Management of type 1 diabetes

The accelerator hypothesis: The plot thickens…

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There was a time when a child with newly discovered hyperglycaemia would have been invariably diagnosed with type 1 diabetes (T1D). These days life is not so simple and in many countries, such as the USA and Japan, type 2 diabetes (T2D) is now a common diagnosis in children (International Diabetes Federation [IDF], 2005b).

The confusion doesn't end there. In 2001, Terry Wilkin from the Peninsula Medical School in Plymouth proposed the 'accelerator hypothesis', which suggested a shared basis for T1D and T2D, with genetic predisposition, insulin resistance and autoimmunity leading to beta-cell insufficiency (Wilkin, 2001). He postulated that the rise in prevalence of childhood obesity might accelerate the onset of T1D (thus explaining the widely reported increase of T1D in younger children [IDF, 2005a]).

Since then, various studies have added or detracted from the hypothesis, with contradictory results appearing from two UK centres (Kibridge et al, 2003; Porter and Barrett, 2004). Two much larger studies from Germany and the USA are now published and it is clear that all is *not* clear with the accelerator hypothesis!

The study from Knerr and colleagues (see right) seems to confirm the theory, with the finding that weight gain in the early years is associated with an earlier onset of the condition. In contrast, Dabelea and colleagues (see below) only found an association with earlier age of diagnosis in those with the worst beta-cell function. Intriguingly, an earlier age of diagnosis was associated with lower birth weight, suggesting that the intrauterine environment may be another factor involved.

So what do these studies tell us? First, they contribute to the ever-growing literature on this fascinating hypothesis. Second, they illustrate the value of having multi-centre or national databases. Let's hope that the UK National Diabetes Audit, which in 2003 took over from the National Paediatric Diabetes Audit and the UK Diabetes Information Audit and Benchmarking Service (UKDIABS), will provide us with the same potential for research.

International Diabetes Federation (IDF; 2005a) *Incidence*. IDF, Brussels. http://www.eatlas.idf.org/Incidence/ (accessed 04.05.2006)

IDF (2005b) *Type 2 diabetes in the young*. IDF, Brussels. http://www.eatlas.idf.org/Prevalence/Type_2_in_the_young/ (accessed 04.05.2006)

Kibrige M, Metcalf B, Renuka T, Wilkin TJ (2003) Testing the accelerator hypothesis: the relationship between body mass and age at diagnosis of type 1 diabetes. *Diabetes Care* **26**(10): 2865–70

Porter JR, Barrett TG (2004) Braking the accelerator hypothesis? *Diabetologia* **47**(2): 352–3

Wilkin TJ (2001) The accelerator hypothesis: weight gain as the missing link between Type I and Type II diabetes. *Diabetologia* **44**(7): 914–22

DIABETES CARE

Accelerator hypothesis link only found in subgroup

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors tested the 'accelerator hypothesis' in 449 young people (<20 years) with diabetes from the USA.

2 Potential correlations between age at diagnosis and body mass index (BMI) or birth weight were analysed.

3 The hypothesised inverse relationship between BMI and age at diagnosis was only seen in individuals with reduced fasting C-peptide (people who have compromised beta-cell production).

4 A 636 g decrease in birth weight related to a significantly earlier diagnosis (by around 5 months).

Dabelea D, D'Agostino RB Jr, Mayer-Davis EJ et al (2006) Testing the accelerator hypothesis: body size, beta-cell function, and age at onset of type 1 (autoimmune) diabetes. *Diabetes Care* **29**(2): 290–4

DIABETOLOGIA

Increased BMI linked to earlier onset of type 1 diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 This investigation was carried out to see if increased body mass index (BMI) or weight is associated with an earlier age of diagnosis for type 1 diabetes.

2 Anthropometric measurements were assessed from 9248 people attending paediatric clinics in Germany and Austria who were diagnosed with type 1 diabetes between 1990 and 2003.

3 Four age-at-diagnosis groups were defined: 0–4.9 years, 5–9.9 years, 10–14.9 years and 15–20 years.

4 Relative to the background population, elevated standard deviation scores (SDSs) were found in males and females for both BMI and weight ($P<0.00001$).

5 Furthermore, the SDSs for BMI and weight were higher in the 0–4.9 years group than the other groups ($P<0.00001$).

6 Another finding to come out of the study was that SDSs for BMI and weight at diagnosis rose continuously during the period of investigation ($P<0.0001$).

7 The authors conclude that clinical trials carried out in children to stop overfeeding and to control weight gain may, in addition to preventing type 2 diabetes in later life, play a role in delaying the onset of type 1 diabetes.

Knerr I, Wolf J, Reinehr T et al (2005) The 'accelerator hypothesis': relationship between weight, height, body mass index and age at diagnosis in a large cohort of 9,248 German and Austrian children with type 1 diabetes mellitus. *Diabetologia* **48**(12): 2501–4

'The authors recommend that young people aim for pre-exercise blood glucose levels >120 mg/dl (6.67 mmol/l).'

DIABETES CARE

Young people should aim for pre-exercise blood glucose levels above 6.67 mmol/l

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The complexity of managing glycaemic excursions during exercise, the authors state, means that trial and error is still the main method.

2 With the aim of providing evidence to guide this decision-making process, the authors analysed the effect of aerobic exercise on blood glucose levels in 50 young people (aged 10–17 years) with type 1 diabetes.

3 The exercise period comprised four 15-minute treadmill walks (with a heart rate target of 140 beats per minute) interspersed with three 5-minute breaks, undertaken at a time when after-school physical activity would typically occur.

4 Based on the American Diabetes Association Work Group's definition of hypoglycaemia (<70 mg/dl [3.89 mmol/l]), hypoglycaemia was detected in 100% of participants with baseline blood glucose <120 mg/dl (6.67 mmol/l), 44% of those with a level of 120–180 mg/dl, and 28% of those with a level >180 mg/dl (10 mmol/l).

5 Accordingly, the authors recommend that young people aim for pre-exercise blood glucose levels >120 mg/dl (6.67 mmol/l).

Tansey MJ, Tsalikian E, Beck RW et al (2006) The effects of aerobic exercise on glucose and counterregulatory hormone concentrations in children with type 1 diabetes. *Diabetes Care* **29**(1): 20–5

DIABETES CARE

Significant U-CTGF increase in diabetic nephropathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 This was the first large cross-sectional investigation (n=347) of urinary connective tissue growth factor (U-CTGF) in people with type 1 diabetes.

2 U-CTGF in people with diabetic nephropathy was found to be significantly higher than in people with microalbuminuria or normoalbumuinura, as well as controls without diabetes.

Nguyen TQ, Tarnow L, Andersen S et al (2006) Urinary connective tissue growth factor excretion correlates with clinical markers of renal disease in a large population of type 1 diabetic patients with diabetic nephropathy. *Diabetes Care* **29**(1): 83–8

DIABETES TECHNOLOGY AND THERAPEUTICS

Capillary 3βOHB may be useful adjunct to SMBG

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The aim of this study was to determine the clinical utility of 3β-hydroxybutyrate (3βOHB) in detecting metabolic deterioration before overt diabetic ketoacidosis in the event of continuous subcutaneous insulin infusion (CSII) interruption.

2 The protocol involved an overnight fast, interruption of CSII at 8 am for 4 hours, and re-establishment of CSII at noon for 4 hours until the study end; eight people with type 1 diabetes participated.

3 Blood glucose, plasma 3βOHB and capillary 3βOHB were assessed every 30 minutes, plasma insulin was measured every 60 minutes and urinary ketones were recorded every 120 minutes.

4 CSII interruption led to a rapid decrease in plasma insulin.

5 The rate of increase in capillary 3βOHB, compared with that of blood glucose, was higher and more clinically relevant ($P<0.05$).

6 By providing information more quickly on metabolic deterioration with insulin deprivation, capillary 3βOHB may serve as a useful adjunct to self-monitoring of blood glucose (SMBG).

Orsini-Federici M, Akwi JA, Canonico V et al (2006) Early detection of insulin deprivation in continuous subcutaneous insulin infusion-treated patients with type 1 diabetes. *Diabetes Technology and Therapeutics* **8**(1): 67–75

KIDNEY INTERNATIONAL

No glomerulopathic progression with antihypertensives and good control

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 Two kidney biopsies were taken over a 6-year period in 29 people with type 1 diabetes.

2 Progression of diabetic glomerulopathy was seen in untreated people with microalbuminuria or hypertension and people without either, but not in people with good metabolic control on antihypertensives.

Perrin NE, Torbjornsdotter TB, Jaremko GA, Berg UB (2006) The course of diabetic glomerulopathy in patients with type I diabetes. *Kidney International* **69**(4): 699–705

'Progression of diabetic glomerulopathy was seen in untreated people with microalbuminuria or hypertension and people without either, but not in people with good metabolic control on antihypertensives.'