Management of type 1 diabetes

NEW ENGLAND JOURNAL OF MEDICINE

Antibody treatment preserves beta-cell function

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

1 A T-cell-mediated autoimmune response causes the major loss of beta-cell function that occurs in type 1 diabetes.

2 Previous studies have suggested that treatment with antibodies raised against CD3 (an antigen present on human T cells) may be beneficial in preventing the progression of type 1 diabetes.

3 This phase II, placebo-controlled, multicentre trial randomised 80 patients with newly diagnosed type 1 diabetes to receive placebo or an aglycosylated human antibody against CD3 (ChAglyCD3) for 6 days.

4 Daily insulin requirements and residual beta-cell function were assessed over a follow-up period of 18 months.

5 Residual beta-cell function was better maintained in those who received treatment with ChAglyCD3 compared with placebo. Required insulin doses did not increase in those patients who received ChAglyCD3, whereas it did in the placebo group. ChAglyCD3 treatment therefore appears to preserve beta-cell function for at least 18 months.

6 The effects of ChAglyCD3 were most prominent in those patients with a higher initial beta-cell residual function.

7 ChAglyCD3 treatment resulted in significant, but transient, 'flu-like' adverse effects in all patients (e.g. fever, arthralgia, myalgia).

Keymeulen B, Vandemeulebroucke E, Ziegler AG et al (2005) Insulin needs after CD3-antibody therapy in new-onset type 1 diabetes. *New England Journal of Medicine* **352**: 2598–608

A step closer to acute prevention of type 1 diabetes?

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Since the discovery of insulin, the medical profession has struggled to deal with the consequences of beta-cell damage and the subsequent complications of type 1 diabetes. We have had nothing to treat the underlying disease process. This paper by Keymeulen and colleagues (see right) goes one step further and describes an experiment to prevent type 1 diabetes progressing shortly after diagnosis – the hugely exciting potential being that we can intervene at an early stage to preserve beta-cell function.

Two well-matched groups of individuals were randomised to receive either an antibody treatment designed to block the T-cell-mediated immune attack on the beta-cell or placebo. The key finding at 18 months was that insulin requirement in the treatment group did not increase, compared with a progressive increase in the placebo group. We would like to have also seen an improvement in glucose control but both groups were intensively managed with an HbA_{1c} of 6.9%.

Individuals that responded best to the treatment were those with the highest insulin secretion at the time of diagnosis. Patients were only enrolled if they had overt diabetes but the obvious implication is that treating as early as possible is best – i.e. during pre-diabetes. If future studies support this group's findings the most difficult question is who should be treated and when?

Side effects were universal in the group receiving antibody therapy and occurred both during the 6 days of hospital treatment and in the weeks that followed. Side effects are to be expected with this form of treatment, and are clearly documented in the paper, but it is difficult to get a feel for how severe the symptoms were. It is thought provoking to put oneself in the position of being newly diagnosed with type 1 diabetes and offered a treatment that will produce a glandular fever-like illness for some weeks (with a possible increased risk of malignancy in the future), but has the potential for significantly reducing the severity of diabetes potentially for many years. I think I would take the 'viral illness'.

DIABETES CARE

Cognitive dysfunction in type 1 diabetes

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

1 Previous studies have shown that people with type 1 diabetes exhibit modest deficits compared to people without the condition in neuropsychological tests.

2 This meta-analysis aimed to assess the nature and magnitude of such cognitive deficits and explore possible associations with other variables (e.g. hypoglycaemic episodes).

3 Studies comparing cognitive performance in people with and without type 1 diabetes were sourced using the MEDLINE and PsycLIT databases.

4 Thirty-three studies met the inclusion criteria. Compared to those without diabetes, effect sizes (measured as Cohen's *d*) were lower in people with type 1 diabetes for cognitive domains including: intelligence, speed of information processing and visual perception. Lower performance appeared to be associated with microvascular complications, but not with poor metabolic control or hypoglycaemia.

5 In contrast, type 1 diabetes did not appear to impede learning or memory.

Brands AMA, Biessels GJ, de Haan EHF et al (2005) The effects of type 1 diabetes on cognitive performance: A meta-analysis. *Diabetes Care* **28**: 726–35

'...the results of this study suggest that aggressive management of HDL-cholesterol may help prevent stroke in type 1 diabetes'

DIABETIC MEDICINE

Aggressive HDL-C management may protect against stroke

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

1 To date, the relationship between type 1 diabetes and stroke has been addressed by few studies.

2 This community-based study in Australia recruited 126 adult type 1 diabetes patients between 1993 and 1996. The participants were followed for a mean of 7.2 years (standard deviation: ±1.6 years) and cerebrovascular events were measured before and after the start of the trial.

3 Participants were divided into three groups: (1) those who had no history of stroke/transient ischaemic attack (TIA) at baseline and suffered no further events; (2) those with history of stroke/TIA at the start of the study; and (3) those who had no prior history of stroke/TIA but who had a stroke during the study.

4 In comparing group 3 with groups 1 and 2 over a range of potential first stroke predictors (including HbA_{1c}), the only significant difference was in fasting serum lipid profile. Patients in group 3 had lower high-density lipoprotein cholesterol (HDL-C) levels than those in groups 1 and 2 (0.68 ± 0.17 mmol/l [standard deviation] versus 1.26 ± 0.42 mmol/l and 1.28 ± 0.45 mmol/l, respectively; $P<0.05$).

5 The authors concluded that a definite link between cardiovascular events and glycaemic control in type 1 diabetes remains to be proven. However, the results of this study suggest that aggressive management of HDL-C may help prevent stroke in type 1 diabetes.

Davis TME, Bruce DG, Davis WA (2005) Predictors of first stroke in type 1 diabetes: The Fremantle diabetes study. *Diabetic Medicine* **22**: 551–3

'The authors concluded that insulin detemir provides a flat and protracted pharmaco-dynamic profile.'

DIABETES CARE

Insulin detemir provides a flat and protracted profile

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

1 This study aimed to investigate the duration of action and pharmacodynamic profile of two basal insulin preparations.

2 In this six-period, double-blind, dose–response trial, 12 people with type 1 diabetes were randomised to receive a specific treatment sequence including five dose levels of the long-acting analogue insulin detemir (0.1, 0.2, 0.4, 0.8 and 1.6 units/kg) and one dose of NPH insulin (0.3 U/kg).

3 Between-individual variation in duration of action was found to be lower with insulin detemir compared with NPH insulin.

4 The authors concluded that insulin detemir provides a flat and protracted pharmacodynamic profile.

Plank J, Bodenlenz M, Sinner F et al (2005) A double-blind, randomized, dose-response study investigating the pharmacodynamic and pharmacokinetic properties of the long-acting insulin analog detemir. *Diabetes Care* **28**: 1107–12

DIABETES CARE

Insulin glargine absorption rate not affected by exercise

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

1 Previous studies investigating the effect of exercise on insulin absorption are conflicting. This study aimed to examine the absorption characteristics of insulin glargine with exercise.

2 Radio-labelled insulin glargine was injected subcutaneously into the thighs of 13 people with type 1 diabetes in the evening before each of two study days on which they were randomly assigned to half an hour's intensive exercise.

3 Plasma glucose and insulin profiles were assessed at intervals throughout the day.

4 The authors concluded that 30 minutes of intense exercise did not increase the absorption rate of subcutaneously injected insulin glargine in people with type 1 diabetes.

Peter R, Luzio SD, Dunseath G et al (2005) Effects of exercise on the absorption of insulin glargine in patients with type 1 diabetes. *Diabetes Care* **28**: 560–5

PEDIATRICS

Improved glycaemic control in children with flexible MDI

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

1 The study aimed to determine the feasibility of a flexible multiple daily insulin (FMDI) regimen in pre-school-aged children with type 1 diabetes.

2 During quarterly diabetes clinic visits over a 2-year period, data were collected from 35 children who had received a multiple daily insulin (MDI) regimen. These children, having followed MDI for 1 year or more, were then switched to FMDI.

3 The investigators found that there was no significant difference in BMI with FMDI therapy. Glycaemic control was improved overall with FMDI (HbA_{1c} 8.8 ± 0.9% versus 8.3 ± 1.0% for MDI therapy; $P<0.0001$), but only in those patients with normal weight.

4 However, the overall rate of severe hypoglycaemia was reduced with FMDI. Again, this effect was only seen in normal-weight children and not those who were overweight.

Alemzadeh R, Berhe T, Wyatt DT (2005) Flexible insulin therapy with glargine insulin improved glycaemic control and reduced severe hypoglycaemia among preschool-aged children with type 1 diabetes mellitus. *Pediatrics* **115**: 1320–4