

Glucose monitoring in diabetes

Prepare for a new era

Dr Tony O'Sullivan was diagnosed with Type 1 diabetes at age 14. He recalls some of the leaps forward in glucose monitoring technology over the years and the exciting future in store

I have been living with Type 1 diabetes long enough to remember the first blood glucose meters in the late 1970s. Compared to urine testing, they were a giant leap forward and offered people with diabetes a chance to chase tight control without risking severe or multiple hypoglycaemic attacks.

Over the years we got human and then analogue insulins, new delivery systems (no, I meant pens!); a move from visual to electronic glucose meters, the development of memory meters, averaging, analytical software, onboard insulin wizards, food and exercise

recording. All brought us incrementally closer to optimum glucose control.

More recently insulin pumps, continuous glucose monitors and sensor pumps have added further flexibility to the situation. Finally in very recent times, the arrival of relatively affordable continuous glucose home sensing will, I believe, represent another giant step forward, just like that prototype meter with its deadly lancet (see *Picture 1*).

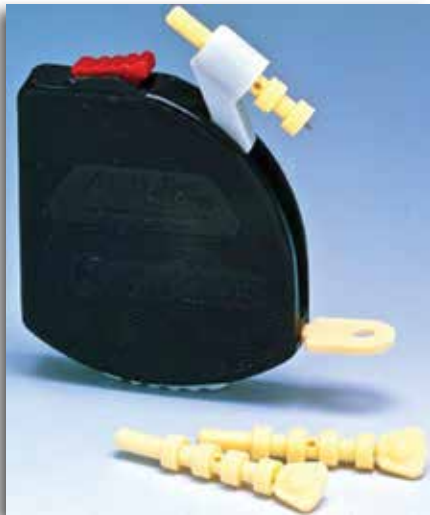
Challenges of Type 1

Type 1 is a challenge for all of us. It is well established that keeping our blood glucose level within reasonable limits

really reduces the risk of long-term complications. We have to juggle many factors, such as food and exercise, with insulin doses to stay low while avoiding severe hypos.

As the condition often starts in childhood, we need to maintain that discipline for a very long time. I see the effort of controlling blood glucose as similar to walking down a long corridor in the dark, trying not to hit off the walls on either side; we need to turn the lights on.

In previous decades, it was all about getting the HbA1c down, and lifestyle



Picture 1. "Deadly" early lancets and meter

restriction was a necessary part of the treatment. More recently, better control for most people is achievable, and we can consider issues of lifestyle, flexibility and adventure alongside excellent control. This has also allowed some of the stigma to dissipate, and some reversal of workplace and sporting exclusions.

No more pre-test fear

Home glucose testing has been with us for some time, but has been developing substantially over time. Since the first electronic sensor strips (see Picture 2) accuracy has gradually improved, blood sample size has fallen, and even the lancets have improved with softer springs and finer needles thankfully. Testing is now often painless and pre-test fear now a distant memory.

Meters come with memories and are downloadable. Most have reasonable software and these add an important source of information. Let me explain.

In Type 2, or those with Type 1 who do not test that often, downloading the meter allows us to put several weeks of readings into one day (provided the clock in the meter was accurate). This 'modal day' view lets us see the wood for the trees, giving a broader view which often points to a time of day where the problem lies.

How often should people with Type 1 diabetes test? Research has shown that frequency of home blood glucose testing over the preceding 12 months



Picture 2. The first electronic sensor strip

predicted HbA1c levels, with lower HbA1c in people testing more frequently, peaking at four times a day.

In some situations more frequent testing is appropriate. These include times of increased insulin sensitivity (childhood, vigorous training), times when very low HbA1c are set (pregnancy), and when there is increased danger attached to hypoglycaemia (driving, occupational risks, adventure sports, travel).



We have to juggle many factors, such as food and exercise, with insulin doses to stay low while avoiding severe hypos.



Testing is usually done before meals and at bedtime. At times it may be useful to check two hours after meals and during the night, if there are concerns about midnight lows.

Also, repeated testing during a period of fasting, perhaps missing a meal, is helpful in the assessment of basal rates for pump users.

So why if someone has good control all day on a Monday, why do we need to repeat these tests every day for the rest of the week?

The reality is that human nature and physiology continuously try to undermine glucose control. Many minor

issues can interfere with control, and modern intensified insulin therapy means that every dose can include an element of correction for the current glucose level.

Wizards

Besides memories, some meters now offer wizards. Imagine a 20-year-old student trying to work out the insulin dose with her lunch, a banana, pack of crisps and a can of diet coke. Her glucose level is 9.7.

To calculate her dose she needs to add up the carbs in her meal (42g), apply a mealtime insulin ratio (eg. 1u to 15g carbs), and add a correction for the higher pre-meal glucose ($9.7 - 6 = 3.7 \times$ a sensitivity factor).

If her meter includes a bolus wizard, she can set this up with her insulin sensitivity and ratios, and simply enter her mealtime carbs and get a calculated insulin dose.

Some meters now communicate with pumps. The glucose reading appears on the pump, launching the wizard to allow calculation of an insulin bolus, which might be 3.6 units. A further press activates the calculated dose – a simple execution of a complex calculation, and clearly an incredibly useful advance in terms of control and safety.

Continuous glucose monitoring

While meters have turned on the lights in my imaginary corridor mentioned earlier, they are widely spaced and there are dark gaps where I still cannot see very well.

What happens between meals, during the night, in the early hours, during exercise or when I'm driving or working? Continuous glucose monitoring

(CGM) offers answers, having developed for nearly 20 years.

Glucose sensors are inserted under the skin and held in place by adhesive. The first systems were wired, and did not give a display of the glucose level. Now, they work wirelessly and display glucose levels in real time on a separate meter or pump. The next generation will communicate with a phone app using Bluetooth or NFC (near-field communication). Sensors generally need calibration with meter glucose readings two or more times a day and last around a week.

Devices include the Dexcom device which is stand-alone or linked to a pump, the Freestyle Navigator which is not yet launched in Ireland as far as I know, and the Medtronic Enlite sensor, which until recently was used exclusively with sensor pumps.

Since 2010 the Medtronic sensor has been able to suspend the Veo pump's basal flow rate for two hours once it records a low blood glucose. The most recent 640G pump allows the sensor to suspend insulin when the glucose level is trending towards a low, and resume when glucose levels stabilise, all without disturbing the wearer. This represents another step towards closed loop therapy in which fluctuations are managed by the pump.

The advantages are many:

- Check glucose levels at any time without having to get a meter out and go through the finger-pricking routine
- Take a correction dose as often as needed
- Get an alarm whenever glucose levels are high, or low
- Download and see a curve representing the day's fluctuating glucose levels and start interpreting these at a higher level than previously
- Put several days together to show a 'modal week' view and see trends to identify where problems lie, including frequent highs and lows, perhaps indicating incorrect basal rates or mealtime ratios.

On the downside, many are not fond of sensors stuck to the abdomen. The

alarms and beeps always come at the wrong time, and may irritate not just the user but anyone around them.

The sensor glucose reading is accurate, but not completely so. It lags behind blood glucose, so hypoglycaemia may be advanced before the sensor picks it up, and it may be slow to acknowledge when it has resolved.

The vast amount of data available from downloads can be difficult to interpret. The biggest issue however is the cost, which to date, has led to limited access to this technology.



Continuous glucose monitoring methods are becoming more affordable, which is very welcome after almost 20 years on the market.



Studies of CGM have struggled to see the full extent of expected benefit. A review in 2013 of several research studies indicated a modest reduction in HbA1c and time spent in hypoglycaemia in children and adults, particularly when used with pump therapy.

The German Diabetes Association support that CGM is most useful for those in pregnancy, those experiencing frequent or severe hypoglycaemia, those failing to achieve targets with SMBG, and motivated people who need to test 10 or more times a day to achieve adequate control.

Affordable options

The recent arrival of the Freestyle Libre has added a new and more affordable option. This device comes with a 14-day sensor, communicates with a phone or a glucose meter (which also takes strips) by sweeping the device close to the sensor, which is placed on the upper arm; it does not need calibration and

records a 24-hour glucose curve once the meter is swept over the sensor every eight hours.

The sensor does not send a continuous signal to the meter so there are no alarms, but this keeps the cost down. Using Libre, people check their glucose 15 or more times a day. Graphs can be downloaded through to their PC or iPad. The ongoing cost for sensors is around 30 euro a week. Although this technology is not yet available on the Long-Term Illness Scheme, uptake has been very significant throughout Europe.

I have used this device myself, and given it to a number of patients with Type 1 and insulin-requiring Type 2 diabetes. I've seen a lot of enthusiasm for the device's ease of use and a significant immediate increase in the amount of testing. Clarity on significant issues in insulin use, has meant these were fixable once the data was downloaded.

Medtronic is about to launch the Guardian Connect device, which uses the Enlite sensor and a transmitter as with the pump, but connects with an iPhone. As this is transmitted continuously, alarms will be possible to alert the user to unnoticed highs and lows.

The Enlite sensor is available on the Long-Term Illness Scheme, but not the transmitter, and the initial cost is comparable to a new phone.

Peace of mind

Modern glucose monitoring includes the rational use of glucose meters, and for an increasing number, the use of more continuous glucose monitoring methods. These approaches are becoming more affordable, which is very welcome after almost 20 years on the market.

They may have a limited impact on HbA1c levels, but do reduce hypoglycaemia and improve control in people who are well motivated. They also give the individual and their family a huge dose of peace of mind.

Studies focusing on HbA1c alone are missing the point: We want our lives back!