits.

5 Reporting an AE was associated with the patient being below the age of 10 years.

Wheeler BJ, Heels K, Donaghue KC et al (2014) Insulin pump-associated adverse events in children and adolescents – a prospective study. *Diabetes Technol Ther* **16**: 558–62

"This paper confirms that human leukocyte antigen genotyping all children with type 1 diabetes at diagnosis is not cost effective and helps resolve at least one of the controversies in the coeliac screening saga."