Timing is everything ... but just add it to the list

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As a research registrar (some time in the last century), I remember staying up all night with people with type 1 diabetes who had foolishly volunteered to undergo total body cooling for the benefit of science (and my MD).

I attempted to maintain the participants' blood glucose within normal limits overnight using intravenous insulin, ready for the diabolical experiment to begin the following morning. Breakfast (two pieces of toast) was permitted and I remember my frustration at watching the participants' blood glucose levels shoot up. Only by increasing insulin doses sufficiently early – so that the blood glucose levels were beginning to fall before the first mouthful – prevented a hyperglycaemic spike.

That experience has influenced my clinical practice since. Whenever I see someone who is struggling to achieve satisfactory glycaemic control, I ask about the timing of injections in relation to meals.

We all know the story: soluble insulin should be administered 20–30 minutes before a meal, fast-acting insulin analogues allow administration immediately before eating. While there is no doubt that insulin analogues have a much faster onset of action than soluble insulin (Rolla, 2008), sometimes I think we expect too much of them. My clinical experience suggests that an increasing number of people using insulin analogues are waiting until after their meal to inject. Yet, depending on the meal, the number of the courses and the company, the time between the first and last mouthful can vary widely.

Cobry et al (2010; summarised below) show that a rapid-acting insulin analogue bolus administered 20 minutes prior to the start of a meal results in significantly better postprandial glycaemic control. This has important implications for people on basal–bolus insulin regimens, and their clinicians. However, the practicalities of applying Cobry et al's findings remain to be seen. Anticipating a meal by 20 minutes can be difficult – especially when fear of hypoglycaemia is involved. Considering the timing of meals and dosing is one more thing for the person with diabetes to think about – along with carbohydrate counting, glycaemic index, injection site, dose in relation to exercise and so on. However, careful insulin dose timing in relation to meals may be the answer for those who, despite their best efforts, cannot prevent postprandial hyperglycaemia.

As an aside, the relationship between insulin administration timing and vascular disease remains controversial but is clearly linked to glycosylation (and hence HbA_{1c} levels), which Cobry et al show can be modified by delayed insulin administration.

Rolla A (2008) *Am J Med* **121**(Suppl 6): S9–19

DIABETES TECHNOLOGY & THERAPEUTICS

Control best when bolus given 20 min prior to meal

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

1 Participants with T1D were exposed to three different meal-time insulin regimens at three different clinical visits: an insulin glulisine bolus 20 minutes prior to a meal, immediately before the meal and 20 minutes after meal initiation.

2 Blood glucose levels were measured for 240 minutes following meal initiation at 30-minute intervals. Mean blood glucose levels (1 and 2 hours after meal initiation) and maximum blood glucose levels were analysed.

3 All participants (n=23; age range, 12–30 years) were receiving insulin-pump therapy at enrolment.

4 Insulin bolus administration 20 minutes prior to meal initiation resulted in significantly lower glycaemic excursions at both 1 and 2 hours following meal initiation than delivery immediately before the meal (all $P<0.040$).

5 A rapid-acting insulin bolus delivered 20 minutes prior to a meal yielded significantly better postprandial glucose control.

Cobry E, McFann K, Messer L et al (2010) Timing of meal insulin boluses to achieve optimal postprandial glycemic control in patients with type 1 diabetes. *Diabetes Technol Ther* **12**: 173–7